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Probing Conformational Preferences in Gas-Phase Chelated Peptide Complexes using Cryogenic Ion Vibrational Spectroscopy

By

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Chapter 1: WISL Chapter

1.0 A Note about the Author

I am something of a hobbyist. What I mean is, for as long as I can remember, I have gotten fixated on an interest – a sport, a craft, an activity – for a finite period of time before I moved on to the next thing. It started with sports. I did ballet, gymnastics, soccer, volleyball, cross-country, horseback riding, yoga. Over the years, it started to include hobbies. I have gardened; read; sewn and mended clothes; embroidered; knit; thrown pottery; made jewelry; written fiction and non-fiction; bound books; woven; painted watercolor. I've had a stint of violin-playing; I used to have a podcast! This is both a blessing and a curse: I have quite a few skills, and I have many more unfinished projects laying around my house. Sometimes I return to them after a year or so, sometimes I don't.

However, there are three interests which have endured the test of time – two I mentioned in the list above, and one yet unmentioned. Reading literature, writing, and chemistry. (Though maybe you already guessed the chemistry part – this chapter only exists in my chemistry dissertation, after all). While these started as discrete interests, they have merged in various combinations over time. I majored in Chemistry; I minored in English literature. The podcast was one I started in my first two years of college with a chemical engineering friend (before having podcasts was trending, mind you) because we wanted people to find chemical concepts just as fascinating as we did. That podcast was how I found the work of Professor Veronica Vaida, who I then did my undergraduate research with. Another member of my undergraduate thesis committee was Professor Rolf Norgaard, who taught *Writing on Science and Society*, a course focused on writing about science for general audiences that I adored. I started writing about the books I was reading and analyzing them after I graduated college, and then I started

writing about the Chemistry Education seminars and papers I was reading in graduate school. I would not be where I am today, or who I am, without these guiding lights. And now, I have the absolute pleasure of combining all three into this chapter for you.

Lastly, I would like to extend my acknowledgements to the Wisconsin Initiative for Science Literacy for this program. In my eyes, sharing scientific research is half of a positive feedback loop: seeing the spark in people's eyes when understanding hits is both rejuvenating and motivating. Long hours in the lab become worthwhile, and it compels me to continue learning so I can share new findings all over again. My thanks go out to Professor Bassam Shakhashiri and the editors, Elizabeth Reynolds and Cayce Osborne, for their help and clarity.

1.1 Literature and (Physical) Chemistry

You may be asking, literature and chemistry? First glance may lead you to believe that these two concepts are disparate, oil and water. I'm here to convince you that they're much more similar.

First, though, I must make a distinction. Chemistry, like literature, can be thought of as having different genres, with each "genre" interested in slightly different chemical "stories." If a mystery novel is a story about "who did it" and historical fiction is "what would this period of time have been like," then organic chemistry would be a story about "under what conditions does this chemical reaction happen" and analytical chemistry would be "which chemical method is best for observing this chemical phenomenon." Of course, these chemical genres are by no means definitive, but they instead serve as general guidelines for what kind of story to expect. A person who prefers science fiction to thrillers is the same as a chemist who prefers physical chemistry to organic chemistry. (I am this person.)

With that in mind, let's consider the original question: what's so similar about physical chemistry and literature? Both seek to answer the same two questions: why and how.

What is literature, or fiction, on a fundamental level? It's a story. Think *Beowulf*, *The Odyssey*, *The Lord of the Rings*, *The Wizard of Oz*. There are many different types of story structures used in fiction, but the most general case works well enough here.

