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From the Editor

Dear Rochester Community,

As we progress in our increasingly specialized academic careers, it becomes especially important to understand how our work fits in a larger framework of knowledge. Insight often comes from unexpected places; Jorge Luis Borges found literary genius in the paradoxical nature of time, while Kekulé conceived the structure of benzene by dreaming of a snake. Some of our greatest thinkers have come to their insights by setting their current problems aside and allowing their minds to roam. The *Journal of Undergraduate Research* (*jur*) editorial board envisioned a non-technical, cross-disciplinary forum that would enrich our knowledge – through primary research – of the subjects we know best, and afford us the opportunity to greater understand those we know least. Our intentions are to foster a culture of research and academic exchange by reading about the accomplishments of our peers, and inspiring others to continue or begin their own. In this spirit, we present the premiere issue of *jur*.

We have included an array of articles that range from topics in poetry to protein biochemistry written by freshman through seniors. We have tried to represent as many disciplines as possible through the excellence and commitment of our contributors. In addition, this journal features a general review, allowing a broader overview of a specific field.

jur is a student organized and produced publication, and I would like to thank our staff for the substantial time and effort required to produce this journal. This has been a tremendous learning experience, and we received excellent advice, guidance and resources from Professor Thomas Krugh. With his encouragment, Deepak Sobti and I were able to initiate this endeavor. Financial support from the Dean of the College, Students' Association, and numerous academic departments has enabled us to provide *jur* free of charge.

We invite the University of Rochester undergraduate community to contribute their original research, letters, or reviews to the Spring 2003 issue of *jur*. Also, we are actively looking to expand the *jur* staff. Please e-mail *journal@rochester.edu* or visit our website jur.rochester.edu for further information.

Sincerely,

Prabhjot "Jot" Singh Dhadialla '03
Editor–in–Chief

Welcome to *jur*

Dr. Debrework Zewdie
Global HIV/AIDS Coordiantor, The World Bank Group

Dr. Debrework Zewdie, a national of Ethiopia, is principal spokesperson for the World Bank's participation in global action against HIV and AIDS. She plays a lead role in developing, implementing and evaluating Bank projects involving HIV/AIDS and also serves as the head of the AIDS Campaign Team for Africa (ACTafrica), a multi-sectoral unit created to mainstream HIV/AIDS into the Bank's operations in the Africa region.

Communicating across disciplines is a challenge that faces students and professionals alike. Over the years, various disciplines have created their own languages, which has made communication across fields as difficult as interpreting new dialects. While members of each discipline can communicate with each other, the biggest challenge, however, is communication across disciplines. The need to communicate across disciplines becomes even more critical for teachers and students, who need to have a broader perspective than the particular subject they are studying.

The ease, as well as medium one chooses to explain and convey a particular subject, is extremly important for the idea to become useful. For example, in a world where there are limited resources, a medical doctor who does not understand the value of cost effective treatment will not be able to communicate with policy makers whose job is to ensure equity and cost effectiveness. There are only very few occasions where the same medical doctor will be able to order tests and drugs without taking the economic status of his patient, and the circumstances under which the insurance or other system operates in a particular place. This becomes even more important in resource-limited settings with multiple priorities.

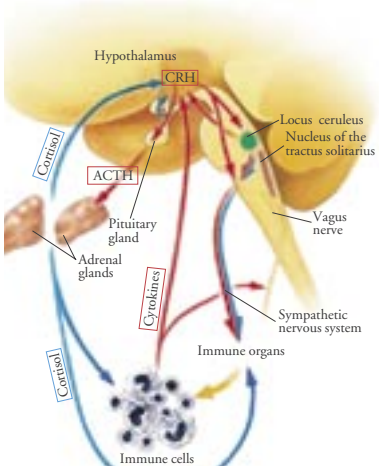
jur provides the beginnings of an interaction across disciplines. Good and simple communication presupposes the knowledge of the discipline that is being discussed. The art of communicating with others in a simple way enables the audience to understand and appreciate subjects beyond their expertise as well as place them in context. Let me cite two very simple examples. In 1984 when the HIV/AIDS epidemic was new to most parts of theworld, a few of us (medical doctors, economists, immunologists and epidemiologists) were asked to explain the HIV/AIDS epidemic to the public. While most were trying to explain the way the virus was transmitted using very complex scientific jargon, the explanation given by one of the panelists using an analogy of two trees, one healthy and another infected with a very common tree bug, made a lasting impression among the public. Similarly, in a recent visit to one developing country that has one of the highest HIV/AIDS prevalence rates, and a reluctant government that has remained unresponsive, we asked the president of the country how devastating a recent bombing in the capital of the country has been. The president, unaware of where the discussion was leading, was explaining the gravity of the bombing. The person who asked the question asked the president if he knew that the number of people infected in his country on a daily basis was like having four of those bombs on a daily basis. The president stood up and said, "Why was this not explained to me in such a way?" This simple manner of communication resulted in the immediate release of a health education material to students that has previously been banned because religious leaders felt that they made young people promiscuous. Communication across disciplines and the ease with which complex issues need to be communicated to those who need to benefit from exciting knowledge is a skill in itself. In my twenty years of professional life, the biggest challenge for me has been to explain the science of immunology and infectious diseases to economists and policy makers whose major concern is cost effectiveness, while mine is saving lives. In time, I have learned to speak the language of policy makers and economists without which I would not be able to be as effective. The paramount goal of communication should be a message that is easily transmitted, as well as understood. I congratulate the *jur* staff for providing a forum that fosters this goal.

Sincerely,

Dr. Debrawork Zewdie

Faculty Interview

jur gets a lesson on opera reconstruction from musicologist Dr. Jennifer Williams Brown Department of Music



jur: What is musicology?

Brown: In its largest definition it means any kind of scholarly investigation of music. Generally, it is used to mean historical musicology. The pieces, the people, the instruments, the kinds of concerts, etc.

jur: So what does that mean in practical terms?

Brown: Well, we take evidence, which can be pieces of music or historical data and draw conclusions. We also run experiments, although not as controlled as one would do in a lab. We also have hypotheses and we test them. The problem is that the data can be hard to get.

jur: How did you come to this field?

Brown: Well this is sort of an unusual story. I actually decided I wanted to be a musicologist when I was 14 years old. Most people don't even know what it is at that age. But I was in social studies class in high school and when we went around and talked about what our parents do, one of the kid's father was a musicologist. Everybody said, "What's that?" After he explained what it was I said, "Well that's for me!" I am interested in music, history, different cultures, art, dance, theatre and all these other activities that intersect with music. That's what I decided to do and I haven't wavered since I was 14.

jur: How long have you been teaching at the University of Rochester and what sort of courses do you teach?

Brown: This is my third year. We have a department of 6 full time faculty here. Two history/musicology, two theory, and two conductors. I am one of the history people and we divide the material into two sections. [I cover] from ancient Greece to the middle of the 18th century and my colleague [takes it] from there to the present. That's one way we divide it, but I do venture outside that territory. I am thinking of offering a Mozart course that would obviously go past the mid 18th century. I am doing an opera course at the moment that is taking me into the 20th century. So it depends on the repertoire.

jur: What do you focus on within musicology?

Brown: What I work on is opera in Italy in the 17th century. More specifically, [I concentrate on] Venetian operas for the fifty years in the middle of the century.

jur: What are some of the methodologies you use and some of the problems you encounter?

Brown: Say you want to study a period of music history. You would generally start by going to the library and checking out some CDs and musical scores so you can follow along with what you are listening to. The trouble is that the 17th century hasn't been studied that well. So there are very few recordings, and even fewer musical editions. That means we need to avail ourselves [of] primary sources. Another problem is that our recordings and editions often tell us more about what we [as modern people] want, what our traditions of musical performance and understanding are, rather than that of the people of the historical period that you are looking at.

So if I want to study how opera was composed, performed, and understood by audiences in this period, we have a certain problem. One, we have no audio traditions and no recordings from this period. We also don't have instruments since it was a vocal music. So what we have to look at it are written documents, the text of the operas. The words that are sung are usually written down in a book called a libretto. And the music was never printed in this period. It was always written out by hand in a manuscript, of which very few survived.

Another problem is that in any century, particularly in the 17th century, operas were never performed the same way twice. Oftentimes directors will make cuts [and give new] arias to different characters. One thing that I think makes this an interesting period to study is how fluid the text of the opera was; the directors were always making changes to adapt it to a particular cost, budget, or a particular audience. They would make cuts and changes, write new music, borrow music from other operas, and

create a cut and paste thing. So every time it was produced in a new city, there would be a new cast and director and so the process would happen all over again. So [after] fifty years, the opera is going to look different from the way the composer wrote it. But that fluidity is what interests me.

[An ever-present question in musicology] is how do we reconstruct that process from the documents that we have, which are few. And they are mostly neat copies that were made years later that cover up all the machinations that went on backstage. It's similar to the way a student might write a term paper. One would give the paper to their teacher, then the teacher would give it back with corrections and suggestions. It was this type of feedback system that composers had with their performers and audiences. And imagine doing this without the use of a typewriter or computer. Everything was written out by hand, and the paper was really expensive. So this paper would be full of corrections and additions, it would be a real mess. This is what would be interesting to study, but most of these things are lost. What we have is a neat copy that a scribe wrote out years later, a person who would have no familiarity with the music at all but was just copying. Then those copies are put into libraries and people regard them as the way the operas were originally written.

jur: So what sort of skills would someone need to do this type of work?

Brown: Definitely language skills. Italian, but archaic, poetic Italian. I'm not so good at conversing with [modern] shopkeepers. Also, music theory to be able to know what the document is telling you and be able to see errors, basically to be able to make musical sense of the document.

You have to have detective skills. To me this is the most interesting thing about the kind of research I do. You have to be able to say, "Hmmm, something doesn't sound right here…" Then you develop various ways of attacking the problem.

It's similar to working on a legal case in many ways.

jur: Why do you feel this type of research is important?

Brown: What started me off is that the music is beautiful. When I heard it in graduate school, I said why is there a whole century's worth of pieces that are languishing, that people aren't listening to. There is much more interest in it, in the past few decades, but there is still a lot of un-mined territory out there.

But it also tells about the culture of other times: what they were doing, thinking, and what sounds were in their ears.

We tend to think that a composer has control over his/her artwork. But what does it mean if these other people are making changes to it and introducing other composer's music into it? What did people of the time think of this process?

jur: How do undergraduates get involved in this?

Brown: The University of Rochester's undergraduate music major program is one of the best programs in the country for preparing students for graduate work in musicology and theory. Well in my course, Ancient Greeks to Bach, I try to introduce musicology to the students. I present it to them by showing them some evidence from the past and this is what some scholars have thought about it, what do you think about it? I try to give them some intellectual puzzles and have them think look at it in different ways.

I also have the students do some of their own type of primary research, for example I took them to Saint Ann's church and had them listen to real time music in a religious context. I also take them to Sibley library and have them look at primary documents from the middle ages and the renaissance.

jur: So what is in your CD player now?

Brown: Stuff for teaching class today! But for fun, different things for different activities. Anything from renaissance to the blues. An eclectic taste.

jur: Dr. Brown, thank you for your time.

Brown: You're welcome.

a. Aurograph manuscript of Francesco Cavalli's opear *L'Oristeo* showing revisions. **b.** Liberetto of Francesco Pallaicino's opera *Vespasiano* (1678).

Freshman Scholarship:

A Cycle of Identity

W.D. Snograss' pseudonym S.S. Gardons.

Catherine Egan

Advisor: William Lavigne
Department of English

A detailed look into what caused W.D. Snodgrass' creation and eventual abandonment of the pseudonymous character S.S. Gardons

What would drive an acclaimed pioneering poet to publish a collection of his works under a pen name? When a writer's work is mass produced and placed on bookshelves in stores across the country, it seems as though the writer would want his name conspicuously scrawled across the cover. This is not always the case. It is puzzling why some writers choose to withhold their names and publish their work under a pseudonym. One might reason that some writers are shy and prefer to keep their careers separate from their personal lives. But to publish only select works under a pseudonym while others bear the writer's true identification raises questions. The subject of the work must be incriminating and of a more personal nature. Following his successful, critically acclaimed first work, *Heart's Needle*, Snodgrass published under a pseudonym for his second collection of poetry *Remains*. While both works were written in a similarly revealing style, something special is contained in *Remains* that set it apart and led Snodgrass to keep his name from appearing on the cover.

Snodgrass is best known for his confessional poetry, a form which he revolutionalized. In a 1970 interview, Snodgrass spoke about what led him to write confessional poetry:

> *It seemed to me that this kind of very personal approach to a poem was something nobody had taken for a long time, so it seemed possible that one might be able to produce something new and different this way and something valuable. But as to whether that way of working is more valuable in itself than another way, I doubt*[1].

Snodgrass achieved a ground breaking level of emotion in his poems written in this style. Poetry had been previously characterized by its symbolism and formal tone. With admirable talent, Snodgrass was up for this challenge to explore new ground in the world of poetry. In the same 1970 interview, Snodgrass expressed a somewhat pessimistic attitude toward writing this personal style of poetry even though he helped develop it. Snodgrass claimed tasks that one knows are possible to accomplish are not worth doing. Only those tasks that may seem impossible are fun. Also, when attempting something new that will not necessarily work, there's no reason to feel bad if it doesn't work. Snodgrass did not have to be concerned with failure[2]. His first collection was critically acclaimed. Many other poets have since followed in his footsteps and his intimate approach to poetry has spread.

Snodgrass is not anxious to take credit for this quite personal style of poetry which has now become popular. He insisted it is the same approach that he has always used. When looking more closely at poets once thought to be impersonal – Eliot and Frost and so forth – one realizes they were writing exceedingly personal poems[3]. Few will argue that the feelings expressed in the poems of Eliot and Frost come even close to matching the emotions expressed in Snodgrass's poems. Perhaps the subject of the poems is similarly personal, but one must look at Sondgrass's language. He chose language that is far less formal and much more accessible than other poets.

Snodgrass's first collection, *Heart's Needle*, contains work about the many emotional and trying events of his life. The poems contained in *Heart's Needle* described his return from serving in the United States Navy during World War II, the ending of his first marriage, and his eventual remarriage. Also serving as the subject of a number of poems was the important separation from his daughter due to his divorce from his first wife. Snodgrass presents these tragic events in an emotional way that touches the reader, but does not evoke pity. He "wears his heart on his sleeve…but refrains from blowing his nose with it.."[4] Snodgrass is aware that revealing too much emotion is unappealing:

> *the personal approach leaves open the possibility of a great deal of sentimentality and foolishness, bedroom memoirs and that sort of stuff, which nobody needs.*[5]

Through this statement, it is clear that Snodgrass set out to write a poem that has a certain feel to it. He not only wants his work to be emotional, but also written in an accessible language. When writing poetry, Snodgrass claims to first write:

> *…a very compacted, intellectual, sad, and obviously symbolic poem with a lot of fancy language in it. But then, as I go on working on it, the poem happily becomes plainer and longer, and seems much more 'tossed off.' The first version*

often seems very labored and literary and intellectual. The final version, if I'm lucky, will seem very conversational, and sort of 'thrown away.[6]

In its final version, his poetry take on a more casual, "tossed off,"[7] feeling, neither over-done nor exaggerated. This balance –portraying emotion without creating a sappy poem–combined with his deliberate use of approachable language, characterizes Snodgrass's work.

Heart's Needle takes on a somber feeling. In a poem entitled "Returned to Frisco, 1946," Snodgrass describes his return home after World War II. Instead of taking on the expected feeling of overwhelming joy that returning soldiers feel, the poem delivers a feeling of apprehension:

We shouldered like pigs
along the rail to try
And catch that first gray
outline of the shore
Of our first life.
A plane hung in the sky
From which a girl's
voice sang: '…you're home one More.'
For that moment, we were dulled and
shaken by fear.[8]

Snodgrass focuses on his true emotion and not what is expected of him or what he supposes the reader would want. Because this poem was not written until years later, the validity of these emotions is questionable.

Snodgrass's daughter, Cynthia, is the subject of much of *Heart's Needle*. From the title alone, one can infer that the poems contained within the compilation are about painful events in Snodgrass's life. The title is taken from an Irish folktale comparing the "loss of an only daughter with a needle puncturing the heart."[9] *Heart's Needle* contains ten poems about Cynthia, one for each season during his divorce and remarriage.[10] These ten poems take on a reminiscent tone, recalling Cynthia's childhood all the way back to her birth:

While nine months
filled your term, we knew
how your lungs, immersed
in the womb, miraculously grew
their useless folds till
the fierce, cold air rushed in to fill
the out like bushes thick with leaves.
You took your hour,
caught breath, and cried with
your full lung power.[11]

Snodgrass's work is very personal and revealing, because his life's events, such as the birth of his daughter, are the basis for his writing. Thus, the reader discovers many details about Snodgrass and his family.

Although each of Snodgrass's collections of poetry deal with certain private events and his feelings about them, Snodgrass chose to withhold his name and published his second collection, *Remains*, under a pseudonym. One might ask why a confessional poet would publish just one of his collections under a pseudonym. Confessional poetry is characterized by honesty and openness, leading to the conclusion that publishing such work under a pseudonym runs counter to the inherent nature of the work. Snodgrass has published other collections before and since the publication of *Remains* using his real name. With this in mind, there must be something special about this collection of poetry to warrant the use of the of the pen name S.S. Gardons.

The fictitious character S.S. Gardons is quite intriguing. When Gardons was first created, little biographical information was published about Gardons. With time, S.S. Gardons became a more complex character. The notion of S.S. Gardons being the author of such a skillfully written collection of poetry became less plausible as more information became available about his background. Included in the biographical information are details assumed to be written by Snodgrass himself, suggesting that Gardons did not have the traditional education of a writer. A resident of Red Creek, Texas, Gardons:

worked as a gas station attendant, although he took a few university classes in Houston, and later became an owner of a cycle shop.[12]

The description continues to include other fanciful details and claims that Gardons was "also a musician, he played lead guitar in the well-known rock group, Chicken Gumbo."[13] If the object of the pseudonym was to conceal his identity, it is puzzling why Snodgrass would make this character so unbelievable. Writing poetry about such a trying time in his life, Snodgrass may have used this publication as a sort of therapy to get past these tragic events. By making Gardons so implausible, Snodgrass is further separating himself from the author of these poems and therefore the events themselves.

There is an interesting pair of poems in *Remains*. The poems "The Mouse" and "Viewing the Body" are linked. The "Mouse" is based on a childhood memory in which he and his sister find a mouse. It was "A dusty gray one, lying/ By the side steps."[14] The poem continues to discuss how they were "Afraid he might be dead."[15] In the end of the poem Snodgrass says the "little animal/ Plays out…Turns from its own needs, forgets its grief."[16] These lines foreshadow the death of his sister. The foreshadowing is made clear in the next poem "Viewing the Body," as Snodgrass describes his sister "gray as a mouse."[17] As a short collection of poetry, Snodgrass clearly and easily links the poems together. The collection, *Remains*, gives an inclusive description of Snodgrass's family when the individual poems are read together.

The next few poems in the collection discuss Snodgrass's family after his sister's death. In "Disposal," Snodgrass describes how quickly and casually his sister's belongings were disposed of after her death. One of his sister's dresses was carelessly "fobbed"[18] off on a friend. "Fourth of July" carries a reminiscent tone, recalling past years and memories when his sister was alive. Finally, "Survivors" discusses the family as it is without his sister. He claims everything is still the same without her there, or at least his parents act as though it is. From this it can be inferred that the nonchalant attitude adopted by his parents upset him. Snodgrass's love for his sister is made apparent through these poems.

