

Metaphors We Think By

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Anxiety seemed like something that happened to other people—something I didn't have to think about—until I found myself in cellular biology class in the first weeks of medical school, unable to think. I hadn't been myself since the early summer, brooding about issues in my personal life, how they would change when I moved across the country. Yet by the time I arrived for school in Boston, I had pored over every relevant thought and circumstance, resolved upon concrete actions, still to no avail. I was stuck in a state of increasing entropy, an unfolding of the mind.

That cellular biology session was our seventh of the semester; the day's topic, protein folding. As any student of biology knows, proteins are incredibly diverse machines, responsible for an astonishing array of cellular and physiological functions. But to function properly, they must first fold into appropriate conformations, and that folding process is highly complex. When a polypeptide does fold properly—into its “native state,” as it's called—the achievement is made possible by segments of the polypeptide which are tailor-made to interact with other segments of the same molecule. But like the Boston green line after a Friday night Celtics game, a crowded cell is constantly pushing new characters into the mix, creating interactions which are, at times, uncomfortable. If two unfolded or misfolded polypeptides come together in just the wrong way, they can bind not only to themselves, but to one another, forming protein aggregates. These aggregates are often deleterious, and several of their associated diseases—Alzheimer's and Parkinson's, to name two—enact their tragic effects on the mind.

In class, contemplating the intricacies of that process, I came upon a peculiar realization: thinking was just like protein folding. Like a nascent polypeptide, thoughts do not form in a neat, discursive order. They are always working in the background, sampling various interpretations of a problem, searching for the lowest-energy emotional state, the most stable conformation. At any given moment, and for any given thought, those conformations might also be productive, reflective of reality: native thinking states, if you will.

But when dealing with stressful or anxious thoughts, they could also misfold, clumping together into ruminations. I, for instance, could turn situations over in my mind, analyzing them with perfect lucidity, until nothing changed. Growing ever more irritated, I would end in perfect frustration, the problems expanding in size and complexity, adding urgency with every turn of the cycle. Yet despite this futility, the anxieties would still seem perfectly logical.

I imagine that misfolded proteins are not so different. Broadly speaking, misfolded proteins aggregate for two reasons: because their interactions are so stable (a thermodynamic explanation), and because of the high energy barrier to move them back in a more productive direction (a kinetic one). Likewise, my thoughts slipped out of hand, into rumination, because the logic of anxiety seemed unimpeachable. And once settled, that logic could hardly be challenged with other, more productive insights, because the activation energy was too high.

As I sat distracted in class, this metaphor—thinking as protein folding—struck me deeply, but offered little benefit. Misfolded proteins are gobbled together, the globs grow larger, and disease follows. This is not exactly a liberating analogy. The same can be said for rumination and brooding: the recurring stresses which, for so many, represent an accosting force to peace and flourishing of mind. Proteins and thoughts both misfold. What of it?

One week later, as I studied with classmates in the Boston Public Library, liberation revealed itself amid of my class notes. I was reviewing the concept of chaperone proteins, molecular quality control systems which prevent protein aggregation and help other proteins find their functional, native states. These chaperones often bind sticky regions of an unfolded polypeptide, allowing the rest of the molecule to fold with less danger of aggregation. They stop destructive molecules from growing too large and too stable. This was an illuminating illustration: if anxiety and rumination behaved like misfolded proteins, perhaps their resolutions could come from the psychological equivalents of chaperone proteins.

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In my case, that meant therapy. Shortly after my realization in the Public Library, I sought out a therapist, an eminently wise woman experienced in the troubles of undergraduate and graduate students. I described to her my personal tumult over the previous months, how I had long since rationalized my way to a solution, and how I nevertheless felt powerless over the recurring distraction. In turn, she offered neither explanation, nor action, nor any result of long, discursive thought. Instead, what she offered was a sharp, purposeful check to my distracted mental cycles: a psychological chaperone.

Over our subsequent sessions, I recounted the paths my mind had trodden, the assumptions and feelings which flickered across my consciousness. I would describe the exact contours of my ruminations, tracing their formulaic patterns from one familiar thought to the next. I would even identify the flaws in those formulae, the instances in which I knew, rationally, that these were not native-state thoughts,

but anchored, amorphous aggregates of the mind. She would listen carefully, empathically, before drawing a slight smile, raising a soft finger, and saying, “Now wait a minute—you don’t really think that. Do you?”

Her questions and insights functioned not to prevent my mind from ever sampling those random, distracting conformations, but simply to keep me from falling too deep, binding too tight to directionless thoughts. That might not sound like a tremendous deal, but by our fourth meeting, I was a different person. I was more attentive in class, better able to recall previous sessions and apply their takeaways to novel concepts. My long runs beside the river were filled with observations of the sailboats, the bursting fall colors. I was, in short, refolded. And for an aspiring psychiatrist—one who yearns to think about the psychological suffering of others, not his own Sisyphean worries—that is an incredible gift.