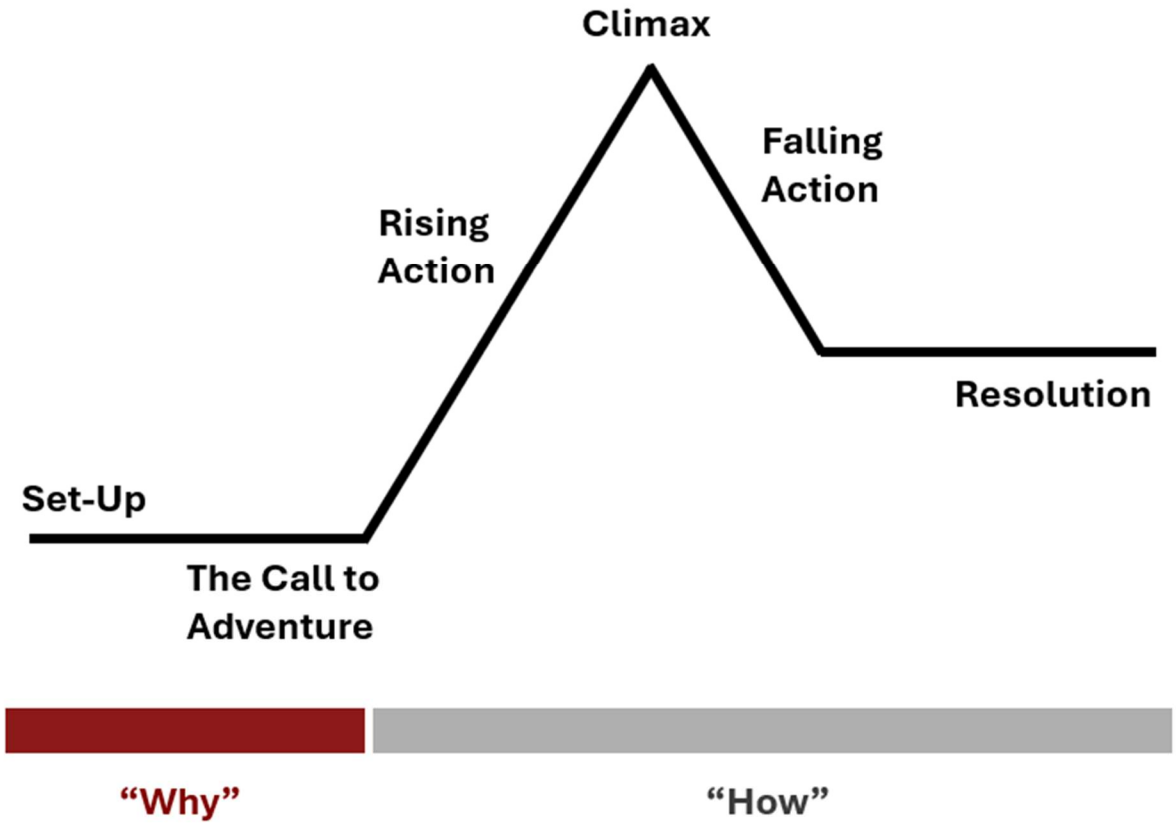

Figure 1: Freytag's Pyramid

Figure 1 shows a very basic story structure, also known as Freytag's Pyramid. The story's setting and characters are introduced in the Set-Up; a person is living their normal life (whatever normal means for them, spaceships and magic notwithstanding), before getting called away on some quest – a war, getting rid of a ring, finding a way home. The "inciting event" that pulls

them away is the Call to Adventure. This person has been given a "why," a reason to leave behind what they know for the strange, unknown world. The rest of the story follows "how" they did it – what trials they faced (the Rising Action and Climax), what realizations they had (the Falling Action), how they returned (Resolution). Even without a story structure in place, literature can show you parts of the world you could not otherwise see. How people live in places you've never travelled, historical events in years you weren't alive for, stories of people you have never met.

Physical chemistry is no different, and its similarity is part of what drew me to this 'genre' of research in the first place. It explained *why* and *how* different parts of the world interacted with one another, parts I could not see with my own eyes – molecules! Take the analogy from the beginning of this section. Oil and water don't mix because oil molecules have an even distribution of charge, while water molecules do not (this is known as polarity; water is considered polar, and oil is non-polar). Molecules with similar distributions of charge prefer to interact with each other over molecules with very different distributions. (These two sentences are your "why.") As a result, when polar and non-polar molecules are placed in the same container, they separate into "polar" and "non-polar" regions, which in turn creates visible layers. (This is your "how.") To me, doing research in physical chemistry is akin to answering the "Call to Adventure" – rather than simply reading about it, I decided to pursue my PhD so I could go on the journey myself.

While I don't expect the question, I want to take a moment to address it anyway: "if you're arguing that fiction and physical chemistry are the same, and fiction isn't real, are you arguing that science isn't?" There's an important distinction here – fiction and physical chemistry are not identical, but how they frame and solve problems utilize similar structures. (In

fact, eagle-eyed physical chemists will note that Figure 1 is just another form of a reaction coordinate: where a starting state is converted into a final state after receiving enough activation energy.) To really prove this point, we'll need to add a third perspective: how physical chemistry research is *written*.

1.2 Scientific Jargon and Translation

Just as authors use literary devices to communicate emotion or experience in fiction, scientists use jargon to efficiently communicate scientific concepts. A literary device is quite a broad umbrella, but it includes metaphors, similes, personification, and allegory, among many others. While not technically necessary to a story, creating one without these devices reduces how much meaning a reader can get from the story. Take an excerpt from one of my favorite novels, *Annihilation*: "The edges of a sharp, golden light [sic] emanated from a place beyond my vision, hidden by the wall, and the brightness within me throbbed and thrilled to it. The buzzing sound again intensified until it was so jagged and hissing that I felt as if blood might trickle from my ears…I did not feel as if I were a person but simply a receiving station for a series of overwhelming transmissions."[1] The "brightness," the loud sound, feeling more like a "receiving station" than a person adds another layer of meaning for the reader to use when imagining the story. This is equally efficient for the author – instead of spending time describing literally how many sounds the character was experiencing, what those sounds were, or how overwhelming it was, Vandermeer can call them a "receiving station…of overwhelming transmissions" and move on.

Similarly, scientific jargon efficiently communicates layers of meaning to the reader. "If theory cannot be relied on to accurately predict the true ground isomer for complexes of the simple aliphatic amino acids, where the binding modes are limited, then predictions for amino

acids with functionalized side chains are also in doubt."[2] "True ground isomer," "simple aliphatic amino acids," "binding modes," "functionalized side chains" – are all shorthand (jargon) that indicate to me (the researcher) which specific aspects of the problem are worth calling attention to. If we removed the jargon, then it would say: 'if computer calculations cannot be relied on to accurately predict the most stable structure between a molecule and a metal atom, when the molecules are amino acids whose side chains contain only carbon and hydrogen, where the number of places a metal atom can bind to are limited, then predictions for amino acids whose side chains are more complex and contain atoms other than carbon and hydrogen, are also in doubt.' (And even that entire sentence still contains some jargon!) It's well worth noting, too, that even within chemistry, jargon is specialized. Half of the battle of presenting scientific research at a conference with other scientists is making sure the language used (the story presented) is told such that scientists outside the field can still understand.

Underneath the jargon, the structure of a research article is quite similar to a story. Usually, research articles are written under 5 sections: Introduction, Methods, Results, Discussion, and Conclusion. These can be directly grafted onto our story structure from earlier.