A possible reason for Snodgrass's decision to publish *Remains* under a pseudonym is its intensely personal content, yet the emotions discussed in *Remains* are not drastically different from those first described in *Heart's Needle*. Perhaps Snodgrass's choice to publish under a pseudonym had more to do with his subject and less to do with his own emotions:

To say that the voice in Gardons's poems is too close to the voice of the author's other work and does not justify or necessitate a pseudonym…is to miss the whole point.[19]

It is not the voice of the poem that needs protection, rather the subject – his family. The relationships that form the basis of *Remains* are too complex, emotional, and descriptive to leave open the possibility for the poems to be traced back to its subjects, at least while they are alive.

While his previous work discussed his daughter and past marriage, *Remains* addressed memories surrounding his parents, the death of his sister, and additional private details:

> *W.D. Snodgrass, in Heart's Needle, wrote a slightly longer sequence with the same grace and control exhibited in Remains, but Gardons touches nerves that are more exposed, probes a subject matter (parents and dead sister as opposed to wife and child) somehow deeper, more explosive, less public.*[20]

The incredibly personal nature of the work can be found by examining any of the poems in *Remains*. Perhaps the most descriptive poem is "Viewing the Body," in which Snodgrass discusses his sister lying in her casket among "obscene red folds of satin."[21] In this poem, Snodgrass accuses the people at his sister's funeral of never deeply caring for her until after her death:

> *They all say isn't she beautiful.*
> *She, who never wore*
> *Lipstick of such a dress,*
> *Never got taken out,*
> *Was scarcely looked at, much less*
> *Wanted or talked about.*[22]

"Viewing the Body" portrays his feelings of contempt and anger toward the people at the funeral, presumably his parents, for never treating his sister correctly. The condemning tone of this poem expresses Snodgrass's disapproval and anger for his parents' actions related to his sister's death. These emotions may have required Snodgrass to use a pseudonym in order to protect his parents' identity.

Another possible explanation for Snodgrass's use of a pseudonym was the pressure from his parents. It is clear that Snodgrass's parents never fully supported his aspirations to be a writer, but rather expected him to continue a family tradition by becoming an accountant.[23] Snodgrass's choice to study English and become a writer was a major source of conflict between him and his parents, especially during his college years. Much later, even though they still did not fully approve of his career choice, Snodgrass's parents eventually stopped criticizing him. He won the Pulitzer Prize in 1960 for his first book, *Heart's Needle*. Snodgrass's success, however, did not curb his parents harping on other aspects of his life.

Tensions between Snodgrass and his parents lie deeper than his career choice. Snodgrass disappointed his father even during childhood. He failed to pick up tennis, pool, or even chess, as his father had hoped.[24] Snodgrass's mother, however, was the biggest cause of his imperfect family relations. She was a selfish, shrewish person who never thought of anyone but herself and always created distress within the family.[25] Snodgrass dedicated an entire poem to describing his mother's detestable character. The damning poem, entitled "The Mother," is the first in the collection:

> *If evil did not exist,*
> *she would create it*
> *To die in righteousness,*
> *her martyrdom*
> *To that sweet dominion*
> *they have bolted from.*
> *Then, at last, she can*
> *think that she is hate*
> *And is content.*[26]

Along with his mother's undesirable disposition were other problems within his family. Equally frustrating to Snodgrass was the way his father dealt with his mother:

> *Some part of me really did despise him—for his weakness, his failure to rescue any of us from my mother's grip, his subtle manipulations of us.*[27]

Snodgrass's father failed to make any effort to ease the ill effects his wife had on their children. Instead, he had an adulterous affair, leaving his children to deal with their mother's moodiness.[28]

Although Snodgrass did not fully respect his parents, he would not have wanted them to see his description of his sister as a corpse with "eyeshadow like a whore"[29,30] These unflattering descriptions of his sister are accompanied by insulting descriptions of his parents. Despite his obvious contempt for his parents, Snodgrass still loved them.[31] He recognized their failings and did not hesitate to write about them. Snodgrass recognized the difference between writing about his parents anonymously and revealing the intimate details of his family life. "I believe that no subject matter should be barred from poetry, but that those matters usually considered personal or private should not be broached for their own sensational sake, where they could damage people still living."[32] By publishing under a pseudonym, Snodgrass spared his parents the humiliation of public exposure:

> *Snodgrass even attributed the character of S.S. Gardons to his parents. "Snodgrass states that he published the collection under the pseudonymous anagram S.S. Gardons because it contains unflattering descriptions of his parents, whose overprotectiveness… prevented his shy asthmatic sister from enjoying life."*[33] *The meaning of such accusations is damaging to his parents' reputation. These statements claim that Snodgrass's parents forced their children to live a life so full of oppression that is was scarcely enjoyable. In this description, his parents are oppressive, harsh, and uncaring. Parents, however severe, still hold a special place in their children's lives. Bearing this in mind, one can understand Snodgrass's decision to conceal his family's identity by using a pseudonym.*

While his true identity was never a secret, few people knew or recognized that S.S. Gardons was W.D. Snodgrass. Snodgrass came forward only after his parents died, sparing them public revile. Considering that *Remains* was reprinted, bearing his real name shortly after his parents' death, one can infer that the pseudonym was intended to protect his parents. But what was the motive to protect is parents? The use of a pseudonym was perhaps a measure of respect, or out of fear. □

Catherine Egan is a sophomore pursuing her degree in English with a minor in Spanish. Her research interests lie largely in works of literature and their authors. She currently serves on the editorial staff of the "Campus Times."

Studies of Emotion

A Theoretical and Emperical Review of Psychophysiological Studies of Emotion

Christopher P. Niemic
Advisor: Kirk Warren Brown, Ph.D.
Department of Clinical and Social Psychology

A discussion of current trends in psychophysiology studies about cerebral laterality and emotion regulation.

For over a century, human emotion has been an important theoretical and empirical idea in psychology. Dating back to the time of William James[1], psychology has accepted the idea that the human experience of emotion is the result of the interplay between an individual's cognitive appraisal of an event and his or her physiological response to it. Since James, psychologists have theorized about the temporal aspect of one's physiological and cognitive responses to a stimulus in the production of emotion,[1,2,3] cognitive strategies for determining physiological emotional valence (*i.e.*, attraction or aversion to a specific object or even),[4,5] and cerebral laterality for its predictive validity for physiological responses to emotion-provoking stimuli.[6,7,8,9,10] This article gives a brief historical overview of the theoretical aspects of emotion; describes the use of electroencephalography (EEG) to study the psychophysiology of emotion and recent developments in this field, including research on cerebral laterality and emotion regulation; and suggests future directions for research in the psychophysiology of emotion.

Theoretical Aspects of Emotion

Among the first psychologists to formally discuss human emotion, William James[1] believed that after perceiving a stimulating event, an individual instantly and automatically experiences physiological changes (*e.g.*, increased or decreased heart rate, changes in respiration rate, sweating). It is in thinking about and assessing these physiological changes that the individual assigns an emotion to them. Take the example of a man being burgularized. Upon witnessing the burglar entering his home, his heart races, he breathes more rapidly, and his hands tremble and sweat. In James's view, it is after cognitively assessing his physiological reactions to the situation that the man is able to assign the emotion of "frightened" to his experience. James believed emotional responses existed on a continuum, and the assignment of a specific emotion to one's experience depended solely on the specific physiological reactions that one experienced as a result of the stimulus. James also believed that emotional reactions were, to some degree, ordered; he listed categories of "coarse" affects (*e.g.*, anger, fear, love, hate, joy), which are coupled with strong bodily reactions.[1,11] In this way, certain sets of physiological reactions could be grouped together in a predictable manner.

Wilhelm Wundt[12] offered a dimensional view of emotion, purporting that human emotional responses could be plotted along a two-dimensional plane, consisting of pleasure and arousal. Wundt's dimensional view did not focus on physiological reactions to stimuli as the origin of emotional responses; rather, he was concerned about grouping and categorizing human emotions. Through his dimensional view, however, he laid the groundwork for the eventual development of the most prominent theory used in contemporary research on the psychophysiology of emotion. Schneirla,[13] following Wundt's dimensional classification of emotions, categorized all motivated behavior into two basic responses: approach and withdrawal. According to this classification, approach-motivated behaviors are those elicited for acquisition, and are generally perceived as positive behaviors stemming from positive stimuli. Conversely, withdrawal-motivated behaviors are elicited in response to external threats and are meant to provide safety for the individual.[11]

Bridging Wundt's[12] two-dimensional view of emotion and Schneirla's[13] classification of motivated behaviors, Davidson[14,15] and Lang[16] have classified emotional responses as being either approach-oriented or withdrawal-oriented. In this classification, the primary view of any emotional response is on direction, either toward or away from an emotion-evoking stimulus.[11] This dimension along which emotion has been separated has been studied extensively in laboratory settings, with results suggesting a neurological basis for this classification of emotions. In addition, there is substantial empirical evidence suggesting that positive and negative affect experienced in response to emotional stimuli is also related to approach- and withdrawal-motivation.[17]

Electroencephalography and Human Emotion

Human electroencephalography (EEG) measures both the frequency and amplitude of electrical activity generated from the brain. The brain site under study is compared to a 'reference site,' a relatively non-active site used as a means of comparison to judge electrical activity. Common reference sites in emotion studies include the ear lobes and the mastoids, because physiologists believe that these specific sites are electrically non-active relative to sites on the brain.

The use of the EEG has enabled researchers to study regional brain activity and brain function, in particular various human cognitive and emotional processes

When measuring emotional response, researchers often focus on the reduction in alpha band (8-13 Hz) activity. Much research suggests an inverse relationship between alpha activity and brain activation in adults.[18] Thus, the level of brain activation increases when emotion is experienced, which is observed as a reduction in alpha band activity as measured by EEG.

With the use of high-density electrode arrays, there exist many possible sources of 'noise' that can disrupt EEG recordings, including muscle activity near the active sites, gross motor movements, and eye movements and blinks.[19] Eye movement artifact can have profound effects on frontal brain sites, specifically mid-frontal sites (F3 & F4), which are used in studying emotional reactivity. Davidson[20] and Tomarken, Davidson, Wheeler, & Doss[21] report that individual epochs of 'clean' data could be as little as 1 second in length, but for each individual emotion under study a minimum of 10-15 seconds of activity must be collected. Although EEG has poor spatial resolution and requires many electrodes placed at various sites on the head, it provides excellent time resolution, allowing researchers to study phase changes in response to emotional stimuli. The use of EEG is noninvasive, fast, and inexpensive, and it is neither painful nor uncomfortable. For these reasons, EEG has become a preferred method in studying the brain's responses to emotional stimuli.

The use of EEG to study electrical activity in the human brain was demonstrated for the first time approximately 70 years ago.[22,19] This development has had far-reaching implications for the study of human brain activity in general and specifically for the study of the human brain's changes in response to changes in emotion. The use of EEG has made possible the discovery of electrical differences in brain activity between resting state and stimulus conditions, the differences that exist between the two hemispheres of the brain (*e.g.*, cerebral laterality), and other physiological activity in response to stimuli (*i.e.*, heart rate, muscle activity, and skin conductance). The use of EEG has also enabled researchers to study regional brain activity and brain function, in particular various human cognitive and emotional processes, individual differences in brain function, and brain activity in psychopathology.[19]

Cerebral Laterality and Emotional Response

The use of EEG has been pivotal in studies concerned with brain asymmetry and emotion.[19] Using EEG to study brain asymmetry in humans, researchers have recently made many discoveries suggesting that physiological reactions play a large role in the experience of emotion and that individual differences in electrical activity between the two brain hemispheres can be used to predict emotional responses to various stimuli. These findings have helped answer the questions concerned with how emotions that shape individuals' everyday life are generated and why individual differences in emotional experiences exist.

To address the question of why individual differences exist with respect to emotional experience, many studies have centered on frontal activation asymmetries. Davidson and his colleagues[23,34] have viewed cerebral asymmetries in the frontal regions as having a basis in approach- and withdrawal-motivation, and thus being of prime importance to the mediation of behavior and emotional response. They hypothesized that the anterior, or frontal, region of the left hemisphere of the brain is specialized for approach behaviors, while the anterior region of the right hemisphere is specialized for withdrawal behaviors.[14,20,23,24,25] This view suggests that individuals who have more activation in the left hemisphere will tend to approach situations more freely and experience positive emotions while doing so, compared to individuals with greater right-hemisphere activation. Conversely, individuals who have predominately right-hemisphere activation tend to withdraw from situations, and in doing so experience more negative emotions, compared to individuals who have greater left-hemisphere activation. These hypotheses are supported by empirical evidence.[8] Researchers have also demonstrated that these individual differences appear at an early age[26], are relatively stable over time,[27] and may be heritable.[28]

These findings suggest that individual differences in cerebral laterality can be used to accurately predict emotional response and valence to various stimuli. Tomarken and his colleagues[6] demonstrated that individuals' measure of resting alpha level could predict both negative affect in response to negative stimuli and affective valence (*e.g.*, the difference between one's positive and negative affect). They found that individuals with greater right-hemisphere activation experience more negative affect in response to negative stimuli, compared to individuals with greater left-hemisphere activation. The same study, however, did fail to demonstrate that greater left-hemisphere activation could predict greater positive affect. Wheeler and his colleagues[8] not only validated Tomarken *et al*'s. findings,[6] but also found that greater left-hemisphere activation predicts greater positive affect in response to positive stimuli. Wheeler *et al.*[8] thus concluded that individual differences in tonic levels of asymmetry have predictive value with regards to individual temperament, affect reactivity, and dispositional mood. The findings thus far concerning cerebral asymmetry and its prediction of affective reactivity have focused solely on anterior cerebral sites (*e.g.*, mid-frontal and anterior temporal). One possible explanation for the difference in predictive validity between anterior and other cerebral sites has been that the frontal and anterior temporal sites have extensive anatomical connections with the limbic structures believed to be responsible for the control of emotion.[29,30]

Relative to research regarding electrical activation in the brain, there has been little research on the muscle and eye movement activity that accompany emotional responses to stimuli. Ekman[31] has suggested that all emotions have a specific physiological pattern that accompanies the electrical activity and subjective experience of that emotion. In studying this hypothesis, Davidson *et al.*[7] found that when averaged across the entire length of the emotional stimulus, the EEG pattern in both the alpha and beta bands could not be used to differentiate between

the emotions of disgust and happiness. Rather, facial (*e.g.*, electromyography) activity have to accompany the EEG pattern to allow for reliable prediction of emotional experience.

Sutton *et al.*[32] studied eye blink reflex and corrugator activity of subjects in response to negative pictures, compared to responses to positive pictures. They found that, compared to positive pictures, subjects demonstrated greater eye blink reflex and corrugator activity when viewing negative pictures. Although females tended to show more aversive emotional reaction to negative pictures compared to males, there were no overall effects for sex on either eye blink reflex or corrugator activity. These findings suggest that physiological activity in the brain, as a response to emotional stimuli, is accompanied by both muscle and eye activity. Furthermore, this eye activity, in addition to EEG patterns, can be used to help predict subjective emotional experience.

The Behavioral Approach System (BAS) and the Behavioral Inhibition System (BIS) are Gray's[33] systems hypothesized to underlie learning and affect.[10] The BAS is utilized when behavior is motivated toward incentives, rewards, or both while the BIS motivates behaviors away from threats that exist in an individual's external world. Furthermore, Gray[34] has suggested that the levels of BAS and BIS activation within an individual can accurately predict predominant personality traits, individual temperament, and the possibility of depressive symptomology. Individuals who have a more active BAS system tend to be more extraverted and impulsive, compared to individuals who have more BIS system activity, who tend to be more neurotic and anxious.[10] Researchers have shown that individuals who have a more active BAS system also tend to have greater left-hemisphere activation. Conversely, individuals who have greater activation of the BIS system tend to have greater right-hemisphere activation (Sutton and Davidson, 1997). These findings suggest that hemispheric activation can predict BAS/BIS activation and could in turn have predictive validity for personality. If future research supports this link, then the accuracy of EEG as a test for personality could be supported as well.

It is important that individual differences in frontal activation is viewed as a diathesis, requiring specific stimuli in order to elicit the emotions to which an individual may be predisposed.[8] Cerebral asymmetries simply give rise to a vulnerability to respond emotionally to a stimulus in a certain way. This view does not suggest that, for example, individuals with greater right-hemisphere activation are destined to become depressed and inhibited. Finally, the discovery of a pattern for frontal activation and its predictive validity for affective response has been shown to generalize to other populations, including people with depression[35,36] and infants.[37,38] This generalizability offers promise that cerebral asymmetry truly can predict affective response and valence as well as individual personality and temperament.

Emotion Regulation

A relatively recent development in the psychophysiological study of emotion has been centered on emotion regulation, focusing on the strategies individuals utilize in order to deal with the negative emotions that they experience. This line of research also investigates the effects of emotion regulation on psychological and physical health, with interest lying in determining the healthiest ways to regulate negative emotions.

Gross[39] has postulated that emotions can be regulated either before an individual response to a stimulus through antecedent-focused emotion regulation (*e.g.*, reappraisal) or after response to a stimulus has been made through response-focused emotion regulation (*e.g.*, suppression). The term 'reappraisal' refers to the reinterpretation of an emotional stimulus, while 'suppression' refers to responding to an emotional stimulus in a way to mask its external display. Both types of regulation strategies were empirically shown to be effective in decreasing emotion-expressive behavior; while reappraisal decreases one's experience of the emotion disgust, suppression increases one's sympathetic activation in response to the stimulus.[39] The results of Gross' study[39] suggests that reappraisal as a regulation strategy decreases the amount of stress an individual experiences, thereby improving psychological health. Suppression tends to increase one's level of sympathetic activation, thus having deleterious effects on physical wellbeing.

In a related study on emotion regulation, Jackson and his colleagues[5] found that emotion regulation has effects on muscle and eye blink activity related to that emotion. Specifically, they found that suppression of a negative emotion tends to decrease eye blink and corrugator activity, while enhancement of negative emotion tends to increase eye blink and corrugator activity. These results suggest that the ways in which individuals cognitively respond to emotion-provoking stimuli have effects on physiological reactions to and experience of a given emotion. The psychophysiological study of emotion regulation could thus have important applications to the enhancement of psychological and physical well-being.

Future Research

Much of the present research on cerebral asymmetry has focused only on female and non-depressed individuals, and thus its generalizability is limited. Future research should attempt to use mixed-sex samples, include both clinical and normal populations, and include a broader age-range. Furthermore, future research in cerebral asymmetry must extend the range of emotions experimentally manipulated; most studies manipulate only happiness and disgust. The limitations of this are obvious. First, the human range of emotions extends far beyond these two basic emotions. If psychologists are to understand the human emotional response, they must study a wider range of emotions. Second, more people do not regularly experience disgust. It serves a useful purpose to be highly withdrawal-motivated, but the inclusion of anger, fear, and sadness as negative emotions to be experimentally manipulated would substantially advance the study of cerebral laterality and human emotion. Finally, the temporal aspects of emotion could be investigated, in which researchers would look into expressive, physiological, and subjective experiences of emotion and their relation to each other through time.

Similar to the study of cerebral laterality, future research on emotion regulation could utilize the experimental manipulation of a

Cerebral asymmetry can predict affective response and valence as well as individual personality and temperament.

wider range of emotions. Also, other forms of emotion regulation, in addition to reappraisal and suppression, could be studied and their effectiveness assessed. Finally, emotion regulation is a commonplace activity for everyone. As such, there exists a need for future research to investigate emotion regulation strategies and their effectiveness as they occur outside of the laboratory.