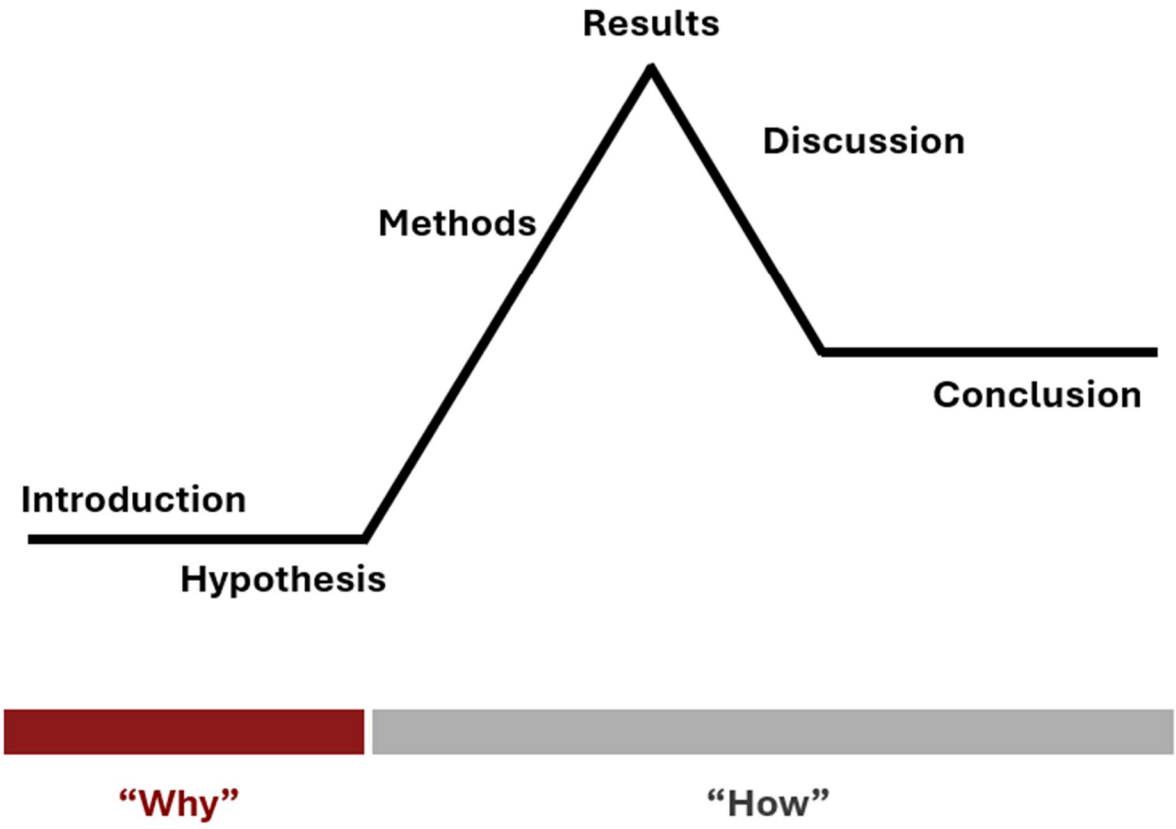

Figure 2: Research Article Pyramid

The Introduction sets up the story – the chemical problem. It discusses where the scientific community is in answering this problem (our story "setting" if you will) and what the current problem is. That problem, along with the Hypothesis, is our "Call to Adventure." The Methods section explains how the authors are going to answer the hypothesis (the trials they face, the Rising Action), and the Results section is our Climax – this is the data the authors found, and now there's no going back to how it was before. The Discussion section (Falling Action) starts drawing the pieces of data together, creating meaning, and the Conclusion (Resolution) wraps the story up (and usually mentions ideas for a sequel).

The similarity in structure means *it is always possible to move between the two*. Scientific research must be shared with the community, and with other scientists. But communicating

effectively means knowing who your audience (your readers) are, and what language to use. Moving between these structures is a wonderful exercise for all scientists (it's what I'm currently doing in this chapter, after all) and I consider it very similar to the act of *translation*. When adapting a novel from a different language, it is the translator's job to move from one language to another, while still retaining the content and meaning of the story.

1.3 Fundamental Research and Close-Reading

For the first few years of my PhD when I got asked about the research I was doing, I would often get the reply, "So, what do you do with that?" This question is fraught, and not uncommon, for researchers studying 'fundamental' chemical problems. Let's first define our terms: fundamental research can be considered as research which has no 'direct' application to current scientific problems. I want to be clear with you – my research does not directly address solving the climate change crisis, discovering a cure for cancer, or newer, clean sources of energy. Fundamental research has a different "why," a different reason for existing. But for that, we need to return to literature.

When I was in high school, a popular class exercise in my English courses was close reading. It did not matter whether it was a book, a short-story passage, or a poem; I had to choose a small excerpt – a page, a paragraph, a stanza – and dissect it. I was taught that, in a piece of writing, there is both the content of the passage (what actually happens) and how the passage is written (how the reader receives that information). This latter aspect is functionally a series of authorial choices: what words did the author use, in what order does the reader receive the information, which character is speaking in the passage, and what is not being said at all. The consideration of these questions can often tell us about the book as a whole. Take my passage from *Annihilation* in the previous section. When you read it, what feeling did it leave you with?

"Edges" of "sharp light," "a place beyond my vision," "jagged and hissing" noises, not feeling "as if I were a person" – it's quite tense and suspenseful language. Something unknown, and possibly not friendly, is about to be revealed. Though you'll have to trust me on this, Annihilation is a tense, suspenseful novel about unknowable creatures! The entire work is nothing but a collection of these small pieces, coming together to tell the full story.

Fundamental research is taking a "close-reading" approach to scientific problems. The important scientific problems in society currently are massive undertakings – climate change, disease, clean energy – each made up of thousands of problems, chemical reactions, and questions. (Why do some important climate reactions only happen at night? How does a mutation in this protein affect the expression of this disease? Which chemical reactions, when used together, create a more efficient battery? Etc.) By taking a close reading approach, we can start to chip away at those many thousands of questions, and by sharing them, come to a more complete story.

2.0 Thesis Project/Story #1: The Room

Now that I've (hopefully) convinced you that physical chemistry and literature are structurally similar, I want to test my theory. The remainder of this chapter discusses two projects that I worked on during my PhD, and while I've "translated" many of the scientific concepts for you, I've gone a step further and added an accompanying story. The projects, and story, are split up according to the shared structure we've already discussed, and the fictional plot will follow the progression of the research findings.