Conclusion

The study of the psychophysiology of emotion has been a recent development in psychology, and consequently has few empirical studies from which psychologists can draw conclusions. In spite of this, the results generated so far regarding cerebral laterality and affective response are promising. With additional research, psychologists can learn much about why individuals respond to emotion-provoking situations in different ways. Furthermore, coping strategies, which occur frequently in individuals' lives, could be more fully understood. Investigation of these issues could have important implications for individual health and well-being.

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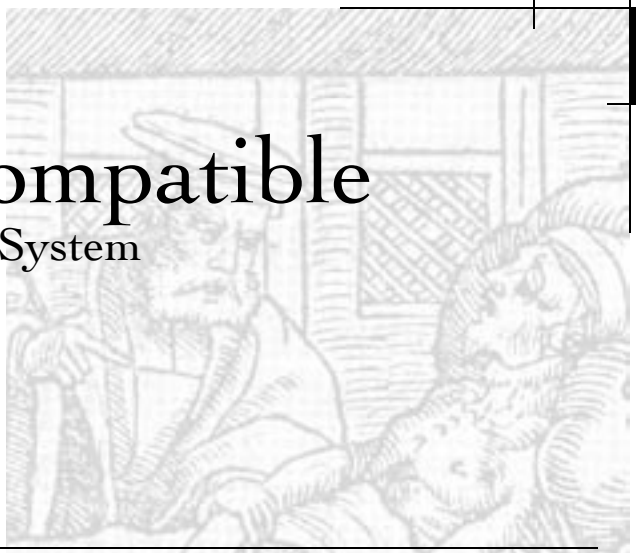
Integrating the Incompatible

The Rise of the Incorporated Immune System

Sahand Boorboor, 2002
Advisor: Theodore Brown, Ph.D.
Department of History



A small discovery at the University of Rochester sparks a revolutionary way of understanding the immune system.

In the mid 1990s, Alan Leschner, the director of the National Institute of Drug Abuse, opened a lecture by stating that dualism was dead. He was referring to the idea that the mind and body were separate entities, a practice that not only pervades Western science but also Western culture. Although dualism's death is questionable, given its long history and firm hold on Western thought, it may well have received a blow from the biomedical community.[1] The 1970s brought a scientific revolution in the way researchers perceived mind-body interactions. This change challenged the belief that the immune system was an autonomous, self-regulating organ system. The reasoning behind this paradigm was that the cells of the immune system worked in culture, devouring microbes as they did *in vivo*. Therefore, the brain would have nothing to do with immune response, an idea perpetuated in medical literature and textbooks. The idea of an independent immune system extended to the vast majority of immunologists, who, if asked in 1970 if the immune system interacts with the nervous system, would have given a resounding no. So deeply entrenched was this belief which experiments that illuminated a link between the mind and immune system were denounced as rubbish in the 1970s and 1980s. Despite this resistance, these experiments introduced a new scientific era in the 1990s.

Along with the skepticism of many scientists, there were internal rifts among the forthcoming revolutionaries of the new school of immune research, leading to the establishment of five definable, and often competing, sub-schools. "Neural-immune interactions" (NII), as the overarching school is often called, will serve as an appropriate title for the purposes of this paper because it avoids the politicization of many other contemporary expressions that signify the entire field. "Neural" encompasses the central nervous system, the endocrine system, and behavior, allowing the term to touch on all aspects of the overarching school. This school, as well as the subschools beneath it, is the result of a scientific revolution whose basic pattern fits Thomas Kuhn's model of scientific change in his essay, *The Structure of Scientific Revolutions*.

Kuhn's Paradigm

Kuhn's theory offers an excellent conceptual framework against which we can view the emergence and development of NII. Kuhn believed that science does not advance in a steady march toward truth, but instead progresses in occasional spurts followed by more extended periods of stability. The stable periods are times of puzzle solving, where the details of a science are examined and explained and advances are made within a "paradigm." Scientists doing research within a paradigm operate in a microculture with a specific theoretical and methodological orientation. Their standards of excellence and rigor are implicitly agreed upon and are so embedded that they are not usually acknowledged. The paradigm is a requirement of science, because "[no] scientific group [can] practice its trade without some set of received beliefs."[2]

When the paradigm fails to explain newly discovered and yet unexplained phenomena, new schools and theories emerge to account for these discrepancies. But the rise of new paradigms is no smooth progression, for "in science…novelty emerges only with difficulty, manifested by resistance, against a background provided by expectation."[3] The change does not follow the progression of anomaly, to crisis, to establishment, and finally to acceptance of a new paradigm in one fell swoop; thus, 'revolution' is a somewhat misleading but necessary term that describes radical changes in the scientific process. Since scientific revolutions shift paradigms and therefore change commonplace facts, rules, and standards taken for granted by scientists, they meet with incredible resistance from proponents of established paradigms. Yet, inasmuch as theory and fact must eventually become compatible again, new schools begin theory creation and shuffle to establish themselves as the new paradigm.

Although Kuhn's theories make up the bulk of our conceptual framework, there are areas where we must stray from his ideas to explain the development of NII. Kuhn never explicitly states that scientific revolutions are self-contained and limited strictly to the scientific community involved, but he makes such an implication. As we will see later, external forces including the lay public and various government institutions, as well as general medical trends and fads influenced the development and acceptance of NII.

The Beginnings of NII

1975 was a benchmark year for NII. Robert Ader, an experimental psychologist

at the University of Rochester, demonstrated a mind-immune link. Meanwhile in Switzerland at the Schweizerisches Forschunginstitut, Hugo Besedovsky, an endocrinologist, performed experiments confirming the thymus's influence on the neuroendocrine system. Simultaneously George Solomon of Stanford University was writing papers that discussed the correlation between stress and immunologic parameters. A new school developed in the mid 1970s because these and other researchers discovered, or in some cases stumbled across, a link between the nervous system and the immune system. This school was a direct challenge to the long-standing paradigm of the isolated and self-regulating immune system.

> Kuhn believed that science does not advance in a steady march toward truth, but instead progresses in occasional spurts followed by more extended periods of stability.

For a paradigm to be questioned and discarded, an anomaly must emerge and be incompatible with the current paradigm. Robert Ader's unfamiliarity with the autonomous immune paradigm was the very reason he discovered an anomaly. As an experimental psychologist, Ader had no idea that the immune system was considered an independent system. His education and experience made him think that every disease had a psychosocial aspect. Ader performed classical conditioning experiments on rats, which, as originally designed, had nothing to do with the immune system or immune function. His research was akin to that of Ivan Pavlov, who conditioned dogs to salivate at the ring of a bell. Likewise, Ader conditioned rats to develop an aversion to water sweetened with saccharin. To do this, he fed the rats saccharin water and then injected them with cyclophosphamide, a nausea inducing drug. Contrary to expectation, some of the rats died after Ader provoked the conditioned response. As Ader soon learned, cyclophosphamide was an immuno-suppresant and through conditioning he assumed the rats had suppressed their immune systems, a process leading to overwhelming infection and, ultimately, death. He did not know how the observed phenomenon worked or if he had committed a simple error in experimental design. With immunologist Nicholas Cohen's help, Ader designed a new experiment that challenged the immune system with antigen to show the rats did indeed suppress their immune systems.[4] At the time, no one could conjecture how conditioning compromised the immune response; nevertheless, the improbable experimental results amazed many and therfore received heated criticism. To a large extent, Ader and Cohen's individual reputations as conservative, rigorous researchers legitmized the results; as George Engel, the priciple architect of the biopsychosocial model of medicine, told Ader: "Your conservatism is going to pay off because people are going to believe this because you said it."[5]

George Solomon published many similar papers on the effects of stress on immunity. A 1969 paper of his, titled "Stress and Antibody Response in Rats," tested various types of stressors on antibody production. Solomon concluded that "the central nervous system might play a role in control of immune response."[6]

Because of advances in medical technology in the 1970s, specifically in the extraction and detection techniques of peptides, researchers from various fields discovered more evidence for an integrated immune system. D. C. Dumonde's work was particularly monumental: he classified a group of non-antibody signal molecules secreted by activated lymphocytes, which he named "lymphokines."[7] In 1974, the term "cytokine" was introduced and by 1979 researchers again changed the name to "interleukin."[8] The discovery of signal molecules secreted by leukocytes created a real possibility for an interactive immune system for scientists skeptical of psychology and stress research, which seemed full of ambiguous ideas. Dumonde's and others' work laid the groundwork researchers needed to demonstrate communication between the immune system and the brain. Convincing skeptical scientists of this relationship depended largely on clarifying the role of cytokines.

The endocrinologist, Hugo Besedovsky, brought a neuroendocrine perspective and "hard science" legitimacy to the field in 1975 with his research on the thymus's effects on the neuroendocrine system. The thymus, an ontologically important immune organ in the middle part of the chest, is the site of T-lymphocyte development. In 1975, Walter Pierpaoli and Besedovsky measured the effects of a missing thymus on the neuroendocrine system.[9] Besedovsky's research suggested that the immune system had a role in neuroendocrine regulation. Two years later he made clear what he and Pierpaoli had suggested in their aforementioned paper: "In order to bring the self-regulated immune system into conformity with other body systems its functioning within the context of an immune-neuroendocrine network is proposed."[10] If taken with previous research, Besedovsky's work allowed for communication and regulation between systems as well.

J. Edwin Blalock's research on lymphocytes, done early in 1981, focused on communication in the same way Besedovsky's did. He and Eric Smith found that lymphocytes produced andrenocorticotropic hormone, previously thought to be made solely by the pituitary gland and to have functioned only in the neuroendocrine system.[11] These results suggested a "circuit" between the neuroendocrine and immune systems and the possible existence of immune regulation of neuroendocrine function.[12]

These major findings of the 1970s and early 1980s constituted the first inklings of a paradigm shift from the autonomous to the integrated immune system. Their immediate significance, however, was the development of a new school of research to challenge the existing paradigm.

Sub-schools Emerge

The first edition of *Psychoneuroimmunology*, edited by Robert Ader, established a new school, NII. The book presented a formal challenge to the autonomous immune system paradigm, and forced researchers from varied disciplines working to bring the subject matter of disparate specialties together. The school had no official members; there was nothing to take membership in, except a belief that the immune system was not self-controlled.

The unity that developed the first edition of *Psychoneuroimmunology* would not last. It was a temporary alliance between individu-

als from different fields with very different scientific backgrounds who were attracted to the possibility a non-autonomous immune system. These researchers shared glimpses of a common vision but had little else that bound them together. In fact, there were rifts between the contributors of *Psychoneuroimmunology* even before the first edition was published.

The existing differences between NII researchers and their methodologies became a greater issue once the field emerged. The paradigms in which they worked could not be avoided or overcome. That one scientist was a psychologist by training and another an endocrinologist made a difference. More important, however, were each researcher's preconceptions of the importance of demonstrable mechanisms or their ideas on the methodology of research; these became some of the important and controversial lines of delineation between sub-schools.

At least five distinct research "approaches" emerged in the 1980s that would eventually become sub-schools. There were scientists who took a psychological approach and asked how stress could alter the immune response. They started from psychology and behavior, and then moved into biological aspects. The neuroendocrine approach did not go higher than the hypothalamus; these scientists looked at the interplay between hormones originating from the hypothalamus, pituitary gland, and the immune system. Neuroanatomists searched for the expression of immune molecules in the brain and other physical connections. A fourth approach was made by scientists who researched sickness behavior; they measured the effects of cytokines on behavior. Finally, the neuroimmunologists who managed to stay outside the politicization of NII made up the fifth approach. They isolated themselves from the other approaches because their research did not cross the blood-brain barrier. Neuroimmunologists measured the effects of immune cells and molecules that were physically in the brain, focusing mainly on multiple sclerosis.

Through development, competition, and external influence these approaches hardened into sub-schools. Some had names reflecting the overall school of NII, whereas others did research under the name of their original discipline. Since fluidity marked the progression of the field, especially in its advance from scattered points of research to definable sub-schools, there are no set dates for when approaches became confirmed sub-schools, only general trends. Scientists, as well as the lay public and media, lumped these approaches under the newly emerging names that the field's leaders created, such as psychoneuroimmunology (PNI), neuroimmunomodulation (NIM), or psychoimmunology.

All of these approaches had roots in the 1970s, and most, with the exception of sickness behavior (which did not appear until the late 1980s), did not realize their boundaries enough to be called sub-schools until the early to mid 1980s. But even as they gained recognition, these research areas transitioned from approaches to sub-schools. In the rest of this section, I use sub-school to refer to the transitional approaches and emerging sub-schools.

The boundaries between sub-schools were often blurred throughout the development of NII in the 1980s and early 1990s. The participants did not live in a vacuum; the crossing of scientific disciplines led to cooperation and communication among researchers, often producing stunning results. Sub-schools are fluid structures whose most defining aspect stems from the paradigm under which its members are trained, whether it is psychology, neurology, medicine, or something else. It must be stressed that the central defining characteristic separating the sub-schools was the content of their science. Neuroimmunology, for example, separated itself from the other sub-schools because its science did not leave

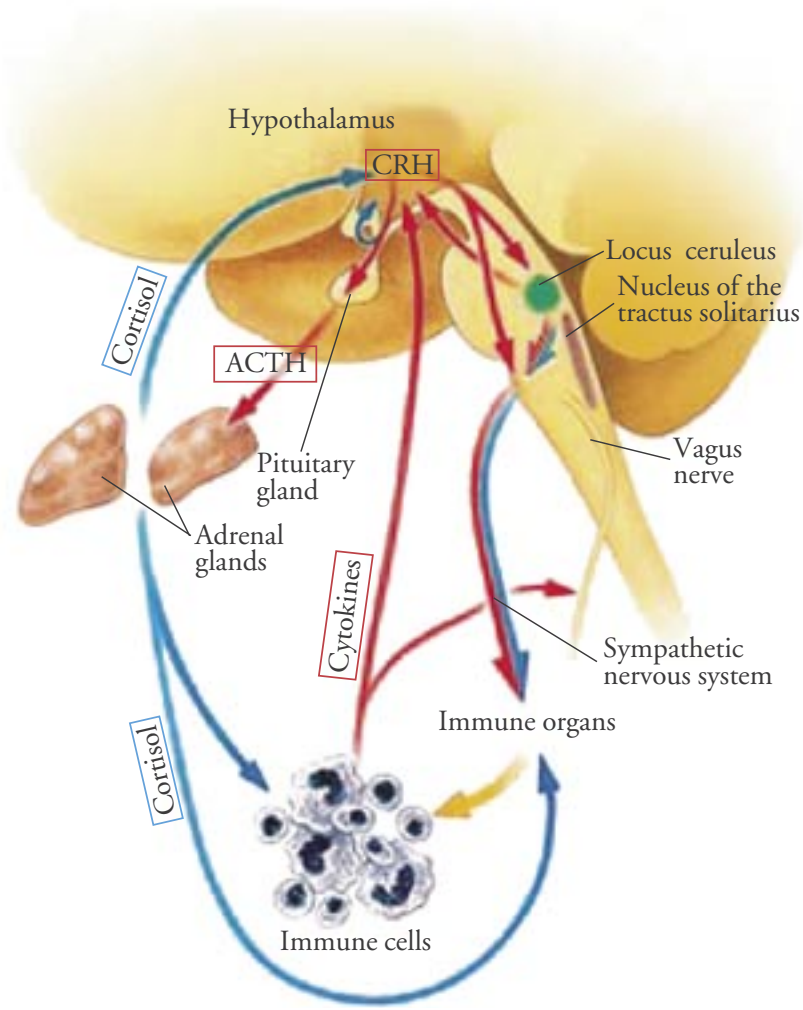


Figure 1. The interplay between the immune system and the brain.

The emergence of NII has changed our concept of disease and opened up new ways that we can use to preserve health.

the confines of the brain. Methodological differences drew lines as well, an example of which is the delineation between neuroendocrine and psychological sub-schools and the weight each put into describing molecular mechanisms. Political squabbles, in terms of recognition, grant funding, and publications, drew very clear lines around the psychological sub-school as well. The cost of being associated with psychology (considered by mainstream biomedicine as 'soft') in terms of wide scientific acceptance and federal grant funding pushed away other sub-schools. Thus, political delineations ran along and, sometimes, away with the scientific delineations of sub-schools. But because of the nature of the sub-schools involved and the fact that the subject involved integrating so many complicated biological systems, scientists would often cross disciplinary boundaries. For example, David Felten, a neuroanatomist, worked closely with Ader and Cohen, editing the second and third editions of *Psychoneuroimmunology* with them.

PNI, as the psychologically oriented sub-school became known, was first termed so by Robert Ader in 1980.[13] Central in the development of the PNI sub-school were also George Solomon, A. F. Rasmussen Jr., and Nicholas Cohen. Solomon and Rasmussen had been exploring the effects of stress on immunity since the late 1960s. For those who did not fully reject Solomon's stress research, a classic argument against its validity was to question its immunologic significance; a precipitous drop in antibody levels will not necessarily mean illness for an organism.

Ader's 1975 conditioning experiment was more dramatic than the earlier work of Solomon and Rasmussen because its suppression effects had high immunological significance: the rats in Ader's experiment died.[14] After these preliminary observations, Ader and Cohen designed more rigorous experiments showing the immunological effects of conditioning. The paradigm they tried to disprove was well situated, and the dedication to its preservation strong. As Esther Sternberg put it:

> *In the 1970s, and even today, the idea that the immune system could be taught was considered an outrageously heretical notion by most classical immunologists. Immune cells respond to molecules that crash up against them, get stuck to proteins protruding on their surfaces, get gobbled up into the cell's interior, and cause other molecules to be made in the cell's protein factories and spit out-magic antibody bullets that surround the prey and destroy it. There is no room for learning here.*[15]

So strange were Ader's results that even supporters of the NII school were skeptical.

The neuroendocrine sub-school, called neuroendocrinimmunology, rose simultaneously as the PNI sub-school with Hugo Besedovsky's research. As early as 1971, Besedovsky had published a paper measuring the influence of glucocorticoids on the lymphoid organs of pregnant rats.[16] His later papers were direct attacks at the paradigm of an isolated immune system.[17,18]

The neuroanatomy sub-school, which often paralleled and progressed with the neuroendocrinimmune sub-school, started in the early 1980s. Many different groups, among which Karen Bulloch's was prominent, started to identify innervations of immune tissues.[19,20,21] These observations provided preliminary evidence for a direct, physical, hard-wired link between the two organ systems. Jean-Michel Dyer's was one of the first to demonstrate the presence of interleukin-1 in the brain and also its *in vivo* synthesis.[22] Bill Farrar and Candace Pert took the next step by identifying interleukin-1 receptors in the brain.[23]

Of the first papers to mark the beginning of the sickness behavior sub-school was a review article by B. L. Hart titled "Biological basis of the behavior of sick animals."[24] The sub-school did not really take off until Robert Dantzer and the team of Steven Maier and Linda Watkins joined the scene in the early 1990s. Dantzer's first papers linking interleukins to sickness behavior were published in the early 1990s;[25,26] the researchers injected animals with synthetic interleukins and measured changes in behavior.

Maier's and Watkins' team did work similar to the Dantzer group. Their studies in the early 1990s helped illuminate the mechanisms of acute responses: fever, fatigue, decreased sexual activity, loss of appetite, and decreased social interaction. By injecting synthetic proinflammatory molecules such as interleukin-1, they elicited acute responses and later found that these responses were largely mediated via the vagus nerve, which connects the gut to the brain (cytokines can either stimulate the vagus nerve and trigger communication or travel to the brain via the blood stream).[27]

The neuroimmunology sub-school was tightly bound with multiple sclerosis and other diseases of the central nervous system. Its roots started in the late 1970s with the work of Henry McFarland and Dale McFarlin. Neuroimmunology dealt mainly with immune effects in the brain, and therefore it did not seriously consider many interactions that the other schools considered relevant. Neuroimmunology gained acceptance from the biomedical community rather early on in the 1980s. *The Journal of Neuroimmunology* started circulation in 1981 and quickly gained respect.