2.1 The Set-up

A run-of-the-mill engineer (and aspiring author) is hit by a truck, only to get transported to a world with huge, incomprehensible buildings. One looms in front of her now; its height only broken by the clouds far above her head. She takes a few steps to either side and sees that the building continues off into the horizon line, twisting left and right in places for no apparent reason. She studies the shape of them for a moment, trying to commit them to memory, but the building's shape gets fuzzier the farther away she looks. With one hand on the building, she begins to walk…

Proteins are responsible for a number of processes in our body – the transport of oxygen in our blood, for example. Scientists have spent many years figuring out the specific function of each protein, where it is located within the body, and what mutations hinder its functioning. We also know that proteins are very large structures, made up of multiple sub-structures. What we are less certain of is how the various sub-structures work together to ensure the overall function. This is because proteins are very dynamic structures – their shape can change depending on what reaction is happening around them. Proteins usually have an "active site" somewhere, which is the specific part of the protein where the "function" occurs (in our story, the active site would be loading dock, where the transfer of materials occurs before being sent off to other places). However, some scientists have tried to change small parts of the protein's structure very far away from the active site and have found that the function of the entire protein (the entire building) stops.[3]

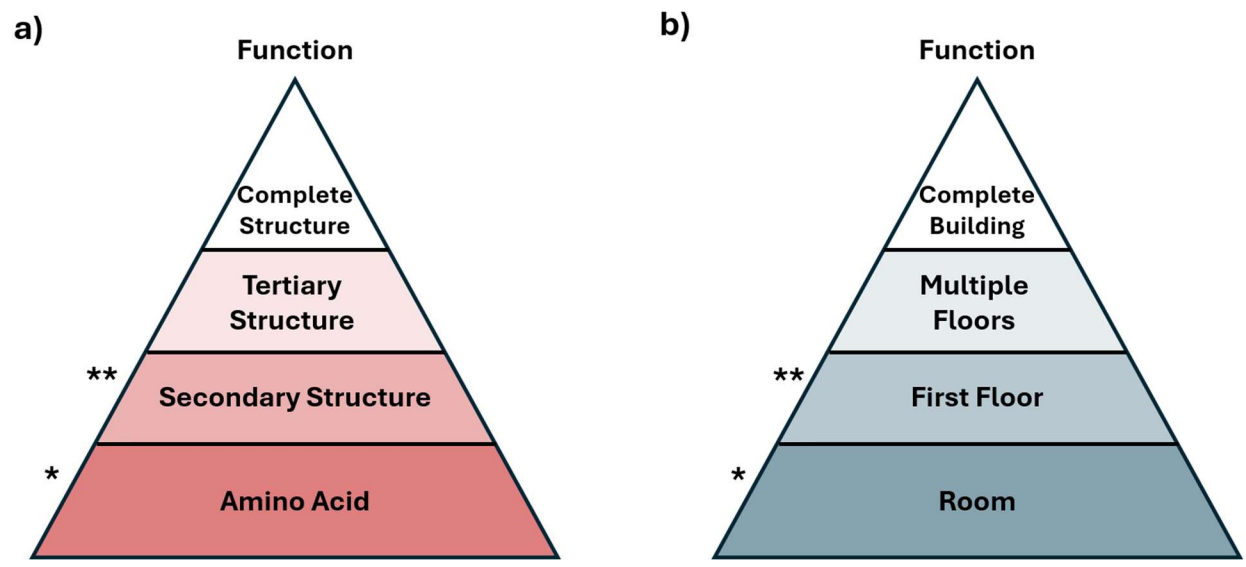

Figure 3: Structures of Proteins and Buildings. Asterisks indicate which levels I researched (and our story discusses).

Luckily, we can split up the sub-structures of a protein into different categories, as seen in Figure 3a. The lowest tier, an amino acid, is a type of molecule that appears everywhere in our body. When amino acids are connected, they form a larger structure (aptly called the secondary structure) just as a collection of rooms can be considered the first floor of a building. Each tier builds off of the one below it, until we reach the complete structure of the entire protein, which performs its specific function. We can directly compare these categories to the buildings in our story, in Figure 3b.

Because proteins can be split into separate tiers, they are a great candidate system for fundamental researchers to study! For my thesis project, I used the "close-reading" technique I described in Section 1.3 to look at the lowest two tiers in Figure 3: first, I studied a complex of an amino acid and a metal cation (a metal with one less electron than usual, thus having a +1 charge), and then I studied a complex of a metal ion with an α-helix, which is a common protein

sub-structure. These projects will get split into their stories– the former in Section 2.0 and the latter in Section 3.0.

2.2 The Call to Adventure: The Hypothesis

She walks for days. Every so often, the ground rumbles, and when she turns back to look, the building has moved. She rounds a corner, and there – a single door. Desperate for new scenery, she passes through the threshold before the door closes behind her. Locked, of course. Now inside, she follows the twisting corridors. Eventually, thankfully, a single sign glows down the hallway. "Analytics Division." There, she finds a long room, the left side lined with windows. Another door, glowing with strange light, shines at the end of the room and another sign above it: "Exit."

Metal ions occur throughout some protein structures, and they are small but mighty forces. If the metal ion is near the active site, then it usually helps progress the reaction that occurs there. For metal ions further away, their role is less certain. What I specifically focused on was investigating how the interactions between a metal ion and an amino acid would change if different parts of the amino acid's structure changed. This was my Call to Adventure. I categorized the structural changes into two separate groups: Group A, where the structural change occurs in the R group (a non-reactive part of the amino acid), and Group B, where the change occurs on the nitrogen group (often referred to as nitrogen substitution). I'll refer to these two groups by their labels for the remaining sections.