All of this work sprouted from different research approaches and backgrounds of individuals. Through refining these works, researchers exploring the nervous-immune connection funneled into sub-schools at different rates. As the field of NII germinated, the singular approaches of exploration turned into sub-schools with more defined methodologies.

Competition Between Sub-schools

That different sub-schools of NII developed is not surprising given the history of competition within medical science. Increasingly, in post World War II United States, medical specialties and subspecialties formed and found their own niches. Medicine transformed from one connected field to many related ones, each steeped in its own methodology. Thus, when NII emerged, each researcher brought her or his own traditions, technologies, and research styles.

The five NII sub-schools drifted apart from each other throughout the 1980s. Subtle scientific difference governed the separation, with each field seeing its specific methodology and pathways of neural-immune communication as the most important. As the incredible ramifications of the field became apparent, NII entered the biomedical research milieu, with all its politicization, research grants, and opportunities for career advancement. The adherents to the new school were treading the dangerous waters associated with competition for scarce resources and recognition. Egos flared as scientists vied to create new ideas and position their work as central to the development of a major new science.

PNI, as a sub-school, was soon isolated from other sub-schools and shunned by mainstream biomedicine, which perceived it as "soft science" psychology, "strategically located at the nexus of natural, biomedical, and *social science*."[28,29] The historical marginalization of psychology led to a "physics envy"[30] among psychologists. As far as the other natural sciences were concerned, psychology was a black sheep, "its subject matter...unquantifiable and its methods mired in a metaphysical morass."[31] PNI, because it contained "psycho-," caused a knee-jerk reaction in mainstream biomedicine, which was concerned with the single cause-single effect "just-associations" provided by molecular mechanisms and not the "simple-associations" psychologically oriented research provided. PNI, as seen by some of the other sub-schools, was not rigorous enough despite Robert Ader 's and Nicholas Cohen's reputations as rigorous NII researchers.

The stakes of association with PNI were raised by scientists outside NII; some of the most scathing remarks were directed against the psychological aspects presumed to characterize the overarching school. Two articles represented the criticism against PNI. One was in the *New England Journal of Medicine* and the other in *Nature*, which repeatedly refused to print PNI research because "...the precise mechanisms involved in the phenomenon" observed were not identified.[32] As the editor of *Nature* argued, not only were mechanisms and thus just-associations not identified, but also the science of PNI falsely sustained the hopes of the ill. This editor, John Maddox, argued that the likelihood of a link binding the nervous and immune systems was high, but that not "enough is yet known to sustain people's hopes of explanation."[33] His skepticism was aimed at the prospect of the seriously ill finding hope in applications of an unproven science, which, under Maddox' interpretation, claimed that a person's state of mind was the road to either health or disease. This view was reflected throughout the biomedical community despite repeated statements by advocates of PNI that the psychological aspects of immunity were just some of the many contributing factors leading to disease. As Robert Ader wrote, "it is unreasonable to suppose that stressor-induced perturbations of the immune system could, *by themselves*, be of clinical significance."[34]

In her 1985 article, "Disease as a Reflection of the Psyche," Marcia Angell recalled the history of scourges such as tuberculosis and the myths that arise with misunderstanding disease. Since uncurable diseases are feared, people attach psychosocial causes to them in an attempt to gain control over the disease. But, as Angell points out, nothing other than a tubercle bacillus causes tuberculosis; she drew a similar parallel to cancer and the 20th Century, recalling that "most reports of such a connection [between state of mind and disease onset and progression] are anecdotal."[36]

Angell's criticism relied heavily on popularizations of PNI since the new research gave an air of legitimization to the already standing biopsychosocial model of medicine. These popularizations ran far ahead of the science of the new field. As the sub-schools were fragmenting in the mid-1980s, magazines were peppered with headlines such as, "Got a Cold? Have you Tried Willing it Away?"[37] and captions such as, "Can you marshal your moods to fight disease? Scientists are discovering the pathways that link your brain with your body's lines of defense."[38] Such media claims made PNI seem ungrounded in the lofty annals of the hard sciences. The neuroendocrine, neuroanatomy, and neuroimmunology subschools, however, were not highlighted by the media because their language would not popularize easily; it did not contain explicit references to emotions and stress. Even though their aim was ultimately the

same as PNI, to show bi-directional communication between the immune and nervous systems, the other sub-schools stayed outside the public view throughout the 1980s. Thus, popularization exposed the sub-school containing the psychological aspects of NII even further than its psychological stance would have by itself. PNI research seemed to give legitimacy to what many in the public wanted to hear. Modern purveyors of "snake oil" even used PNI to give credence to odd curatives, such as crystal therapy.

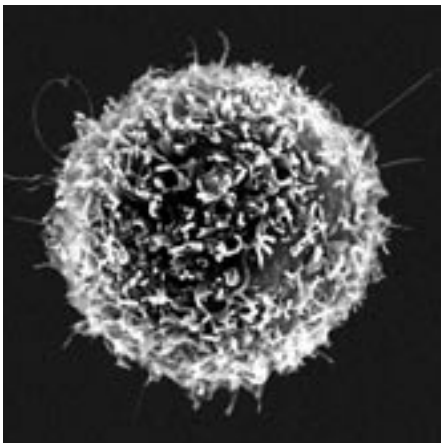
External criticism of PNI paralleled its internal problems with the other sub-schools and the general field of biomedical research. Ader summed up some of the major differences in his 1979 Presidential Address to the American Psychosomatic Society:

> *One simple, universal observation underlies psychosomatic research: that when a population of individuals is exposed to the same environmental pathogens only some individuals manifest disease. Despite the most sophisticated strategies designed to achieve uniformity, variability remains one of the ubiquitous results of all natural and contrived biological experiments. The biomedical scientist, operating within the conceptual and technical constraints imposed by the disciplinary boundaries of a reductionistic philosophy, attempts to control or minimize (or ignore) variability. For the psychosomaticist, such variability is the starting point of his research: it defines the operation of variables with which to be concerned.*[39]

This type of statement seriously discouraged mechanism-oriented researchers who had to limit variables in order to observe cause-effect type relationships on the molecular level. In terms of scientific content, the stance on variability and PNI's unquantifiable aspects were the major reason for tension between it and the other sub-schools. Thus members of the other sub-schools, in particular the neuroendocrine sub-school, tried to distance themselves from PNI.

Outside influence did not serve a strictly negative role in setting PNI off from the other sub-schools; special funding opportunities arose because of this sub-school's stress oriented research. The military financed a great deal of PNI research because they had encountered illness among members of the armed forces that if not caused by stress, were at least exacerbated by it. More important for PNI's growth, however, was the immense amount of money made available in the late 1980s for AIDS and HIV research. The disease and the research sub-school became intertwined for a brief period of time into the early 1990s until the "unrealistic expectations" projected onto the possibilities of PNI treating AIDS did not yield incredible results.[40]

Novera Herbert Spector, who held an administrative role at the NIH throughout the 1980s, coined "neuroimmunomodulation" (NIM) in 1979 as a substitute for "nervous system influences upon immune responses," a cumbersome term that researchers in the emerging field of NII frequently used.[41] As tensions between the sub-schools ran high,



many researchers distanced themselves from the science of PNI as well as the word by using NIM in reference to the overarching school. Both expressions were, and still are, used to signify NII or certain combinations of sub-schools. PNI and NIM also function as benchmarks demonstrating the union of the overarching school in the very early eighties and the separation and politicization of sub-schools shortly thereafter; NIM appeared in the first addition of *Psychoneuroimmunology*. It was only afterward that proponents of each term began to actively avoid the other term. And as will be shown later, when the sub-schools started to accept each other's work as complementary to their own, PNI papers constituted a significant portion of the meetings of the International Society of Neuroimmunomodulation and appeared very often in their journal, *Neuroimmunomodulation*.[42]

Of the other sub-schools, neuroimmunology and sickness behavior hold special positions, the former because it effectively separated itself from the rest of the sub-schools by virtue of its scientific content and the latter because it did not fully develop until the early 1990s. There is no evidence of the neuroimmunology sub-school interacting with the other sub-schools until the mid 1990s. The constituents of this sub-school were either pure immunologists or neurobiologists who extensively researched multiple sclerosis and other neurological diseases of the central nervous system; thus they were able to insulate themselves from the mind-body controversy the other sub-schools dealt with.

Solidification and Acceptance

As sub-schools distinguished themselves, their members conducted research, thus creating a sound foundation upon which they could establish a paradigm. Little of this research represented a collaboration between sub-schools; each traveled down its own road of solidification beyond the original introductory experiments described earlier. The body of research under the NII school burgeoned in the mid-1980s through the 1990s, each experiment reinforcing another so that, when taken in totality, the findings explained to even the most skeptical of critics that the immune system was integrative. Solidification was a requirement for paradigm establishment because scientists are skeptical people who need irrefutable evidence that an established paradigm is obsolete. Initial experiments created an introduction but were not convincing on their own; it was only when these experiments were repeated with greater precision, or simply repeated by different researchers, that skeptics considered them sound. Introduction of a new concept concerning the immune system eventually led to rigorous experimentation and thus solidification and acceptance. Some experimental results seemed so outlandish, as conditioned immune responses did, that no matter how rigorously carried out, they had to be repeated by a variety of people, many of whom aimed to refute the original results.[43]

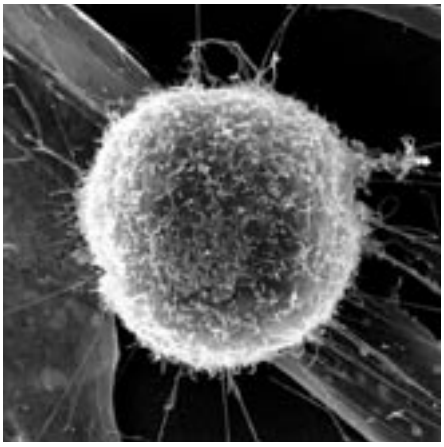
Solidification of the neuroanatomical and neuroendocrinimmune sub-schools came in two waves, a supplement to the August 1, 1985 issue of the *Journal of Immunology* and three influential articles in the October 23, 1987 issue of *Science*. The supplement contained 28 diverse papers that

centered mainly on the neuroendocrinimmune and neuroanatomy sub-schools, but they also addressed PNI.

Perhaps the most striking of the articles and what constituted a landmark achievement of the neuroantomy sub-school, as well as that of the NII school, was David Felten's "Noradrenergic and peptidergic innervation of lymphoid tissue." The paper solidified Karen Bulloch's earlier work and thus achieved greater acceptance. The Felten group firmly established an anatomical connection between the immune and nervous systems.[44] Also in the same issue was a paper by Candace Pert, "Neuropeptides and their receptors: a psychosomatic network," in which her group "develop[ed] the concept that neuropeptides and their receptors form a network of information exchange which extends throughout the brain and body, including the immune system."[45] The paper furthered Jean-Michel Dayer's identification of interleukins in the brain, because they now had an identified target in the brain upon which to act.

The October 23, 1987 issue of *Science* convinced many skeptical neuroendocrinologists with its mechanistic evidence for neuroendocrine-immune communication. The research in all three papers, printed in succession, was made possible by the cloning of the interluekin-1 gene, first done by Charles Dinarello. By injecting pure, recombinant interluekin-1 into mice, researchers could measure the effects on the neuroendocrine system and establish a direct cause and effect relationship between the nervous and immune systems.[46,47,48] The three independent papers constituted an enormous landmark in the progression of NII. However, there were still many scientists, especially immunologists, who found these studies to be incomplete or unconvincing. This is evidenced by the small amount of attention given to NII in immunology textbooks up to the present. While immunologists were willing to accept that the immune system was integrated into the rest of the organism, they questioned the immunological importance of the communication. As immunologists argued, just because there is an interaction between the nervous and immune system, even if it produces statistically large variation in immune cell and antibody populations, does not necessarily mean the interaction is immunologically important. The immune system's flexibility, its overabundance of leukocytes and antibodies, allows for a drastic fall in immune cell number without effecting immune efficacy. The importance, however, lies in the combination of multiple inputs leading to compromised immunity and, ultimately, the difference between health and disease.

Other researchers, who did not author papers in either of the two above landmark issues but were of incredible scientific and political importance to the neuroendocrine sub-school, included Samuel McCann, Seymore Reichlin, Alan Munck, Esther Sternberg, Robert Dantzer, and Janice Kiecolt-Glaser. The first two men contributed to NII in both research and funding areas. Munck produced important work on the role of glucocorticoids, steroid substances released when we are under stress that have an anti-inflammatory role;[49,50] Sternberg established the biological and immunological



importance of the nervous immune connection;[51,52,53] Dantzer illuminated some of the mechanisms of sickness behavior[54] and Kiecolt-Glaser added legitimacy to PNI and the link between stress and repressed immune responses.[55,56] All of these experiments and discoveries, along with more persuasive research of the 1990s, legitimized the field of NII and allowed it to achieve paradigm status. Each study fed off the previous one, creating an exponentially growing body of research that gained viability with each passing year. New journals that contained research strictly from the sub-schools of NII started to appear and gain respect in the 1980s. Ader and Cohen started *Brain, Behavior, and Immunity* in 1987; *The Journal of Neuroimmunology* began circulation in 1981 and became a highly respected and cited journal; and in the winter of 1988, the first volume of *Progress in NeuroEndocrinImmunology*, which later switched names to *Neuroimmunomodulation* in 1999, debuted.

Paradigm Achieved

The revolutionary period of the 1970s and 80s finally led to NII's establishment as a new paradigm in the early 1990s. But this was only the beginning of paradigm status: it would take more research for the paradigm to eventually solidify in the late 1990s. The struggle to convince skeptics that the nervous and immune systems did communicate was not completely over; the extent, pathways, and importance of the interaction remained hotly debated. Some researchers, though fewer than in the 1980s, still questioned the existence of bi-directional communication between the nervous and immune systems. However, the communication between two organ systems, previously thought to be autonomous, was accepted by a majority of the biomedical community, leaving only details to be resolved.

One of the best indicators of NII's raise to paradigm status appears in the 1992 *Encyclopedia of Immunology* with the entry on "Neuroendocrine Regulation of Immunity."[58] This entry, along with the huge number of publications printed in prestigious journals such as *Science* and *The New England Journal of Medicine*, marked NII's into mainstream legitimate, paradigm-driven science. We also see recent immunology texts with references to modulation of the immune system, especially through the use of cytokines;[59] some texts even include small sections on the neuroendocrine modulation of immune function.[60] Although immunologists were the most skeptical about the integration of the immune system, their questioning faded to an eventual acceptance of communication between the nervous and immune systems.

Scientific Détente

As NII became paradigmatic, the subschools started to accept each other. The pressure for precedent faded, and internal differences made way for cooperation as each sub-school acknowledged the varying, yet complementary, pathways of communication between the immune and nervous systems. The science binding the two most complex parts of human beings attained ever-greater clarity from the early 1990s, and by the mid-1990s on the various sub-schools saw more similarities than dif-

ferences between their research. However, tensions still run high within the field, especially among pioneers, and NII remains the subject of criticism, although it no longer has to fight for survival.

In 1993, Seymour Reichlin published an article in the *New England Journal of Medicine* reviewing some of the important pathways of communication associated with NII. He identified research from most of the sub-schools and synthesized a broad overview of their contributions, though he did manage to identify Ader and Cohen's conditioning experiments as "neuroimmunomodulation."[61] His professional position and the article's publication in the *New England Journal of Medicine* gave credence to a template of cooperation and synthesis of varied research for NII that coincided with its rise to paradigm status.

"Dualism is dead"—Alan Leschner

Some researchers who started investigating areas within NII in the late 1980s and 1990s were able to move between subschools and in doing so consolidated the field. Chief among these was Esther Sternberg whose education and background in immunology made her research acceptable to the other subschools. Her book, *The Balance Within*, a personal account of her experiences with NII, included all of the sub-schools and adamantly emphasized that they all worked toward the same goal.

Younger researchers entered the field by the late 1990s and received training under an integrated rubric, one furthered by trainee grants issued by the National Institutes of Health. These students of the new paradigm are now learning within an integrative field and are being taught to conduct research in an integrative manner, thus allowing them to bring together not only the scientific aspects of NII but also aspects of all the sub-schools.

Yet the most convincing marks of détente are the scientific content and members of meetings, societies, and most importantly, journals like *Brain, Behavior, and Immunity* and *Neuroimmunomodulation*. The editorial boards of these two journals exemplify détente quite well. The editors of *Neuroimmunomodulation* are Samuel McCann and Jim Lipton. Robert Ader serves as the editor-in-chief of *Brain, Behavior, and Immunity*. The two journals, whose principle editors were among the leading figures of some of the sub-schools (Ader of PNI, McCann of neuroendocrinimmunology), have many common associate editors and editorial board members: Hugo Besedovsky, Robert Dantzer, Adrian Dunn, Kieth Kelly, Seymour Reichlin, Eric Smith, and Esther Sternberg, who serves as an associate editor for both journals.

Reports such as *NeuroImmunology and Mental Health*, put out by the National Institutes of Health in 1994 and edited by Ljubisa Vitkovic and Stephen Koslow also hint at the beginnings of integration of sub-schools. Some of the notable names previously mentioned were on the advisory panel: David Felten, Ronald Glaser, and Samuel McCann. More importantly, the subject matter of the report covered all of the sub-schools and contained references to work that came from across the board.[62]

By the late 1990s, the sub-schools were nearly completely brought together in a loose scientific détente. The NII paradigm was not at the time a rigid structure, but rather something people still debated. Its final position in medicine is still to be determined.

Conclusion

Scientific revolutions are long processes with neither clear beginnings nor endings but with distinguishable trends that let us mark their progression despite their fluid nature. They are a broad series of events with numerous inputs and ramifications, not only for the science involved, but also for society at large. The emergence of NII has changed our concept of disease and opened up new ways that we can use to preserve health. While NII has not completely matured into a fully developed field of science, there still remains controversy about its efficacy, and a textbook, which Kuhn suggests is the mark of a matured science, is not evident. There are many proto-textbooks, such as Bruce Rabin's *Stress, Immune Function, and Health*, but they are neither comprehensive nor fully integrative. There remains room for ever greater integration.

NII has blurred the duality of mind and body, showing us that they are indeed two parts of a whole that are entirely reliant on one another. If we expand on the findings of the past three decades and view them in totality, we can see that the state of the immune system effects our emotions and vice versa. This is not, in any way, to say that emotions and the stresses they cause lead to or cure disease, but that they are one aspect of health and illness and belong with the other inputs modern medicine considers when treating a patient. Emotions should be considered along with genetic predisposition to disease and the pathological basis of disease when a physician makes a diagnosis and prescribes therapies. NII, by providing the pathways and outcomes of neural-immune communication, allows us to seriously consideration the mental and social circumstances underlying the disease process. The body of research is, at this time, so large that it cannot and must not be ignored.