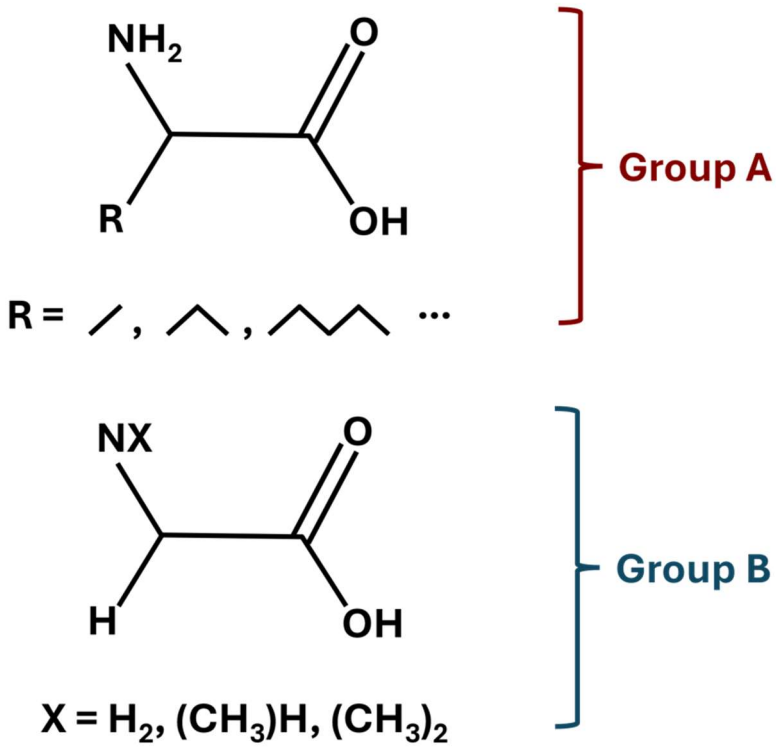

Figure 4: Structures of Amino Acid Groups A and B

2.3 The Rising Action

In this strange world, she takes the glowing door as a good sign – this must be a test, then. Through each of the seven windows is a black nothingness, but at each one, she finds a set of controls: two knobs (R, X) set at zero, a button with a lightbulb on it, and a switch labelled 'Roof.' In fact, the button at the first window was already glowing. Placing her trust in glowing objects once again, she hits the button. Light bursts through the window – in the void are two cubes, a large red one and a small blue one. Flipping the roof switch makes the top of each cube disappear, revealing two different rooms. The Engineer relaxed for the first time since landing here; she needed to run experiments.

In order to answer my Call to Adventure, I needed to know two things: first, what the structure of the amino acid-metal ion complex was, and how the structure of the complex

changed when I changed structural parts of the amino acid. Each structural change in Groups A and B corresponds to a unique amino acid, and luckily for me – remember, organic chemistry is not my genre of choice – I could purchase all 7 of them (4 in Group A, and 3 in Group B) pre-made. Then I mixed them into a solution with a metal salt, sodium carbonate, before loading them into my instrument.

If you're wondering how I was sure that I was making the sodium-amino acid clusters just by dumping them in a solution together, good on you for catching a potential plot hole. In fact, I made many different compounds, and I was only interested in the sodium-amino acid clusters. How I was able to differentiate them comes down to the instrument I used; with it, I could separate chemical compounds by their mass and investigate what structure they had.

In order to do the first task, everything in the solution gets collected and released down a long tube with the same amount of force before getting detected. Heavier chemical compounds move slower, while lighter compounds move faster, and I can monitor when each compound arrives at the detection region. To do the second task, I intersect the compounds with infrared light. Light can come in many different colors – the visible region (the type of light we can see with our eyes), for example, goes from red light to blue light and is associated with a certain value of energy. Infrared light is lower in energy than visible light and induces certain parts of a molecule to vibrate. Each structural part vibrates at a different value, so I can link whichever values of light I see with the structure of the molecule. This general technique is called infrared spectroscopy. And because I'm comparing many molecules together (the 4 molecules in Group A and the 3 in Group B), I get an added bonus: when the structural parts change – when the metal moves closer to the amino acid or farther away, for example – the value light I see also

changes slightly. By recording in which direction the light moves (either higher or lower in energy), I can know how certain parts of the complex have changed in relation to each other.

2.4 The Climax

The Engineer knew from her research – changing two knobs at once would get her in hot water, fast. She moves to the next window in the room and turns the R knob a quarter clockwise. Button, switch, and now the red room is slightly smaller, the blue room slightly bigger. Interesting. At the third window, she gets another stroke of luck; there's a small sheet of paper filled with notes about the R knob. Using the notes, the Engineer confirms the first 5 windows. The sixth and seventh window stare at her – the notes mention nothing about them. Time to test the second knob. She sets the R knob back to zero and moves the X knob. Now, the blue room is the largest room, while the red room is tiny. Excited, she arrives at the final window. This time, only the blue room appears…

Previous research groups have looked at which structures the complex formed when investigating Group A, and they categorized them into two types (Type 1 and Type 2, shown in Figure 5). A Type 1 complex has the sodium ion in between two different functional groups, and the proton (H) is on one of the oxygens. The only positive charge in Type 1 complex is on the sodium (keep this in mind). A Type 2 complex looks…frankly, like it's uncomfortable. Most importantly, though, Type 2 has a lot of discrete charges! There's a positive charge on the sodium, like Type 1, but there's also a negative charge between the two oxygens, and another positive charge on the nitrogen. When a molecule has two different charges in different locations (like the amino acid in Type 2 does), we call it a "zwitterion:" a zwitterion is technically neutral, because the positive and negative charges sum to 0, but usually, it's also less stable. In fact, other

researchers have noticed that, without the sodium ion, the amino acid zwitterion would not exist in the gas phase at all. We can say that the sodium ion stabilizes the zwitterionic structure.

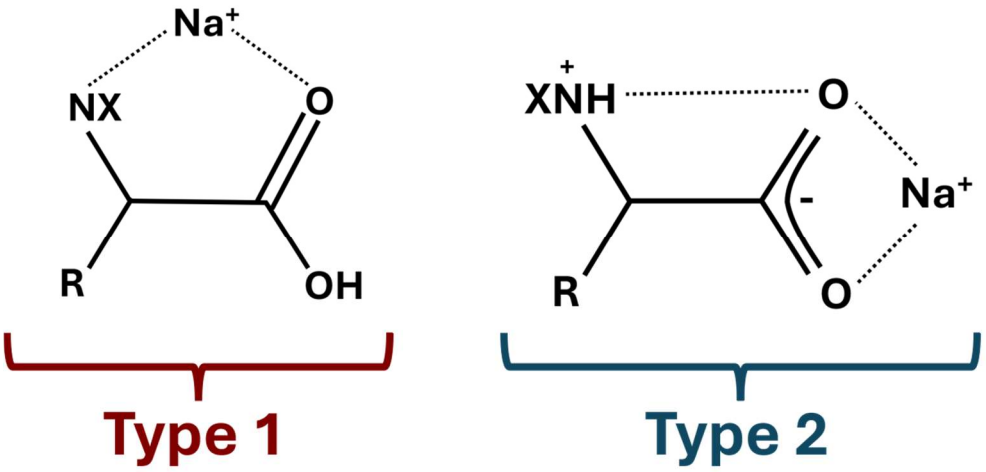

Figure 5: Structure Types of Sodium Ion-Amino Acid Clusters

When I looked at Group A with my technique, I was able to confirm that I saw both Type 1 and Type 2 complexes. While not the most exciting discovery, within the scientific community, results which match between different groups, using slightly different techniques, are worthwhile results. It means that the behavior we're trying to characterize is consistent, and not a behavior which occurs because of the type of technique used to investigate it. In our story, this is the equivalent to the engineer re-creating the room from the notes she found – when given the type of materials, and in what order to use them, her results matched the note's results. However, the technique I used has another advantage, something other groups could not do: I could quantify how much of each complex type there was for every structural change that occurred. I'll talk more about why quantification is important in the following section.

When I looked at Group B, I saw that the relative amount of the Type 1 and Type 2 complexes changed drastically! The largest amount of the Type 2 complex I saw for Group A

was around 30%, but I saw roughly 80% for Group B. In fact, the last molecule in Group B was entirely the Type 2 complex! I've shown you this same information graphically in Figure 6 below. This was quite the interesting finding – because I separated Group A and Group B by their structural differences, I could now link those differences to the switch between the Type 1 and Type 2 complexes.

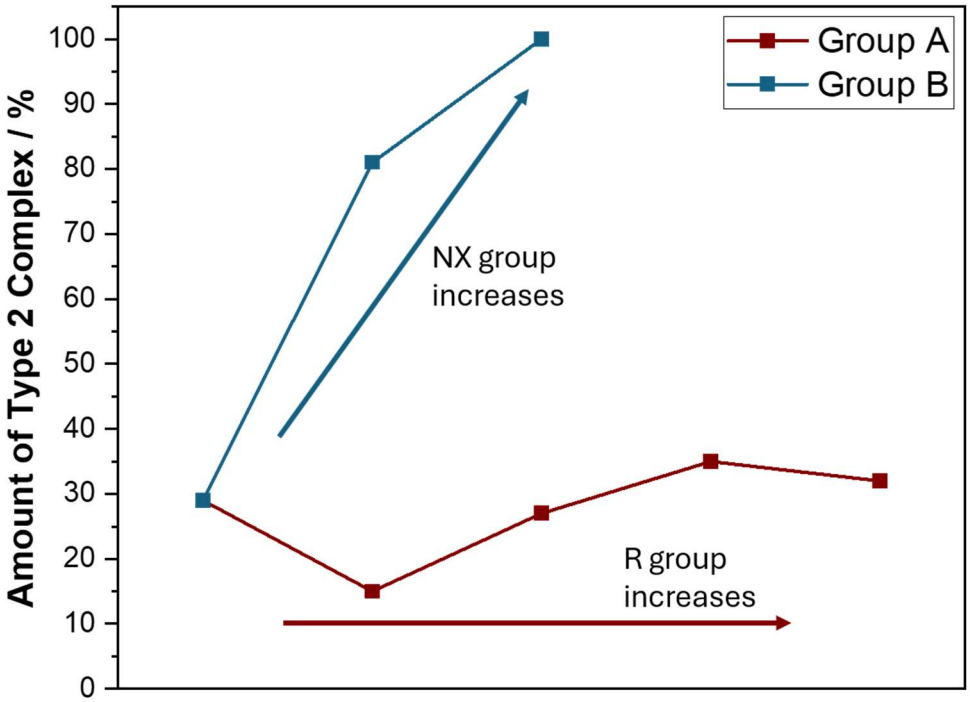

Figure 6: Amount of Type 2 Complex seen in Groups A and B. Note the difference in slope!

2.5 The Falling Action

The Engineer paces up and down the room. There are no more windows to check, no more switches to flip. The glowing door remained tightly sealed. She passes by all the windows again, peering inside. There was nothing else in the room to do! She debates banging her head against the wall, literally, when she realizes. This room is the Analytics Division. Reviewing all the information she had learned from the windows, she begins to speak…

Quantifying how much something changes is useful for researchers because it allows us to be specific. Remember – my thesis project is a close-reading exercise. The more precise I am about the behavior I see, the more useful the information will be when I start to build off of it. While it would be true to say that *Annihilation* is a story about surrender or liminal spaces, if I wanted to recommend the story to someone else, it would be more useful to say that it's a story about whether humanity will surrender to nature when it's given power, or how staying in liminal spaces can infect one's way of life. (I did say it was a tense novel.) It provides more precise information that a person can use to decide whether or not to read it.

When I looked back at both groups of amino acids that I was studying, I realized that there was another trait that changed between each group. By definition, an amino acid contains two parts: an acidic group and a basic group. In general, acid and base chemistry describes a molecule's relationship to a proton (a small positive charge, +1). An acid gives away a proton to other molecules, and a base wants to take a proton from other molecules. The stronger the acid or base, the more easily it can donate or accept that proton, respectively.