David Felten questioned our ignorance in the second edition of *Psychoneuroimmunology* and asked, "Can we afford to ignore the role of emotions, hope, the will to live, the power of human warmth and contact, just because they are difficult to investigate scientifically and our ignorance is so overwhelming?"[63] The research is certainly abundant and the ramifications of NII are now seen in policy decisions about healthcare and even in the medical school curriculum, although they still represent only the slightest inklings of influence.[64]

The mind and body, held in separate regard for centuries and therefore believed to be incompatible, have been integrated. Thus, the development of NII did much to integrate the incompatible by changing our conceptions of mind and body, nervous system and immune system, and the specialties and divisions within medicine. The recent entrance of NII into the biomedical milieu marks the beginning of change. Whether these changes will manifest themselves in any revolutionary manner outside the annals of science (or even outside NII) remains to be seen. □

This article is an abridged version of Sahand Boorboor's senior honors thesis, for which he received the Wilson Coates Award for the most outstanding senior honors thesis in history. Sahand received a B.A in history from the University in 2002. He is currently at the University of Cologne (Germany) studying German literature and the German healthcare system.

Organic Light Emitting Diodes

Developing Chemicals to Light the Future

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New platinum-group metal complexes have surprising potential for smaller, lighter, and more energy-efficient flat-panel displays.

The demand for flat, lightweight television and computer displays has given rise to many different flat-panel display technologies. Recently, much emphasis has been placed on organic light emitting diodes (OLEDs), chemical systems which have the potential to be not only smaller and lighter, but also more energy efficient than other current display technologies.[1] The most common form of television and computer displays now in use are cathode ray tubes, often referred to as CRTs. These devices accelerate electrons (cathode rays) through an electrical potential until they strike a certain area on a screen. Attached to this screen are phosphors (luminescent compounds) that emit a photon (or "particle") of light when the electron strikes it. The color contrast and resolution from a CRT is very good, but the device is bulky and thus impractical for portable and lightweight applications. The current technology used in portable televisions and lap top computers is liquid crystal displays (LCDs). These displays utilize liquid crystals, compounds that align in certain conformations when an electric potential is placed across them, to create an image on a screen. Aligning the crystals with electricity is very energy efficient, but LCDs require a great deal of energy to back-light the display in order to make the image visible. The high energy input required to back-light the display makes the LCD screen very inefficient, and consequently many portable devices that utilize this technology, like lap top computers, have short battery lives.

OLEDs make use of a phenomenon known as electroluminescence in which electronically excited materials emit light. An OLED consists of three basic layers of different chemical compounds sandwiched between an anode and a cathode (Fig. 1). When an electric current passes through the diode (from cathode to anode), electrons and holes (units of positive charge) travel through their respective transport layers until they recombine in the light-emitting layer. This process is called light-emitting charge recombination.[2] The light-emitting layer contains the electroluminescent material, which emits photons that produce the visible image on a screen. The materials that occupy the light-emitting layer of the OLED must luminesce a desired wavelength so that a full range of colors can be created on a display. These considerations

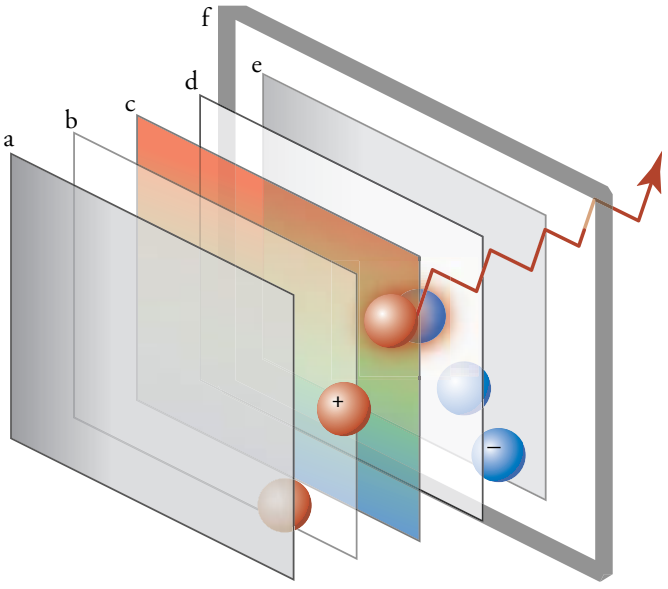


Figure 1. An OLED consists of three basic layers of different chemical compounds sandwhiched between an anode (a) and a cathode (e). When an eletronic current passes through the diode, electrons (blue spheres) and holes (units of positive chage, red spheres) travel through their respective transport layers (b, d) until they combine in the light-emitting layer (c). The OLED is fused to a glass plate (f), the front of the screen.

have prompted research chemists to examine new luminescent transition metal complexes with long-lived excited state and solid state luminescence, such as platinum group systems, as potential materials for OLEDs.

Platinum group metals are those elements located near platinum on the periodic table, such as iridium and gold. In compounds, these elements tend to adopt electronic configurations similar to that of platinum, which gives them similar chemical reactivity. Emission from these complexes generally involves transfer of an electron from an orbital on the metal to an orbital associated with the ligand (*i.e.*, the molecule bound to the metal). This type of electronic excitation is referred to as a metal-to-ligand charge transfer (MLCT). Ligands possessing low lying π^* orbitals, such as dithiolates and diimines, are usually involved in these types of transitions because the energy of their lowest unoccupied molecular orbital (LUMO) is comparable to that of the metal. The directionality of charge transfer in these systems is normally assigned as (metal)$d \rightarrow$ (ligand)π^*, although the nature of the highest occupied molecular orbital (HOMO) may not be entirely *d*-orbital (metal) in character.[3] Consequently, the energy of the MLCT excited state is sensitive to both the bonding character of the acceptor ligand and the electronic environment around the metal.

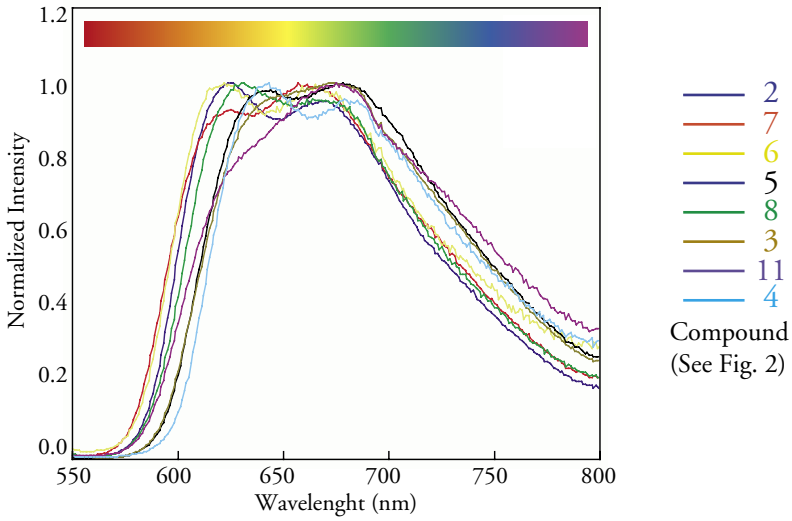


Figure 2. 298K solid state emission spectra of TBA[Ir(CO)(PR_3)mnt)] complexes.

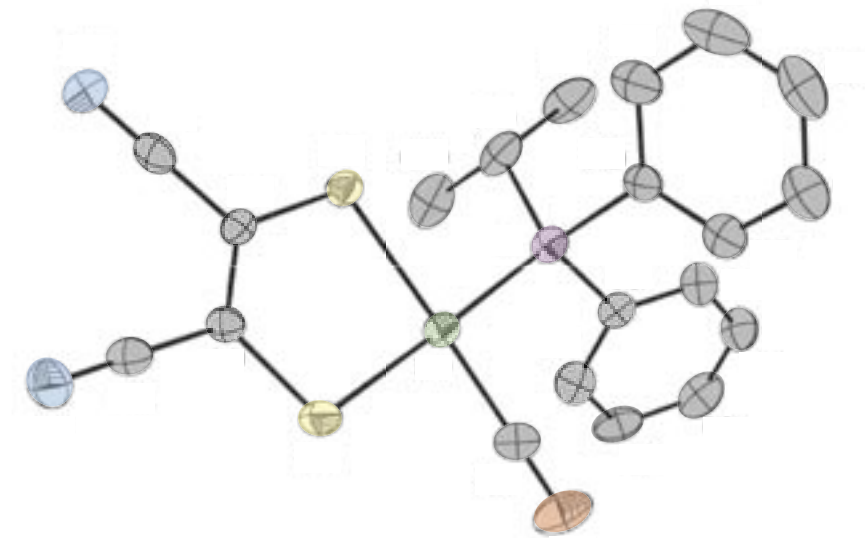


Figure 3. Crystal structure of compound 9, showing the square-planar geometry expected from iridium-mnt complexes. Black ellipses are Carbon, lavender is Phosphorous, yellow are Sulfur, blue are Nitrogens, and green is Iridium.

The ligands that surround the metal play a significant role in modifying the energy of the complex's excited state; it is the energy of the excited state that accounts for the color and intensity of the luminescence. The ability to tune this excited state by varying the types of ligands has produced many compounds with emission energies spanning the visible spectrum. Many of these compounds are already used to manufacture simple devices, and the number of OLEDs containing platinum group complexes continues to grow.[4]

From Ligands to Light

My work in the Eisenberg Group Laboratory at the University of Rochester has focused on the photochemistry of square planar platinum group complexes. Emission from these systems has been observed in both solution and the solid state. The solid state luminescence of iridium (I) dithiolate complexes has been particularly interesting from the standpoint of possible OLED materials. In complexes containing the *mnt* (maleonitriledithiolate) ligand, emission from this charge transfer gives rise to intense luminescence in the solid state and in frozen glass media. Previous reports of these systems involved complexes of the type $[Ir(CO)L(mnt)]^-$, where L (ligand) represents either CO (**1**) or PPh_3 (**2**) (Fig. 4).[3]

The focus of the present investigation was to prepare a series of iridium (I) dithiolate complexes with hopes of tuning the emission energy by varying the dithiolate and L-type ligand. Our research has been successful and we have characterized a series of new iridium dithiolate complexes and examined their emission energy. Systems involving dithiolates other than mnt were found to be non-emissive, while complexes of *mnt* containing different monodentate phosphine ligands were found to display intense solid state luminescence. The luminescence is tunable through approximately 25 nm in the red region of the electromagnetic spectrum, which is consis-

tent with the electron donating capacity of the phosphine ligand. These results are promising and suggest that mnt complexes may be a viable option in developing OLED technology.

Complex Luminescence

Our research examined 15 complexes that are similar in structure and composition to two previously reported iridium (I) dithiolate complexes (Fig. 4).[3] Compounds **1** and **2** had been reported previously and were used as a template for the synthesis of **3** - **11**. The new dithiolate complexes, *tdt*, *ecda*, and *dmit* (**12** - **17**) were prepared in similar fashion to compound **1** with slight variations.

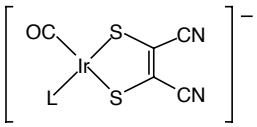
Compounds **3** - **11** exhibit solid state luminescence similar to complex **1**. However, the other dithiolate complexes failed to show any luminescent properties in the solid state, which may be attributed to the energy of the π* orbitals in these complexes. The mnt ligand appears to be the most electron-withdrawing of the dithiolate ligands studied. Consequently, its π* orbitals are closer in energy to the metal *d*-orbitals than the other dithiolates. The stretching frequency of the carbonyl bonds (CO) in the $[Ir(CO)_2(mnt)]^-$ complex vibrate at higher a frequency than the corresponding bonds in compounds **12**, **14**, and **16**, indicating that there is substantially less electron donation from the metal. Such a situation arises when the metal is made more electron deficient by means of an electron-withdrawing ligand (in this case, the mnt ligand). With the other dithiolates, the electron-withdrawing character is less, and the energy of the π* orbital may be elevated to such an extent that the highest energy metal orbital ($d_{x^2-y^2}$) of the iridium falls below that of the dithiolate. In this situation, the MLCT transition may not be observed to the same extent as in the mnt complexes, and weakly emissive ligand field transitions (transitions between metal orbitals) may dominate.

We hypothesized that the electronic character of the phosphine ligand would partially determine the electron density surrounding the iridium center for compounds **3**-**11**. By varying the phosphine R-groups (R = Me, Ph, tolyl, *etc.*), the energy of the metal-based HOMO could be changed in such a way as to produce a series of luminescent compounds with predictable emission energies, and therefore predictable colors. Results from room temperature emission measurements in the solid state indicate that the emission energies of the complexes are, to some degree, controllable. Emission maxima for the compounds encompass a range of 25 nm, which corresponds to an energy difference of approximately 500 cm^{-1} (approximately 6 kJ/mol) (Fig. 2). The reddest emissions come from the compounds containing aliphatic phosphine ligands, (**3**,**4** and **5**) as expected from a simple assessment of the electron-donating capacity of each phosphine ligand. Aliphatic phosphines are better able to donate electrons to the metal orbitals and increase the energy of the HOMO (d_{xy}), which causes a red-shifted (lower energy) emission. In contrast to aliphatic phosphines, the aromatic phosphines are less efficient electron donors and tend to decrease the relative energy of the HOMO leading to a slightly more blue-shifted (higher energy) emission (Table 1).

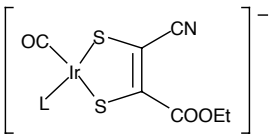
All of the $[Ir(CO)(PR_3)(mnt)]^-$ compounds (**3** - **11**) synthesized are yellow or yellow-orange powders. A crystal structure of compound **9** was elucidated, which showed the expected square planar geometry (Fig. 3). The compounds appear stable in the solid state for months if kept in a sealed vial. However, the complexes begin to turn orange after extended exposure to air, which is probably due to oxidation of the phosphine part of the complex. The compounds decompose rapidly in solution, changing color from yellow to deep orange in a matter of minutes. Although this decomposition might appear problematic, the mnt compounds do not exhibit any luminescence when in solution, so their chemical instability does not pose any serious problems to their potential industrial application.

Iridium-mnt Complexes

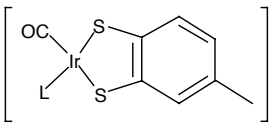
L =**1** CO
2 PPh_3
3 PBn_3
4 PMe_3
5 PCy_3
6 $P(p\text{-tolyl})_3$
7 $PPh_2(p\text{-tolyl})$
8 PPh_2(2-pyridyl)
9 PPh_2(i-propyl)
10 $P(p\text{-}C_6H_4F)_3$
11 $P(p\text{-}C_6H_4Cl)_3$



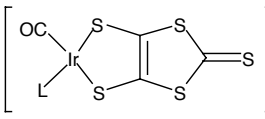
Iridium-dithiolate Complexes



L =**12** CO
13 PPh_3



L =**14** CO
15 PPh_3



L =**16** CO
17 PPh_3

Figure 4. Light emitting complexes synthesized and examined for this study.

Conclusion

We have synthesized thin films of these compounds by preparing a solution of 90% dichloromethane, 9% polycarbonate, and 1% metal complex, and then applying this polymer to a glass slide. The films exhibit the characteristic luminescence of the solid compounds, which is encouraging because incorporating the metal complex into a polymer (doping) is one of the chief means toward industrial application. The doped polymer films can be coated onto a glass surface to create a device that contains an evenly distributed amount of the luminescent material.

The results presented here demonstrate that luminescent compounds with predictable excited state energies can be produced successfully. Bolstered by this knowledge, chemists can produce more highly emissive and thermally stable compounds with the properties necessary for complete display manufacture. With new compounds such as these iridium complexes, the OLED industry can press forward and create the displays that will light the future. □

Zachary Tonzetich graduated from the University of Rochester in 2002 with a B.S. in Chemistry. His work on luminescent transition metal complexes for OLED applications was part of his senior thesis work under Professor Richard Eisenberg. He is a National Science Foundation predoctoral fellow currently working toward his Ph.D. in inorganic chemistry at the Massachusetts Institute of Technology.

Explanations Matter

The Interplay Between Family Instability, Parental Communication Patterns, and Preschool Children's Family Representations

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Department of Clinical and Social Psychology

Positive and informed explanations by parents to their children may buffer children from the ill-effects of family instability.

Family instability, as a state of chronic chaos and unpredictability, is an accumulation of family events that challenge the continuity and cohesiveness of a child's daily life and environment.[1] It is one factor that can lead to an increased risk of child maladjustment.[1,2] Even within the context of other family variables, such as conflict, the way in which caregivers express their emotions and parenting, family instability uniquely contributes to children's wellness. Thus, it may be a threat not only to children's perception of security in the family[3] but also to their own sense of control over their environment.[1]

Previous research indicates that the relationship between adversity and child wellness needs more investigation: studies of family instability have typically focused on outcomes such as symptoms (*e.g.*, depression) and behavioral traits (*e.g.*, aggression). Consequently, research psychologists know little about how family instability affects children's functioning at a process level of interpreting and coping with family adversity. Ackerman and his colleagues[1] defined family instability and isolated some risk factors that challenge a family's ability to provide a stable environment for its child; residential moves, changing intimate adult relationships that involve a primary caregiver, serious childhood illnesses, changing families with whom the child lives, and other recent negative life events (*e.g.*, death of family member, job change) are all specific indicators of instability that may create adjustment problems for children when they grow older. Furthermore, Ackerman *et al.* indicated that these risk factors predicted adjustment problems even after controlling for variables such as family conflict and caregiver emotionality.

These results attest to the importance of studying instability, for it is a risk factor that can predict an array of negative outcomes for children. These past studies, however, have focused on outcomes such as symptoms and have not addressed how instability affects children's coping processes and interpretations. Therefore, this study focused on the influence instability had on the development of children's internal working models (Fig. 1a).

The typically modest to moderate associations between family characteristics and children's adjustment suggest that potential moderating factors are important; few studies, however, have considered aspects of family life that may exacerbate or ameliorate the effects of family instability. Hence, the second goal of this study was to examine how parental communication patterns with their children may potentially moderate the relationship between instability and children's internal representations of their families (Fig.1b).

> The quality of a parent's explanation strongly influences his or her child's perception of the family.

Family instability embodies events that are pervasive and/or occur repeatedly over a child's lifetime. It also depicts a chaotic and unpredictable environment that often results in stress for the child.[1] Disruptive family events and challenges, such as divorce, can increase a child's vulnerability to a wide range of psychological problems. Links between any single disruptive family event and a child's adjustment, however, tend to be more suggestive than conclusive. Therefore, psychologists need new conceptualizations of family instability that address children's cumulative exposure to multiple disruptive family events. These models should more adequately and realistically represent the difficulties families face when creating a cohesive, predictable, and safe environment for their children.

Internal Working Models and Communication Patterns

Internal working models (IWMs) can index how children perceive and cope with life events. Early experiences with caregivers contribute to children's development of sets of social expectations, which then become their IWMs.[4] Children use IWMs as 'social lenses,' or mental rules, that provide information and structure to events in their environment. These social expectations guide a their information processing (*e.g.*, their emotions, behaviors, beliefs). IWMs serve as both a framework for future interactions and children's perception of others and the self.[5-10] IWMs become more stable with time, and children begin to use them outside of their families, such as in peer groups, school, and the surrounding community.[10]

Parents who provide explanations that promote strong family security recognized concern for their child. Such explanations emphasized that parents would ensure their childs' safety, support, and protection.

Since the caregiving environment has been associated with children's IWMs, and family stability can be conceptualized as part of the caregiving environment,[9-11] we predicted that greater stress (as indexed by more frequent unstable life events) would relate to more negative and destructive IWMs.

In addition to considering children's IWMs as indices for functioning, this study is also unique in that we tried to account for some of the heterogeneity that is usually made evident in children's outcomes, such as their behavior. Research suggests that even under severely adverse social conditions some children adapt and adjust to meet and overcome their personal challenges.[12] Sandler and Block[13] found that social circumstances may affect the relationship between children's instability and their poor behavior. Many psychologists are now interested in identifying the factors that may promote more positive and effective IWMs.