I found that the structural changes occurring in Group A were also changing the strength of the acidic group, and likewise, the changes occurring in Group B were affecting the strength of the basic group. If you'll remember, in Group A, the non-reactive R group was changing between the amino acids. As the R group got larger, the strength of the acidic group increased. In Group B, the structural change was on the nitrogen group. As the nitrogen got further substituted, it became a stronger base. Scientists in the 1950s figured out a way to quantify how acidic or basic a molecule was and assign it a numerical value. I used those values and found a correlation between the acid/base value of the amino acid, and which complex structure (Type 1 or Type 2) was most stable.

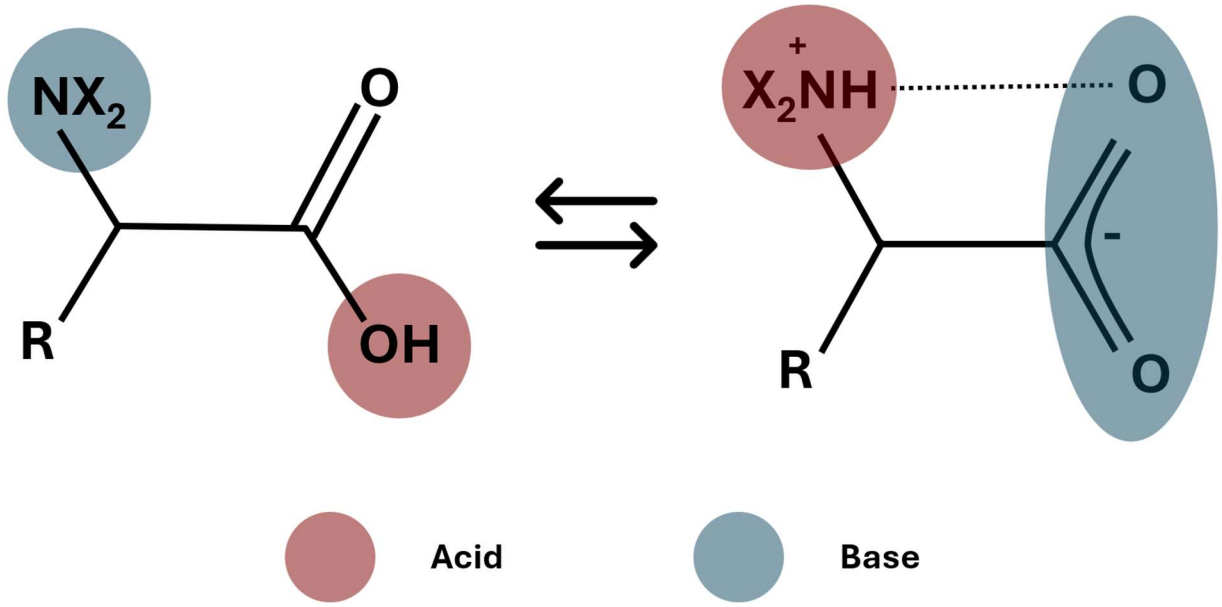

Figure 7: Acid and Base Groups in Neutral and Zwitterionic Amino Acids. Note that the neutral form of the amino acid is seen in the Type 1 complex, and the zwitterionic form in the Type 2 complex.

What I also noticed was that in both complex types, the metal ion was centered around the opposite acid/base group from the proton. In Type 1, the acid is the OH group (where the proton is) and the sodium ion is near the NH2 group (the base). In Type 2, the acid is now the HNX group (where the proton is) and the sodium ion is by the OO- group (the base). This is visualized in Figure 7. It turns out that the sodium ion's positive charge, +1, means that it, too, can act like an acid. But, importantly, it is also much larger in size than a proton.

2.6 The Resolution

Success. She had just finished her discussion of relative room sizes, adding that returning to Earth would be quite nice please, when the building starts to shake. She turns around, the glowing door nearly blinding her, and she hears the lock flip. The Engineer runs, she could not get stuck in this building again, and barrels out to… her lab office. Sunlight shines through the window, and in the distance, the buildings. Normally sized this time.

What does this all mean? It means that what I first believed was a correlation (one behavior causing another) was actually a tug-of-war! (A twist ending!) Let's review our story thus far:

1. I knew that the interactions between metal ions and the surrounding amino acids within a protein sometimes changed, which affected its structure, but…
2. …I didn't know how.
3. I found a way to change specific parts of an amino acid in two different ways, which formed Groups A and B. I then used a tool which allowed us to see what type of complex formed when I added a metal ion to the amino acids in each group.
4. I found two different complexes, Types 1 and 2, where the metal ion was interacting with different parts of the amino acid. When I looked at complexes formed with amino acids from Group A, I saw Types 1 and 2. With complexes formed from Group B, I saw mostly Type 2.
5. I could calculate how much of each complex type I found for Groups A and B. I also realized that I could relate the structural changes in each group to acid-base strength. I noticed a correlation: as the amino acids in Group A got more acidic, the amount of Complex Type 1 increased. As the amino acids in Group B got more basic, the amount of Complex Type 2 increased.
6. The switch between Complex Types 1 and 2 is a competition between a proton and a metal ion, each with a positive charge. The most basic part of the amino acid will grab the proton, and the less basic part will interact with the metal ion.

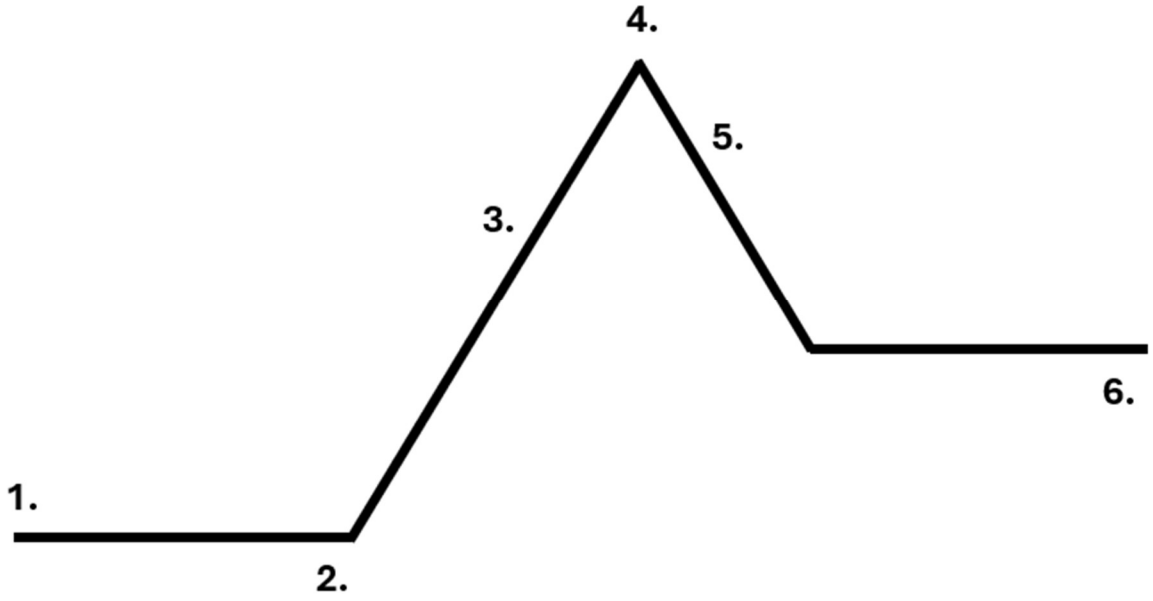

Figure 8: The Return of the Pyramid.

This is important because of new developments made in designing proteins. Rather than modify already-existing proteins, some scientists are interested in creating proteins from scratch. To do so, they'll need to start from the bottom tier – a sequence of amino acids – before moving up. If we're able to describe how metals interact with amino acids, we can more accurately predict what structures will form.

Unfortunately, it's not a tidy ending. First, the way that scientists have historically measured the acid/base strength of a molecule is not precise enough for a molecule which contains both an acidic group and a basic group. We would need that information to be fully certain of our hypothesis (our "how"). Second, now that we have a better understanding of how the lowest tier in a protein works, what happens when we go up a level?

3.0 Story #2: The First Floor (a Sequel)

3.1 The Setup and Call to Adventure

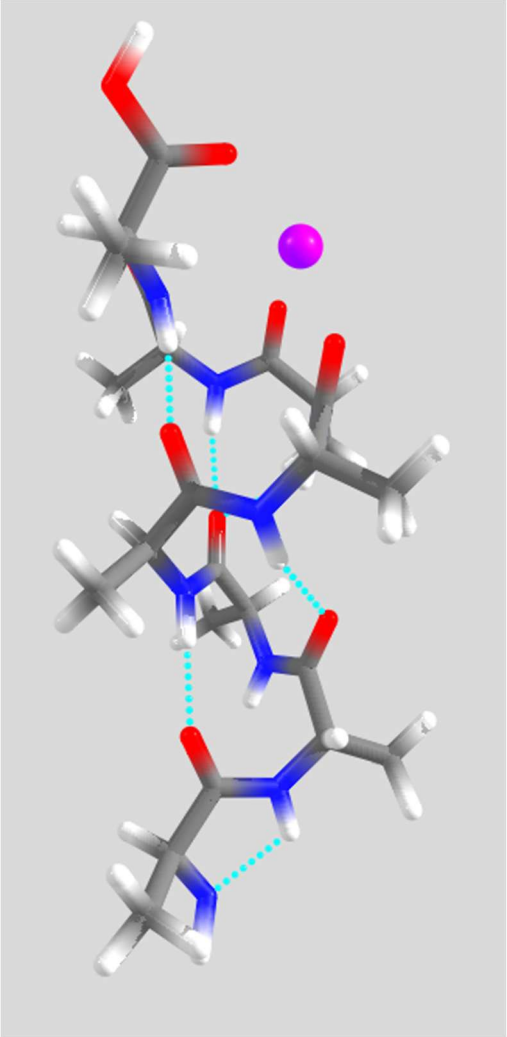

Figure 9: Structure of an α-helix. Carbon atoms are in gray, hydrogen in white, oxygen in red, nitrogen in blue, and the sodium ion in purple.

The Engineer shocks herself on a circuit board and returns to the world of Buildings. This time, to escape, she must build an entire floor…

The next tier in protein creation (refer to Figure 3) is called Secondary Structures. Secondary structures describe how an amino acid sequence folds around itself – how a set of rooms, ordered in a certain way, creates the floor plan for a house, an office etc. In proteins, there are two main types of secondary structures: an α-helix and a β-sheet. An α-helix resembles a curled piece of ribbon, held together by a series of special chemical bonds called hydrogen bonds. (Hydrogen bonds can only occur between a hydrogen atom, and a carbon, nitrogen, or oxygen atom.)

Researchers who want to build proteins from scratch have a large task ahead of them. They're primarily interested in building proteins that have never been seen before in nature, which means that there's even more permutations of structures to consider. Our Call to Adventure was wanting to know how far a small structural change diffuses, or spreads.

3.2 A Story in Progress: Community in Research and Multiple Authors

I did make some progress on this project, but it is nowhere near completed. The reason I leave this project uncompleted highlights a key difference between chemistry research and (most) literature: chemical 'stories' rarely get completed by a single author.

Five years seems like a long time to spend answering a question, and that is partially true. For my research, a lot of that time was spent troubleshooting rather than data collecting; my instrument is very sensitive for what I want to study and it's equally as prone to breaking. Often, the media's perception of graduate researchers is that we are solitary, strange creatures, fixing our tools under a single lamp and muttering to ourselves. That perception couldn't be farther from reality. My day-to-day work is communicating – with my coworkers to brainstorm, with my PI to think about next steps, with my mentees to teach them. I have only gotten as far as I have by learning through the community around me. One hero's journey to save the world is a fine story, but real progress comes from collective efforts. It's with great joy that I leave the story unfinished, waiting for another researcher to pick up the baton.

3.3 Chapter 1 References

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