Protective factors, embodying environmental characteristics and events in addition to individual attributes, are not as strongly associated with negative outcomes in children as some psychologists predicted.[14] Therefore, protective factors like family warmth and emotional support,[14] children's temperamental adaptability,[1] competent parenting involving nurturing involvement and consistent disciplinary practices,[15] responsive parenting,[16] and children's competence level,[17] may weaken the effects of risk factors on children's symptoms. Wyman *et al.*[15] propose that research psychologists must look beyond children's characteristics and extend their inquiry to family contexts and relationships; they argue that parent-child interactions give children the ability to learn and internalize attributes associated with positive adaptation and coping. In this study, we wanted to examine how explicit parental communication patterns related to family instability and children's internal working models.

Researchers have postulated that communication patterns may moderate children's reactions to dimensions of the caregiving environment. For example, Cummings, Simpson, and Wilson[18] found that children showed less negative reactions to conflict among adults when these arguments were followed by explanations and rationalizations. Children's reactions to discipline also tend to vary as a function of the quality of explanations that parents offer during disciplinary interactions.[19]

Furthermore, researchers concerned with emotion expression have found that parents' discussion of emotion-related behaviors can predict children's social competence,[20] altruism, peer functioning, understanding of emotion,[21] and social-emotional development.[22] These findings indicate that parental communication is important to not only children's reactions and symptoms but also their emotional responses to conflict and discipline. Moreover, these results indicate that specific parent-child communication patterns directly related to the discussed issues might be important factors in children's development.

Although most developmental psychology research has overlooked how parental communication patterns affect children's reactions to family instability, Bretherton[6] found that children's ability to form coherent representations of family relationships is supported by emotionally open and sensitive parent-child communication. Nancy Eisenberg[23] found that when parents talk to their children about emotions and why specific emotions are expressed at certain times, children are generally well behaved and more socially adapted. Although Eisenberg *et al.* demonstrated that communication patterns are significant to children's social adjustment, developmental psychologists still know little about how they function as a protective factors against family instability. Parents may protect their children from the effects of family instability by providing explanations, but no previous research has addressed this issue. We predicted that good communication between parents and their children would ease the ill effects of family instability on children.

The FEQ and Story Stems

This study is part of a larger one at the University of Rochester that is investigating characteristics that may affect children's internal working models. Thirty-eight preschool age children (16 girls and 22 boys, with a mean age of 4.5 years) and their primary caregiver or parent, who was often female, were interviewed as part of this study. Seventy-nine percent of the families were Caucasian, 18% were African-American, and the remaining 3% were of other ethnicity. We recruited families from 3 separate pre-school agencies in urban Rochester, NY. Preschool children, unlike older primary school children, interact mostly with their primary caregivers.

We interviewed parents by telephone at a time of their choosing and asked them to describe their demographic backgrounds and family communication patterns and to fill out a questionnaire. The questionnaire, the Family Event Questionnaire (FEQ), was a self-report questionnaire adapted from two previous forms developed by University of Rochester researchers, one by Evan Forman and Patrick Davies[24] and the other by William Work and his colleagues.[25] Interviewers asked parents to describe the preceding three years of her or his child's life in an attempt to measure cumulative life events. Studies show that maladaptive events in a child's life can accumulate and have more significant effects on the child's adjustment than recent and singular life stressors.[27] The questionnaire included questions about 19 specific events that we consider unstable, threatening, or disruptive. Fourteen of the questionnaire's 19 items addressed the number of instances the parent and child had experienced each unstable event. For example, how many times had a close family member lost a job or been unemployed; or, had an adult in the home and a romantic partner separated? The remaining 5 items assessed problems that tended to be more pervasive, like drug or alcohol abuse. For these questions, the parent indicated if each situation occurred within the past three years. These data became a measure of overall family instability.

In addition to those on the FEQ, parents provided answers to questions that would illuminate communication patterns among adults and between adults and children. Interviewers presented hypothetical vignettes

that described events indicative of instability within the family. These events included: (1) a parent or caregiver losing a job that is important to the family's financial security; (2) adult relationship troubles; (3) the death of a close family member; (4) a residential change; (5) and a serious drug or alcohol problem within the family. Interviewers read each vignette to the caregiver and then asked whether or not she would say anything to her child, and if so, what she would say. Their responses were written down verbatim. Since the purpose of these interviews was to examine the explicit messages children receive, interviewers prompted parents for direct quotes if necessary ("What would you actually say to your child? For example, if I was your child, what would you say to me?").

This study relied on a common technique called coding to quantify the data collected and make them accessible. With coding, data reviewers assign a numerical value to different types of responses to a given question or prompt. Coding allows researchers to look for trends in and correlations between data and variables. In this study, multiple researchers coded each interview and statistical tests for variance between reviewers indicated that coding scores were consistent and reliable.

Parents' narratives were coded separately along five-point continuous scales for each hypothetical vignette and then summed across all vignettes to illuminate trends in relational harmony and overall security. Relational harmony ranged from very discordant (low scores) to very harmonious (high scores) and was designed to highlight the ways in which parents' explanations represented the social world and interpersonal relationships.[28]. Higher ratings reflected more harmonious and positive interpersonal relationships that portrayed positive, caring, and loving relationships (*e.g.*, concern for others). Conversely, lower ratings portrayed relationships as threatening, dangerous, chaotic, or all three, in which parents placed little value on the well-being of others.

Coding for overall security ranged from strong insecurity (low scores) to strong security (high scores).[28] Explanations were coded based on the degree to which they reduced the proposed threat while promoting a sense of security from the child's perspective. Parents who provided explanations that promoted strong security recognized concern for their child. Such explanations emphasized that the parent would ensure her child's safety, support, and protection within the family. Explanations with low scores, however, indicated that family members could not provide physical and psychological safety, support, and protection for their children. Conversational attributes that could influence children's understanding, such as brevity and complexity, were also considered in coding the explanation.

Children were interviewed in their preschools in an area separate from other children to minimize their distractions and so that we could videotape the interview. Interviewers used story stems to elicit children's narratives about unstable family events from which we could measure children's IWMs. Story stems elicit children's attitudes, feelings,[29] and developmental understanding of family representations by creating a contextualized narrative that he or she must complete.[30] Some studies have found linkages between the way pre-school children play and how parents and teachers report problem behaviors.[30] These studies suggest that researchers can garner additional information about children from less structured assessments like story stems.

We used two story stems that were based on the MacArthur Story Stem Battery paradigm (MSSB).[31] The first story stem was adapted from Bretherton *et al.*, while the second was created for this study. Brotherton's story stem involved an adult argument about lost car keys. Our story stem concerned a lost job resulting in financial trouble. Each story stem depicted two adult dolls (one male and the other female, both of an ethnicity similar to the child's) engaged in a discussion that indicated family instability, while a child doll (of the same gender and ethnicity as the participating child) looked on. The interviewer presented each story stem to the child and then asked him or her to complete the story using the dolls. The interviewer also asked the child to demonstrate what would happen the next time the characters (dolls) interacted. We added this additional prompt because we wanted to examine how children's expectations corresponded to the amount of instability in their home lives. Children's verbal narratives, along with their physical manipulation of the dolls, are meant to represent their IWMs.[29,30,32]

Children's interpersonal discord and overall felt security were assessed using five-point continuous coding scales similar to those used for the adult interviews. For interpersonal discord, higher scores indicated intense strife characterized by multiple threats to a person's well-being or survival (*e.g.*, physical aggression, death, profound physical or emotional injury). Lower scores reflected benign interactions free from any discord. Overall felt security captured the holistic quality and patterns of security within relationships as described by the children;[3] it considered how children viewed themselves in the context of family relationships in regard to both short- and long-term feelings of safety and security. We also accounted for the cohesiveness of each child's story: higher scores (strong security) depicted predictable, cohesive, and

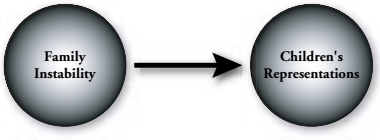

Figure 1a. Family stability can be conceptualized as an important part of the caregiving environment parents create for their children. Therefore, a disruptive and unstable caregiving environment (indexed by family instability) may produce negative and destructive family representations (indexed by internal working models).

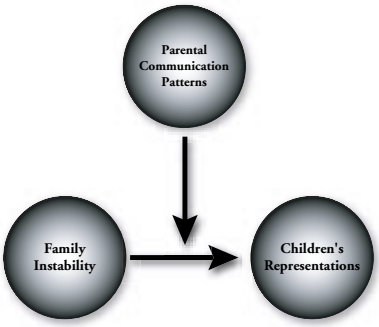

Figure 1b. One purpose of this study was to examine how parental communication patterns with their children moderated the relationship between family instability and how children mentally represented their families.

understandable relationships. In these situations, children represented adults as able and willing to effectively manage stressful events while simultaneously supporting and comforting them. Lower scores (strong insecurity) indicated that children considered adults to be unpredictable, dangerous, or ineffective at solving problems. Children whose responses were coded low presented few, if any, positive descriptions of adults.

Interpreting the Data

Family instability appears to be associated with children's internal representations of their families. Children feel less secure about their families when their parents do not effectively explain both the causes of an argument and that they are not responsible for the argument. While negative representations of family life may be detrimental to children's long-term psychological adjustment, these representations may have some short-term adaptive value. They may function as a cognitive warning signal for children and prepare children to adapt and protect themselves when faced with a potentially threatening event. Our findings demonstrate the value of addressing children's functioning at a process level (*i.e.*, how children process information that contributes to their IWMs) and not at an outcome level.

Since some children who are exposed to family instability still develop adaptively, we examined whether associations between family instability and children's internal representations may depend, in part, on the quality of explanations parents provide to their children about the meaning of unstable family events. The data from this study partially supports this proposed moderator model. Our hypothesis predicted and our results suggest that family instability led to greater discord and less security in family representations only when parental explanations depicted family life as disruptive. In other words, when parents in unstable families portrayed relationships as threatening, dangerous, or chaotic in their explanations of family events, children represented simulated family events (*i.e.*, story stems) as hostile and insecure. This suggests that the quality of a parent's explanation strongly influences his or her child's perception of the family.

When characteristics of family cohesiveness and harmony were emphasized in parent's explanations, greater family instability was a predictor for less discord and more security in children's internal representations of the family. This finding is consistent with Garmezy, Masten, and Tellegen's[17] "challenge model," in which stressful events are conceptualized as fostering children's understanding, appraisal, and coping with subsequent stressors if they occur in manageable and mild doses. If we extend this model to incorporate our results, we can infer that explanations that emphasize positive attributes of interpersonal context may help reduce children's stress associated with unstable family events to manageable doses.

There are several limitations to these conclusions that warrant discussion. First, the small sample size limited the statistical power of our findings and our ability to generalize them beyond our sample population of children. Even with a small sample size, however, the magnitude of the moderating effects was relatively large. Second, the measure used to index family instability contained diverse dimensions of instability (*e.g.*, change of primary caregiver, placement in foster care, move to a new residence). Different aspects of family instability may have varying effects on children, some of which may be especially potent while others may be benign. Our conceptualization of family instability is nonetheless consistent with earlier research that focused on this issue. Ackerman *et al.*[1] argued that an accumulation of experiences, and not simply a specific event within the family, indicates if a family is able to provide a predictable and cohesive environment for its child. This accumulation of events is a more robust predictor for a child's psychological wellness than any single experience. Third, parents' explanations were not measured directly within a natural context, their homes; we created hypothetical situations to create a similar environment. Thus, some researchers may question the ecological validity of this measure. The hypothetical situations, however, were designed to activate similar psychological processes (*i.e.*, explanations) that probably occur in common family contexts while also controlling for variation in explanations that may emerge from experiences with different types of family instability.

Despite these limitations, this study extends earlier research by addressing the influence of family instability at children's processing level while simultaneously accounting for some of the heterogeneity in children's outcomes. Family instability is a significant proxy for children's internal representations of their families. The findings discussed in this paper emphasize that researchers should consider children's mental processing of family events and life experiences, for it appears to have a noticeable affect on how children process family events and life experiences. Future studies should examine how children may mediate between their personal adjustment and family's instability as portrayed in their family representations. Moreover, future research should look for specific aspects of instability that are most influential to children's processing and adjustment. Parental communication patterns partially moderate the relationship between family instability and children's internal representations of family, indicating that future efforts should consider aspects of the family that may exacerbate or ameliorate the effects of family instability. □

> Negative representations of family life may function as a cognitive warning signal for children and prepare them to adapt and protect themselves.

This article is a summary of Sara Meyer's senior thesis, for which she received the 2002 Zimmer Award for Research in Psychology from the Department of Clinical and Social Psychology at the University of Rochester. Sara graduated from the University in 2002 with a B.A. Honors Degree in Psychology; she is currently working toward her Ph.D. in Developmental Psychology at the University of Nebraska, Lincoln.

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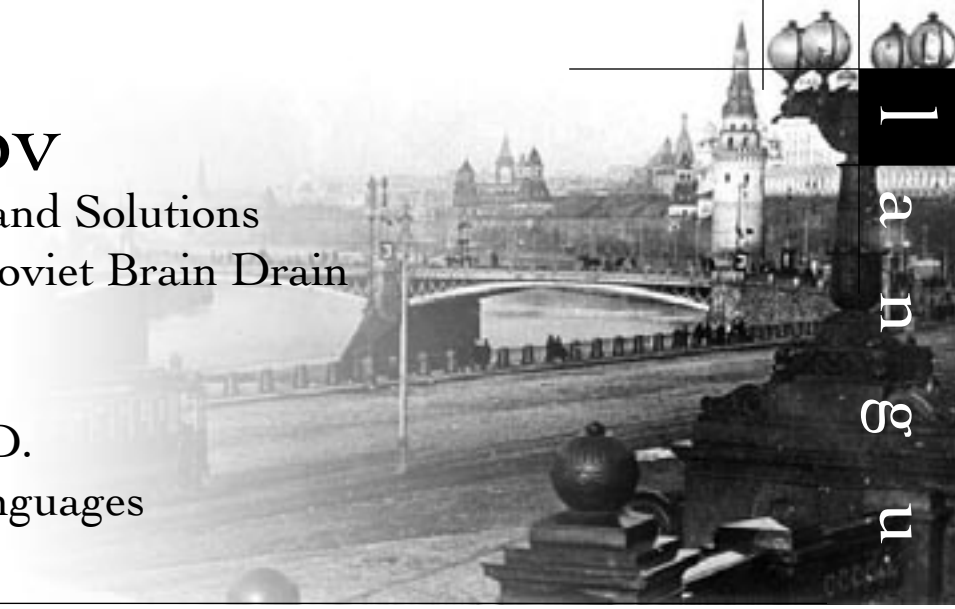
The History, Implications, and Solutions concerning Russia's Post–Soviet Brain Drain



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Department of Modern Languages

How serious are the economic, political, and social consequences of an exodus of intellectuals from Russia?

Russia's Post-Soviet brain drain is not a sociological process that lends itself to easy analysis. Brain drain has persisted in Russia since before the dissolution of the Soviet Union to the present, all-the-while on the backdrop of massive social and economic upheaval. Any treatment of Russia's ongoing brain drain must account for the prevalent political, economic, and social conditions in Russia. Following the dissolution of the Soviet Union, Russia has entered into a deep and prolonged economic depression spurred by the chaotic transition from a closed to free market economy. Although the consequences of this chaotic transition are well documented, they are, at best, only partially understood. Between 1989 and 1999, the Russian gross domestic product (GDP), a measurement of a nation's monetary value, contracted by 43%. The striking growth of 2000-2002 has only slightly offset this massive economic depression.[1] Statistics that measure the basic human welfare of a nation, such as longevity, infant-mortality, crime, and morbidity, have all dramatically changed for the worse. As Russia copes with these problems, the brain drain is sometimes disregarded as a trifling and inevitable consequence of the current economic and political instability afflicting the country. In truth, Russia's brain drain is closely interconnected with these economic and social problems: brain drain is both dependant on the prevailing economic and social conditions in a country and a factor in determining these same conditions.

Brain drain, broadly defined, is the permanent emigration of individuals with skills and knowledge of commercial, economic or strategic importance to a given country. There have been many instances of brain drain in the past century. Following both of the world wars, European intellectuals and scientists, like Goedel and Einstein, immigrated to the United States en masse, enriching America's research potential and transferring leadership in scholarship across the Atlantic. The current brain drain from the former Soviet Union is on the same scale and importance as earlier brain drains. It is also critically different, because it is driven by turmoil within Russia rather than by international upheaval.

The unique and turbulent historical conditions that accompany Russia's Post-Soviet brain drain preclude an easy comparison to other well-known and understood examples. Traditional brain drain analysis, which focuses on relative demands and wages for scientific personnel and relative national investments in human capital, have no relevance to contemporary Russia, where volatile currencies and chaotic accounting and record keeping makes a scientist's relative welfare difficult to determine. Additionally, the expertise of Russian scientists frequently does not neatly match Western categories, further compounding the comparison difficulties. Russia's current predicament with respect to the emigration of scientific personnel is unique and requires careful consideration before sound conclusions can be drawn.

Uncertainties about many aspects of the migration make studying it a complex and confusing process. Migration analysts only recently determined the exact size of the exodus due to poor record keeping in the past. Fundamental questions about the emigration, such as the demographic composition of the outflow, what industries and fields were most affected, and the primary motivations for emigration remained unanswered years after the main population movement. Thus, the best understood aspect of the Post-Soviet Russian brain drain is its cause, namely the economic and social havoc wrought by the disintegration of the Soviet Union, even if this is only partially understood.

The Motives for Migration

Russia's economic weakness is only half of the economic explanation. The fall of the Soviet Union coincided with a growing international trend toward economic globalization. The integration of markets, the destruction of state-imposed barriers to trade, and the movement of people have led to an especially competitive international labor-market for scientists and intellectuals. Nation-states competed for human-capital in science and technology, much as corporations have always competed for consumers and market niches. Western governments tried to attract talented international intellectuals with fellowships and joint ventures with foreign scientific institutions. In the midst of this hyper-competitive environment, Russia's incapacitated economy and government found themselves unprepared to face Western advances toward its scientific personnel.

Analysts, however, often focus too heavily on the economic stimulus to emigration while downplaying other important factors,

particularly in the former Soviet Union where there are abundant social and political forces also contributing to the phenomenon. The economic incentive to emigrate actually played a secondary role to other factors, such as ethnically motivated emigration, which tend to be especially widespread among intellectuals. Ethnic migrants, with their connections abroad, education, financial resources, and employability, often have the greatest means to emigrate. Therefore ethnic migration, and not just economic migration, has been and continues to be a major component of Russia's brain drain.

There was a noticeable rise in emigration from the Former Soviet Union during the late 80s and early 90s when restrictions on human mobility were gradually eased. Between 1986 and 1992, more than 600,000 people left Russia for at least temporary residency abroad.[2] This outflow coincided with a large contraction in Russia's scientific workforce: in the same period, 1.4 million workers (representing approximately 30% of Russia' scientific workforce) left domestic scientific institutions. Russian analysts naturally feared that many of these personnel had immigrated to competing nations. Even if aspects of this emigration were not well understood, such as its composition and magnitude, they were nonetheless conspicuous, and Russian brain drain became a heated topic of debate within the media and among politicians. Politicians and diplomats feared that scientific departments would become so small that they would be unable to reproduce the high-quality personnel who sustained them. Others feared that prospective new scientists would not inherit Russian technological expertise because talented faculty were leaving their teaching posts. Russian citizens, who had instilled in these scientists a great deal of national pride, were especially alarmed by the potential implications of brain drain. They feared that further advances in science could be rendered impossible in the future by lack of relevant and skilled personnel. A survey conducted in 1997 by the Russian Federation Center for Scientific Statistics (Tsentr isledovaniy i statistiki nauki) found that 51% of Russians believed that even temporary emigration abroad by scientists does harm to the nation's science, economy, and national security. 29% did not think brain drain was a concern and the remaining 20% were unable to answer. Thus, many Russians had unambiguously negative views toward the emigration of scientific personnel.

The West was also deeply concerned about the potential ramifications of Russia's brain drain. Many Western politicians worried that the formidable technological and military expertise accumulated by the Soviet Union would be transferred to unreliable and dangerous regimes. Indeed, this has happened, as there have been reports of Russian scientists with specialties in nuclear technology and aeronautics working for Iran and China. In one famous example from the early 90s, nearly 30 Russian scientists working on missile-design were arrested by Russian Federation police as they boarded a plane to North Korea. Each scientist allegedly had been offered $150,000 (USD) in compensation for functional ballistic missile technologies.[3] Thus, the relative ease with which dangerous technology could be bought from Russia forced Western nations to address Russia's Post-Soviet brain drain.

For Good or For Bad?

Since the early 90s when concern about brain drain was first raised, the debate about it dynamics and characteristics has followed several main lines. One debate centers on the dearth of reliable data and lack of knowledge about the true magnitude of the brain drain. But even in the most concrete cases, when evaluating the economic consequences resulting from brain drain, analysts must rely on elaborate cost-benefit systems and not on simplistic calculations that address average productivity for a given number of scientists. When a scientist emigrates, he or she often benefits the home economy in new ways: remittances, improved business and research connections abroad, and new business and political representation at the international level. Furthermore, many Russian scientists are only temporary migrants. Some of them return to their homeland, and in doing so they bring back not only foreign expertise and technology, but also the financial assets they accumulated while abroad. A minority of migration analysts have even argued that the benefits of Russia's Post-Soviet brain drain outweigh its costs. Such statements, however, are cursory and speculative; a thorough analysis of new and more detailed data would make them more conclusive. Analysts have made some progress in improving these data and the fruits of their efforts are outlined in this paper.

Politicians and academics disagree about the best method needed to resolve Russia's ongoing brain drain. Some nationalists see the core of the problem in labor's new mobility and therefore seek a return to closed borders and a state monopoly on research activity. Most economists, however, have accepted that Russia will inevitability reform its economy and become integrated into international markets. Thus, the Russian State, which currently has few resources at its disposal to tackle such issues, is in a predicament: how to stem academic decay? Western governments face a similar puzzle, since Russian brain drain poses many security risks that must be addressed and remedied. The Russian government has conducted several studies that address these risks, and Western countries have provided several aid programs designed to bolster Russian science. But in spite of these initiatives, there is still significant debate about how to stop or reverse this intellectual exodus.

Finally, Russia's experiences with brain drain are quite unique and unlike other historical migrations. Therefore, Russia's Post-Soviet brain drain may furnish valuable lessons for international migration studies and sociology in general. Russia's Post-Soviet brain drain raises interesting questions about the changing nature of Russian national identity as an ever larger proportion of ethnic Russians settle in the far-abroad, creating what is essentially a diaspora. Brain drain also raises questions about the rights of individuals versus the welfare of the state and society, for it offers a concrete example of the interests and freedoms of the individual that are not coincident with the interests of the government. Should a poorly compensated and unrecognized scientist continue to work in Russia, or should he emigrate to where his work would be more recognized and more widely received? The move may be prudent at the individual level, but may be counterproductive to national security and economic strength. Any proposal to solve the brain drain must account for this conflict of interests, as many plausible solutions tend to favor only one faction.

The Russian Scientific Workforce

Before any of these debates can be resolved or even tentative solutions to Russia's brain drain can be explored, policy makers must determine the real composition and

Above: Leading physicists Aleksei A. Abrikosov, Lev P. Gor'kov, and Anatolii I. Larkin left the Landau Institute in 1993.

magnitude of the brain drain as it has occurred since the dissolution of the Soviet Union. With the aid of modern data and analytical techniques, it is possible to address the question of whether Russia's Post-Soviet brain drain has been as cataclysmic as some first feared.

In the early 1990s, as the average yearly wage of Russian scientists plunged to the equivalent of 25 USD, many analysts in Russia and throughout the world feared an exodus of Russian scientific personnel. In 1992, the Ministry of Economy of the Russian Federation predicted that 200-250 thousand scientists would emigrate each year for permanent residency abroad, implying that by the year 2000, up to 1.5 million scientists would emigrate.[4] Presently, it is clear that this prediction, and many others like it, were grossly exaggerated.

A brief examination of the number of scientists on the Russian government's payroll provides a rudimentary understanding of why there was so much panic in the early 90s. Not only had the number of Russian scientists in national technical institutions fallen 30%, but also the wages of those personnel who remained within state research institutes by 1994 were only 75% of the average wages in the Russian Federation. In 1991, those wages were 116% of the national average. By comparison, scientists in the United States who hold doctoral degrees earn nearly twice the national US average salary.[5] As relative wages in Russian fell, so too did interest in scientific and research occupations. The number of doctoral degrees awarded by Russian schools fell steeply in 1991-1993, from approximately 17,000 to less than 13,000. This constitutes a 25% drop compared to previous numbers. The number of applications to doctoral programs has fallen by a similar percentage. Thus, there are far fewer qualified scientists in Russia than there are open research and teaching positions.[6] Given the sizable disproportion between the status and earnings of scientists in the West to scientists in the Russian Federation, it was natural for people to fear the worst and assume that a majority of Russian scientists were trying to emigrate. Analysts assumed that this outflow of skilled personnel would represent a major threat to national security, in terms of its effect on the Russian economy, national research potential, and military development.

These initial and alarming forecasts were false, and, in retrospect, we can see that they were based on several misconceptions, foremost among them that Russian scientists held skills that were in demand abroad. The single greatest shock to many analysts who forecasted extensive brain drain was the degree to which Western nations did not court Russian scientists, except for the very elite. Most Russian scientists were neither educated nor worked with the same rigor and in the same competitive atmosphere as their peers in Western nations. During the Soviet period, many institutions trained personnel and awarded them advanced degrees on the basis of quotas rather than on genuine marginal benefit. The Soviet Union felt pressured to produce as many scientific personnel and academics as the West, and in the process produced more personnel than the economy demanded. Many undeserving individuals received degrees and were then placed in work-environments in which no significant demands for research or creativity were placed on them. Hence, much of Russia's current scientific workforce has never faced the demands of a competitive workplace and has not developed the skills to act accordingly. Their poor academic flexibility made them liabilities to highly funded Western research institutions, and they were consequently unattractive career applicants on the international market

Early panic over the extent of brain drain was also based on the assumption that a large proportion of those leaving the state-science sector actually had active interest in working abroad. The results from surveys conducted in 1992 suggest that not more than 20% of scientific workers across multiple fields had any interest in working abroad. Many scientists were deterred from opportunities to emigrate or work temporarily abroad by difficulties of bringing their families with them. Cultural and linguistic barriers also discouraged many potential emigrants. A small minority of those who expressed interest in emigration actually had the ability to do so.[7] Lastly, many analysts falsely assumed that people who left the Russian state science sector, if not immediately emigrating, were at best adding to Russia's structurally unemployed, and by implication then becoming more likely to emigrate for economic reasons. In fact, people with higher education who left state science tended to be among Russia's most entrepreneurial people and were some

of the quickest to capitalize on the new opportunities provided by the decentralized economy. Very few of those who left state science actually moved into new scientific careers; rather they filled small gaps in the Russian economy left open by the former command economy. They became mechanics, shop-owners, repairmen, and technicians. The contraction in the number of scientific personnel downsized bloated and inefficient state research institutions. Thus, these career shifts may have been, in many circumstances, a positive influence on the Russian economy.

New Demographic Data

If the extent of Russia's post-Soviet brain drain is not as severe as some early forecasters projected, then the question remains, what is the real extent of the brain drain and what are its likely ramifications for Russia and the world? Although the extent of the Russian brain drain can be safely reduced to less than the estimated 1.5 million, it is difficult to determine its true magnitude due to a variety of complicating factors. Analysts can provide an accurate picture of this phenomenon only if they have detailed statistics concerning the population movement with respect to educational level and employment. Unfortunately, these statistics were not collected from Russian emigrants until 1994, when it became mandatory for them to fill out a questionnaire detailing their level of education and work-experience while in Russia. Before this policy change, researchers relied on surveys from various scientific institutions that detailed the status of their current and former employees. Such surveys were understandably inadequate, as few institutions had reliable data on the whereabouts or activities of those who had left the institutions. In 1992, RAND, a private organization which collects and analyzes sociological data, conducted its own survey of Russian scientists in an attempt to overcome the shortcomings of existent statistics and to create a realistic estimate of the size of future brain drain. The survey of 774 Russian scientists working in national aeronautics and nuclear research institutes asked these scientists to detail their future plans and proclivity to emigrate. The results tended to confirm alarmists' worst fears. Inferences based on these surveys suggest that nearly 20% of Russian mathematicians preferred to emigrate.[8] These numbers, however, only formed an upper bound for potential future emigration. Additional analysis showed that only a small fraction of those who voiced a strong interest to emigrate actually did so. The difficulty of finding adequate work abroad, separation from family, and linguistic and cultural adaptation discouraged the majority of those interested in emigrating. The study predicted that the likely rate of emigration would be in the range of 6-7% of Russia's scientific personnel.

Posterity has validated these RAND findings. The alarming predictions made by many in the government and media appear to be spurious. E. F. Nekipelova, a demographer with the Russian Federation Center for Research of Scientific Statistics, concluded that, by 1998, only 0.2% of Russia's workers occupied in science or research had actually emigrated for permanent residency abroad. The percentage is slightly higher if workers on temporary contracts abroad represent 6% of the Russian scientific labor population. Many workers who have temporary contracts become permanent emigrants; therefore, it is reasonable to place the true value between 1-3%. Furthermore, only 2% of emigrants who leave Russia have a background in Russia's science and research sector.[9] Ironically, a Russian emigrant working for RAND in the United States made the most accurate measurement of the scale of brain drain.

Brain drain is heavily drawn from only a few fields, foremost among them mathematics, but also physics, chemistry, and biology.

These early surveys were valuable not only because they were honest, but also, and more importantly, because they built a strong statistical picture of the average Russian scientific emigrant. The surveys tested for a correlation between the likelihood for emigration and the age, sex, field, location, family composition, and income of the potential emigrant. Age was the most strongly correlated variable. Young scientists were far more likely to emigrate than older scientists.[10] Official statistics from 1994 confirm that these findings are not an artifact of the study: by 1994, 45% of Russian researchers abroad were younger than 40 years, but only 33% of Russian researchers both at home and abroad conform to this age group.[11]

Men expressed a far greater interest in emigration than women did.[12] While there was a positive correlation with a person's academic and professional success, there was a surprisingly negative correlation with his income. Well-paid Russian scientists were less inclined to emigrate. This finding may support the "income-dispersion hypothesis," which posits that an employee is more concerned about his income relative to his national peers than his income relative to his international peers. Interviewees with obvious pro-Western political views were unsurprisingly more likely to emigrate.[13] These findings, combined with the relatively small scale of Russia's Post-Soviet brain drain, suggest that the greatest danger of Russia's ongoing brain drain is not its numerical magnitude, but its composition.

As young scientists move abroad in significant numbers, Russia may lose an entire generation of scientific and academic elites. Without young scientists to guide and educate the next generation of Russian researchers, Russia's current scientific and technical expertise may be preserved only in history books. Furthermore, most professionals are their most productive in their first years of work. Therefore, emigration of Russia's most youthful stratum of scientific personnel implies that the loss of productivity is more significant than just the number of emigrants. Russian policy makers are also very much concerned about the number of pro-Western emigrants. These citizens are crucial to Russia's future, because they are often the most supportive of national reforms that follow Western examples. Russia's potential to reform its economy, as well as its future relations with the West, depend on the strength of these Russians; their loss should alarm not only the West, but Russia as well.

The Threat to Academic Institutions

Survey statistics also suggest that brain drain represents a specific threat to certain academic and research institutions and to certain fields of research. Brain drain is heavily drawn from only a few fields, foremost among them mathematics, but also phys-

ics, chemistry, and biology. Russia and the former Soviet Union enjoyed international prestige in these areas, especially in physics and math. Scientists who share the collective prestige of their national science can easily find employment abroad. Knowledge can be a commodity, and like other goods and services, an ample supply is always welcomed when demand for it is high. The boom in biotechnology and nanotechnology has created a high demand for trained biologists, chemists, and physicists. Not surprisingly, these very categories of scientists are leaving Russia for the West.

Russia's brain drain from the mathematical field has been especially severe. Demand in the United States for academic posts in mathematics is currently heavily dependent on immigration from abroad, and the Former Soviet Union has become one of the prime suppliers. By some estimates, approximately 50% of America's demand for mathematicians in the past 20 years has been satisfied by immigrants from the Former Soviet Union.[14] According to official statistics from the Russian Academy of Sciences, approximately 15% of its members in the field of mathematics emigrated between 1991 and 1992; 10% of them were on temporary contracts and 5% emigrated permanently during the same time period. These values are glaringly disproportionate to the statistics for other fields; the average loss across disciplines is only around 3.5%.[15]

Unfortunately, these losses are taking place simultaneously to a contraction in the number of professionals created by the educational system. Between 1990 and 1993, the number of doctoral dissertations in the field of mathematics fell by more than one half.[16] The main reason for the current dereliction in Russian academic mathematics is an economic one: a mathematics professor cannot make a respectable living with the wages currently distributed by the dominant state university system. Foreign universities, however, are usually willing to accept distinguished foreign mathematics professors. Emigration has dissolved entire mathematics cadres in Russia. S. Novikov, the president of Moscow Mathematical Society, has indicated that at least half of Moscow's 200 leading mathematicians have permanently transferred abroad since the late 80s. Current mathematics students repeatedly indicate that their primary career goal is working at a foreign university. Meanwhile, Russia's best mathematical research has moved out of the state university system into new private universities, such as the "Independent (Nezavisimiy) Institute of Moscow" (IIM). Coincidentally, the IIM is largely funded by joint ventures with Western institutes.[17]

Physics has suffered a similar plight. The Russian Academy of Sciences estimates that almost 8% of its members in the areas of general and nuclear physics emigrated in the early 90s.[18] As with mathematics, the number of doctoral degrees has fallen sharply since 1990 by almost one half.[19] There are many examples where individual cadres of physicists and institutes have lost overwhelming amounts of human capital. For example, in 1986 the Landau Institute was established for the study of high-temperature super-conductors. But by 1993, all of the leading researchers at the institute, such as the widely published physicists Abrikosov, Gor'kov, and Larkin, had emigrated to the United States (Fig. 1). The institute is now essentially non-functional. In this particular example, the effect of foreign interest in promising research areas is especially apparent.

Ethnic Migration

It appears that the greatest forces compelling Russian scientists to emigrate are opportunities to earn more money and to advance their careers. One primary, and perhaps dominant, driving force behind emigration, however, is completely independent from Russia's economic and institutional conditions, namely factors stemming from ethnic tensions or the desire for national repatriation. Ethnic migration threatens to diminish a natural diversity of the Russian nation and alienate it from countries representing the origins of the various ethnic groups. Ethnic migration also represents a significant component of Russia's brain drain. Ethnic minorities in Russia account for a disproportionately large percentage of the nation's university graduates. Also, those citizens of the Russian Federation who belong to an ethnic minority group and are well-educated are more likely to have an opportunity for emigration. Their education will provide them with the intellectual resources and economic means to move abroad, while their ethnic status will likely provide them with contacts abroad to make the transition easier.

Evidence for the existence and magnitude of ethnic migration is found in several forms. In the early 90s, when reliable data about the composition of the emigration were generally scarce, the primary gauge for measuring ethnic migration was simply the destination of those travelling abroad. Since most ethnic migrants are not only fleeing perceived oppression based on their identity, but also seeking national repatriation, it follows that most ethnic migrants travel not just to the most economically convenient location, but also to the traditional homelands of their people. Thus, by determining ethnic migrants' final destinations and examining migrants' decisions which appear economically imprudent (i.e., those destinations which are unlikely to attract migrants who are motivated by purely financial concerns), analysts approximate the number of those who emigrate for ethnic reasons.

> Ethnic migrants often have the greatest means to emigrate.

There are three primary ethnic groups that constitute the majority of ethnically motivated brain drain in Russia, and someone not well-informed about the history of Russia's ethnic minorities may be surprised not only by these groups identities, but also by their relative weight in contributing to brain drain. The groups in question are ethnic Jews, Germans, and Greeks. A cursory glance at the relevant statistics gives a telling picture of the magnitude of ethnic migration: in the period 1987 to 1994, 86.7% of those emigrating for permanent residency abroad were travelling to only three countries: Germany (65.5%), Israel (11.3%), and Greece (9.9%).[20] More specific statistics, based on surveys conducted by the Russian Federation State Committee for Statistics (RFSCS), exist for the period of 1992-1993. The study asked emigrants to indicate their ethnic identity. More than 50% of the respondents identified themselves as ethnic Germans; 20% identified themselves as Jewish; and a scant 2% identified themselves as Greek. Only 20% identified themselves as ethnic Russians. These statistics are surprising for two reasons. First, they confirm that ethnic migration is the most dominant force driving Russian brain drain, especially during the early 90s. Second, these statistics cast new

light on the ethnic composition of Russia's migration of intellectuals. To people in the United States, where the status and plight of ethnic Jews in Russia receives attention from the media and politicians, it may be surprising that Jewish emigration accounts for about 20% of the total emigration in the Post-Soviet period.[21] These surveys suggest that ethnic Germans constitute the largest segment of Russia's academic decay.

Analysts, however, should be leery of any generalizations drawn from these data that do not first account for some important considerations. The predominance of ethnic minorities among emigrants in the early 90s does not necessarily imply that ethnic tension was the primary motivation for emigration in this period. Other factors, such as decreased assimilation costs and improved contacts abroad, may have made the decision to emigrate easier for these ethnic minorities. According to some surveys, 91% of emigrants cite economic factors for their primary reasons for leaving Russia. Only 8.5% of respondents indicated that ethnicity was their primary motive.[22] Secondly, the RFSCS data suggest that ethnic emigration was a significant factor only in the early 90s. The importance of ethnicity as a decisive factor for emigration has declined throughout the 1990s. Additionally, countries to which ethnic migrants move necessarily receive lower proportions of economic migrants, where the latter tend to be more educated and therefore qualify as factor in the brain drain. Therefore, ethnic migration is an important factor to brain drain, but those countries accounting for large proportions of ethnic migrants are not necessarily attracting the most intellectuals. It may be assumed that no one is migrating to the United States for purposes of national repatriation, but the composition of immigrants from the former Soviet Union to the United States is by far the most educated of all major flows of such migrants.

The future role of ethnicity in the migration choices of intellectuals in Russia largely depends on the policies of the various countries involved, namely Germany, Israel, Greece and Russia itself. The two largest migrant sinks, Germany and Israel, provide the greatest comparison and contrast in terms of migration policy. Israel has encouraged, and continues to encourage, Jews to emigrate from Russia and the Former Soviet Union to the Jewish state. There is, however, relatively little economic opportunity in Israel and little demand for Russian scientists, engineers, and academics. Unemployment rates among immigrants from the Former Soviet Union are incredibly high in Israel, yet Israel continues to encourage migration by providing generous subsidies and unemployment benefits to new Jewish residents. Germany has adopted a much different policy. The German government has worked with former Soviet governments to improve the quality of life for ethnic Germans abroad, thereby curbing migration to Germany. Considerable amounts of money have already been spent on such programs, and various agreements have been signed with states in the Commonwealth of Independent States (CIS) which are designed to restore political recognition to ethnic Germans. With the aid of the German government, nearly one million ethnic Germans currently settled in Kazakhstan have made plans to resettle in their former locations in Ukraine. Similar repatriation is taking place in the former German province of Kaliningrad. Demographers estimate that there are more than one-million ethnic Germans living in Russia who may migrate. It remains to be seen whether the moves taken by the German government will have any effect on stemming that potential population movement.[23]

Ethnic migration presents a special challenge to those who would reverse the brain drain, since a remedy can be neither a simple institutional restructuring nor the creation of new economic opportunities. To encourage ethnic migrants to return to Russia, historical grievances have to be addressed, security of minority interests have to be guaranteed, and bitterness for past conflict has to be assuaged. Unfortunately, the ethnic migration component of Russia's contemporary brain drain appears to be irreversible.

Irrespective of these issues, ethnic migration is being resolved without any active state policy from the Russian government. Sociological data suggest that ethnic migration, while still significant, is tapering off considerably from its levels in the early 90s. But even if the tumult of the early 90s has passed, it is nonetheless a major factor. Positive economic growth rates and a more stable democracy are giving Russian ethnic minorities greater hope for their future in Russia.

Concluding Remarks

The large-scale migration among Russian scientists has been restricted to alienated ethnic groups in Russia. Brain drain within these groups also appears to be the most hopeless form of brain drain, insofar as there are no means within the reach of the Russian authorities for reversing or stemming it. The one positive aspect of this specific type of brain drain is that, to a large extent, it seems to have run its course. Fewer emigrants are going to Israel and Germany now than in previous years; far greater proportions are now going to other West European countries and the United States.

It is also apparent that the brain drain is problematic because it is concentrated on certain groups, like young scientists and those with pro-Western views. But the greatest danger brain drain poses to Russia is its concentration on certain fields, such as mathematics and physics. Entire institutions and academic departments have fallen victim to drain brain.

Russia's experience with Post-Soviet brain drain can provide powerful lessons to the rest of the world. Post-Soviet Russian brain drain offers a compelling example of several important global phenomena. Both the labor-mobility that accompanies economic liberalization and the destruction of trade barriers has numerous complicated and ambiguous repercussions, all of which Russia is currently experiencing. This liberalization brings with it the potential (so far unrealized in Russia) for long-term economic growth; but it also evokes risks of weapons proliferation and short-term economic instability. Brain drain is also a symptom of the disintegration of national solidarity. In some respects, this is a global cultural phenomenon contemporaneous with globalization. Russia's experiences are perhaps the most extreme repercussions of brain drain, but many countries have had similar experiences. Further study of Russia's Post-Soviet transition and brain drain may lead to a greater understanding of how to cope with and prevent similar upheavals in the future. □

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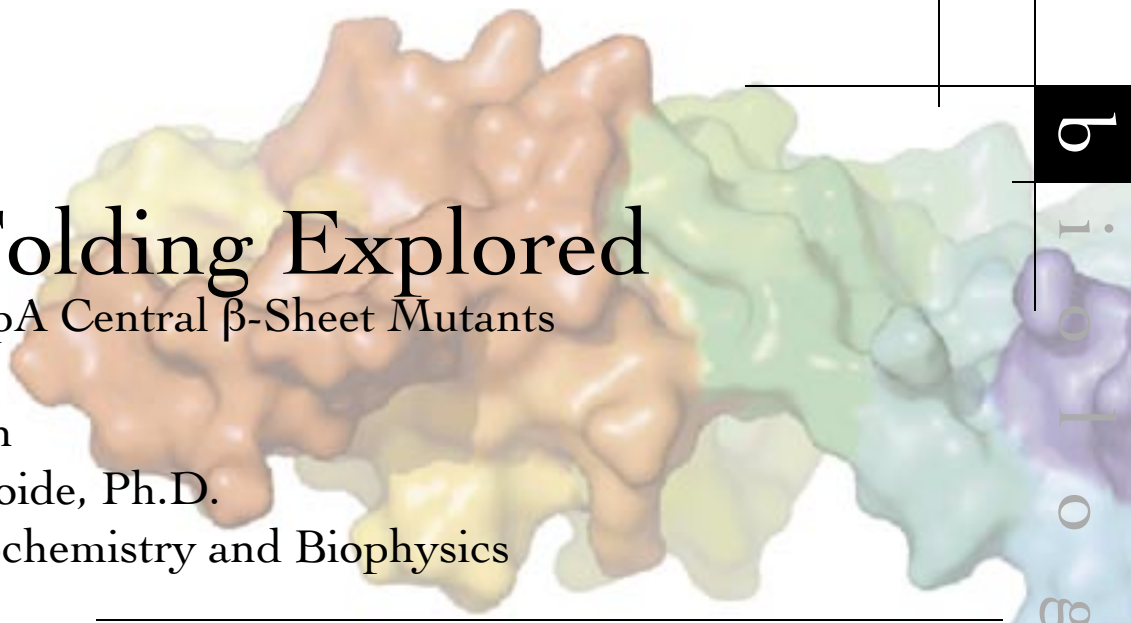

Protein Folding Explored

An Analysis of OspA Central β-Sheet Mutants

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A deeper understanding of the body's most essential molecules may be the key to a cure for many terminal illnesses.

Proteins are essential; their diverse functions range from carrying oxygen through the bloodstream to breaking down sugars for energy. Almost every process in the cell is controlled in some way by these complex molecules. It is clear that these large molecules are able to function because they have very specific three-dimensional shapes. For example, sucrase, the protein which breaks down the sugar sucrose into smaller components, has a shape which allows it to selectively bind to sucrose and no other molecule. Surprisingly, very little is known about how these molecules attain their shapes. Proteins are made within cells by the attachment of the 20 different amino acids together in different combinations as directed by the corresponding gene. Proteins can be hundreds of amino acids long and each one is composed of a unique sequence of amino acids. This string of amino acids, however, exists only transiently in the cell before quickly folding into a more compact three-dimensional shape. A Columbia University biologist, Cyrus Levinthal, showed that even for a small protein (*e.g.*, 40 amino acids), it would take about 10^{18} years to sample every possible structure in order to find the most stable configuration! This clearly cannot be what is happening, and this has come to be known as Levinthal's paradox. Much of the current research indicates that the folding process requires a transition through an intermediate state, which greatly limits the search for the final conformation. Also, it appears that this folding process is driven mainly by the fact that the folded state is considerably more energetically stable than the unfolded state. This is very significant because, if given a choice, molecules will always prefer to exist in the lowest possible energy state.

Looking at the properties of the individual amino acids gives great insight into the forces that are important to folding. For example, some are positively charged while others are negatively charged. Thus, these amino acids would be attracted to each other in a protein chain. Others are said to be hydrophobic and cannot be dissolved in water. Such amino acids tend to congregate together in the centers of proteins where they are sheltered from the polar environment created by water. Also, some amino acids favor certain types of bonding over others. The combination of all these forces contribute to the overall stability of the native (folded) state.

> ...Amyloid plaques may be a primary cause for diseases such as Alzheimer's and Mad Cow disease...

Two common structural motifs in folded proteins have been identified, α-helices and β-pleated sheets. These form due to intramolecular hydrogen bonding in the peptide backbone. Despite the tremendous progress that has been made to understand factors that influence α-helix formation and stability, there is still little known about the other major class of secondary structure, β-pleated sheets.

Understanding β-sheets is of special interest, as mutant forms seem to contribute to the onset of many neurodegenerative diseases. The problem results when the protein folds incorrectly. It appears, as a result of either mutation or intrinsic properties, that some proteins have a tendency to aggregate together and form undesirable structures called amyloids. The consequences of amyloidogenesis can be quite tragic. The formation of amyloid plaques may be a primary cause for diseases such as Alzheimer's, Mad Cow disease, and many other disabling illnesses. The buildup of these structures in brain cells can result in blocked communication between the cells as well as many other notable toxic effects. It is clear that β-sheets are responsible for inducing this aggregation.

In the past decade there has been an intense effort to make sense of these complex molecular problems. More effectively designed peptide drugs would be a critical step in bridging the worlds of research and medicine. It is incredible to imagine that in many cases a doctor might know molecular details of what has gone awry in a diseased patient, yet still be essentially helpless in terms of actual treatment. This is not to say that dramatic progess has not been made, but it is a sign that there is still much to accomplish. With the recent sequencing of the human genome, research will inevitably be more focused on the study of protein structure. The study I undertook investigates protein folding and demonstrates how some well established techniques can be used to research this problem.

Even though the specific protein looked at here is not directly involved in any neurological disease, it is very attractive from a research perspective because of the unique structural features it possesses. The hope in studying models such as this is that universal principles can be established which can eventually be applied to creating rationally designed drugs for the aforementioned diseases. Specifically, we used the Outer Surface Protein A (OspA) from the bacterium *Borrelia burgdorferi* to study the folding problem. This 31 kilodalton protein consists almost exclusively of β-pleated sheets. It has two globular domains, an amino (N-terminal domain) and a carboxyl (C-terminal domain) connected by a central three β-strand region (strands 8, 9, 10) (Figure 2). This central β-sheet is very unusual, as it lacks a large hydrophobic core and is exposed to the solvent on both faces. These features make the protein useful for examining interactions that contribute to its stability in the absence of an overwhelming hydrophobic core. The contributions of weaker forces are often difficult to measure in the presence of a dominating hydrophobic core. The OspA protein is the only protein known with these interesting properties. It has been previously reported that OspA fits a three-state model.[1] Evidence exists that in addition to the fully folded and fully unfolded states, there is a stable partially unfolded intermediate state that forms as well. This intermediate seems to play such a critical role in guiding the folding of OspA, that this *third state* is included in the general scheme. Specifically, the C-terminal domain seems to denature, or unfold, first, leaving part of the central β-sheet and the N-terminal domain structured in the intermediate. Thus, an equilibrium situation between the native, intermediate, and denatured states exists (Figure 1).

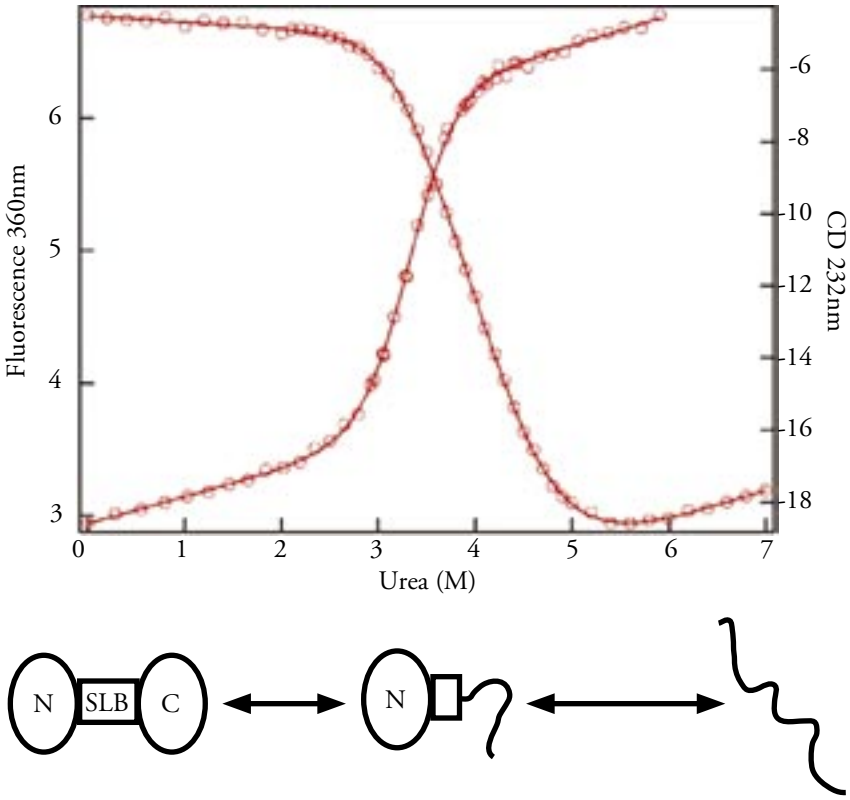

Figure 1. An example of typical denaturation curves. Both fluorescence and CD 232 signals are shown for this urea titration of wild-type OspA. The CD 232 signal corresponds to the curve with a decreasing signal as the [urea] increases. The cartoon representations show what the majority of the population of OspA looks like at different urea concentrations.

Previous Page. Surface WT OspA. N-term blue to C-term red; the central β-sheet (strands 8, 9, 10) shown in turquoise and green. Rendered in PyMol (www.pymol.org) from PDB 1OSP.

In order to gain more information about the central β-sheet, a series of mutant proteins were engineered. On the ninth strand of the central β-sheet (β-9), each amino acid was individually substituted with the amino acid alanine. Each mutant protein that was created had an alanine substitution at a different position on β-9. Alanine was an appropriate choice as it did not introduce any new interactions due to its simple nature. It simply removed the contributions of the original amino acid. Thus, by comparing the stability of wild-type (WT) OspA to each of the mutant OspA's, we could determine the contribution of each amino acid to the stability of the protein. For example, if we observed that a particular alanine mutant was less stable than the WT protein, then this would suggest that the amino acid which had been removed in the mutant was important for stabilizing the folded protein. If the stabilities of the WT and a particular mutant were about the same, then this would indicate that the original amino acid was not playing a significant stabilizing role.

We made a series of measurements for each of the eleven alanine mutants. The experiments that were performed took advantage of the fact that certain chemicals called denaturants will cause proteins to unravel from their native shapes. The higher the concentration of denaturant in a protein solution, the lower the concentration of folded proteins. Since secondary structure, such as β-sheets, can be detected by certain types of spectroscopy, the amount of folded protein can be detected at each new denaturant concentration. As the denaturant concentration increases, the signal will decrease because more proteins in the solution will lose their secondary structure.[2] More specifically, an increase in denaturant concentration causes a shift in the equilibrium constant, K, to the right. Since equilibrium is proportional to free energy [$\Delta G^\circ = -RT \ln K$], the free energy at each equilibrium position can be calculated. This simply means that by knowing how much of the protein in a solution is folded and unfolded at a particular

concentration of denaturant, the amount of energy it takes to unfold the protein can be calculated for that particular denaturant concentration. The amount of energy required to unfold a protein is a good measure of the protein's stability. When enough free energy values have been computed, the free energy of unfolding when no denaturant is present can be extrapolated.

These denaturations were performed twice for each mutant, and a denaturant called urea was used. The same theory explained above was applied to each run, but we used different types of spectroscopy to monitor the unfolding. The fluorescence-monitored denaturation took advantage of the fact that OspA contains a single Tryptophan amino acid at position 216 in the C-terminal. These titrations provided information about the local environment of the Trp216 residue, and thus about the unfolding of the C-terminal domain (Figure 1). This signal actually increases as more of the protein unravels as the tryptophan is free to fluoresce into the solution more. Also, far-UV (λ=232nm) monitored denaturation was performed for each mutant. This effectively allowed observation of global changes in the structure of OspA, as this signal is responsive to β-sheets.

Using *Igor Pro* software, the combination of fluorescence and far-UV data were fitted globally with a three-state model. Since there is an unavoidable error associated with extrapolated values, it was decided that the free energy value at 3M (denoted as ΔG^3) should be used instead (all ΔG^3 values have a std. dev. less than or equal to 0.1). The results using ΔG^3 are much more trustworthy than the extrapolated $\Delta G°$ values. Parameters in the curve fitting were added in order to make predictions about the intermediate. Free energy values for both transitions were also calculated for each mutant.

The results were very informative about not only the contributions of the individual residues to the stability of OspA, but also in providing evidence for what the structure of the intermediate might look like. The Phenylalanine126 and Asparagine127 replacements had the greatest destabilizing effects. This observation supports the importance of the hydrophobic effect and hydrogen bonding in protein stabilization. The Phenylalanine126 mutation greatly disrupted the small hydrophobic core that exists and as a result greatly destabilized both transitions. The small amount of hydrophobic amino acids that do exist play the most important role for stabilizing the central β-sheet. The Asparagine127 replacement also destabilized the protein. In the wild-type OspA, this residue's side chain is involved in three hydrogen bonds with other amino acids. The alanine mutation effectively removes these hydrogen bonds and the result is a significant destabilization of both transitions. Another interesting observation is that Lysine119, Glutamic acid128, and Lysine129 replacements behave almost identically to the wild-type. All of these residues play similar roles in the β-sheet; they are all amino acids involved in the connection of adjacent β-strands. Thus, residues at these turns seem to not contribute significantly to the stability of the β-sheet.

The transitions from the intermediate state to the unfolded state were affected by the alanine substitutions. This strongly suggests that β-9 is structured in the intermediate. If β-9 was already denatured in the intermediate, then further denaturation of the structured portion should not be affected by the alanine mutants. However, this does not appear to be the case. This is supported by the fact that the Glutamic acid123 mutant significantly destabilized the second transition but not the first transition. This indicates that β-9 is structured in the intermediate and β-10 is not. This makes sense if one realizes that on β-10 Glutamic acid123 is interacting with an isoleucine residue, which should not be greatly affected by the alanine replacement on β-9. This is consistent with the observation that the first transition is not greatly affected for the Glutamic acid123 mutant. However, Glutamic acid123 also forms a salt bridge with a lysine residue on β-8. Glutamic acid has a negatively charged side chain and lysine has a positively charged one. This interaction stabilizes the WT OspA. An alanine mutation eliminates this interaction and the destabilization is experimentally observed for the second transition. It should be noted that these results are in contrast with the data published in the Biochemistry paper cited earlier. The results from this previous study indicate that neither β-9 nor β-10 are structured in the intermediate. Thus, it seems that more experiments will have to be performed so that more definitive conclusions can be made. Determining the structure of the OspA through the use of a technique called NMR at a concentration of denaturant where the population of the intermediate is the greatest could provide a solid resolution to this debate.

These experiments demonstrate that hydrophobic shielding, hydrogen bonding and salt bridges all contribute significantly to the stabilization of the central β-sheet. It appears that the surface salt bridges contribute the least of these three interactions. A better idea of the overall electrostatic contribution could be obtained by performing these denaturation experiments at high salt concentrations. Most importantly, however, these experiments support the idea that β-9 is structured in the intermediate and β-10 is not. Thus, these experiments help to better quantify the contributions of various forces to the stability of β-sheets, and give some insight into the process of protein folding. If this process could be fully understood, proteins of any shape, and therefore any function could be designed. The potential for the drug industry and for biomedical science is truly astonishing. □

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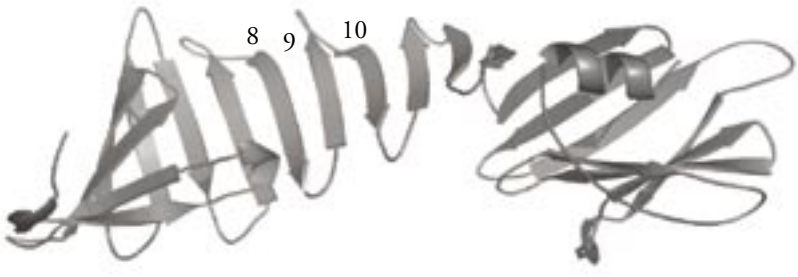

Figure 2. Cartoon of OspA. The two globular domains, an amino (N-terminal domain) and a carboxyl (C-terminal domain) connected by a central three b-strand region (strands 8, 9, and 10). Rendered in PyMol (www.pymol.org) from PDB 1OSP.