GERALD EDELMAN

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GERALD EDELMAN was a complex individual of diverse and deep talent, with wide knowledge and a boundless nervous energy. In addition to his skill as a biological scientist, he was an accomplished writer who enjoyed poetry, read and was quoted widely in philosophy, and was both practiced in and appreciative of music. These were not just separated avenues of his life: he integrated them to bring an elegant style to his science and to compose his more speculative intellectual works in a characteristic literary format.

Raised in a fairly tough area of Queens, N.Y., Edelman initially studied medicine (his father was a physician) but turned to research in immunology and spent the major portion of his career leading a laboratory at Rockefeller University. His early focus was on the primary (polypeptide composition and amino acid sequence) structure of antibodies, which led to his sharing the Nobel Prize in Medicine with Rodney Porter in 1972. As impressive as that work was, two major advances in immunology (the role of Darwinian-like selection in the immune response and the precise source of diversity upon which that selection operated) had been defined largely by others. A man of his skill and ambition was hardly going to be satisfied.

After the Prize, Edelman's laboratory group comprised several sub-teams, which moved subsequently into several current areas of biology, including carbohydrate-binding proteins, the molecular basis of cell-cell recognition, and tissue morphogenesis. However, his personal focus turned increasingly toward the challenging allure of the vertebrate nervous system and the nature of cognitive brain function, leading him to form and direct a Neurosciences Institute at Rockefeller, which eventually moved to the Scripps Institute.

At Rockefeller University, Edelman appreciated that he was a faculty member as well as a research scientist and took keen interest in training members of his group. He deeply understood the research process in terms of formulating an important and testable hypothesis, and he instilled an effective attitude toward (a) experimental design (specifically, "in an emergency tracheotomy, use anything pointy" and "the refrigerator principle"—which meant that ideas sometimes were created from the ready availability of good reagents); (b) the dangers of distraction by potential competition ("don't look sideways"); and (c) the value of interpreting results in both a valid and interesting context.

Training with him was intense, particularly once a senior student received notice that "it's your year, son, to be in my nitric acid sitz bath." Thesis presentation before the Rockefeller community in the legendary Caspary Hall amphitheater was preceded by weeks of his direct scrutiny, with rehearsal sessions critiqued by the entire research group. Edelman required us to write clearly and succinctly in

publications, often commenting that "less is more." He also warned not to become overly defined by societies, administrations, or clubs.

Before delving into his work on the brain, it is interesting and perhaps illuminating to take stock of the widely-observed personal quirks of this never-boring individual. A close associate once commented that it was hard to believe that a diamond as big as Gerry could have so bad a flaw as to render it nearly worthless. And therein lies the continuing challenge posed by this complex individual man: how to see through the flaws so as not to obscure the value that might lie within or beyond. His passing will, to some degree, facilitate that process, and Ralph Greenspan (of the Kavli Institute for Brain and Mind at UC San Diego, and who enjoyed a period of close interchange with Edelman) suspects that "Gerry's scientific reputation will likely improve steadily now that he is gone."

Edelman was not oblivious to his behavioral shortcomings, in particular an explosive anger and a need to wall himself off from perceived detractors. Nevertheless, they gradually defined much of his outward persona. Despite these bristles, Gerry loved a good (or bad) joke, both hearing and telling, possibly through the influences of professors Shedlovsky and Marc Katz, who were exceptional raconteurs and reigned over a jovial atmosphere with good beer nearly every afternoon in the Rockefeller Faculty and Student Club. But the humor could never be directed at him—this is not a man who could laugh at himself. He did urge trainees to "do as I say, not as I do," but this was not offered in jest.

Would Gerry Edelman have dedicated half of his career to a Darwinian theory of cognitive brain function with a less imperial personality? Perhaps his multiple facets reflected on each other, including some essential reinforcement, influencing not only the style but also the content of Edelman's most far-reaching thought.

So how to view the flaw, often evidenced as an abrupt and brutal condescension based on the premise that he operated intellectually at a level well above his colleagues (for example, "any idea shared by both of us must be trivial")? Edelman would occasionally open up about his inner life to close friends, such as his trusted elder colleague at Rockefeller, chemist Theodore Shedlovsky, and these stories would then percolate on to Teddy's friends. A perhaps telling one concerned young Gerry's studies as a gifted violinist. The question arose as to how special he could become, and his highly respected teacher offered that he would be very good but not Jascha Heifetz (considered by some as the greatest virtuoso of the twentieth century). The studies apparently ceased, with a clear message to the young boy: if you are not going to the best ever at something, don't waste your time. Being recognized as

the best ever at anything is not easy territory and involves attitude and tactics, in addition to exceptional talent.

In any case, given his broad intellect and family traditions, the focus turned from music to medicine and then shifted into the more individualistic challenges of biomedical research. With that came a watershed moment in his life: the opportunity to enter the select student program in the rarified Nobel Laureate-studded atmosphere of Rockefeller University. The doctoral student program at Rockefeller had recently been founded by its president, Detlev Bronk, who consulted with the likes of Lord Adrian of Cambridge so as to establish a unique haven for generating the finest gentleman scholars, with emphasis on broad training and with no expense spared—in other words, a perfect incubator for what Edelman needed to achieve.

Coming from medicine, Edelman chose to do his thesis studies with a noted immunologist, Henry Kunkel. Because of a disagreement about research findings, this relationship suffered an acerbic and permanent breach. But Gerry also had acquired the admiration and steadying support of chemistry Professor Shedlovsky (with whom he also shared an appreciation of the arts) and President Bronk, who placed students and faculty on a remarkably level platform. That support and those findings soon provided Edelman his own laboratory, and within 12 years, he had secured a Nobel Prize.

The Prize gave Edelman a platform from which big ideas could be launched. But high status and driving ambition alone do not produce great thought. Equally essential was his timely exposure to the revolutionary idea posed by Niels Jerne that the immune response operated via a type of Darwinian selection. This idea was accompanied by the Nobel-winning studies by McFarland Burnett, showing that this selection operated on a repertoire of pre-existing cells producing different antibodies, giving rise to clonal cellular expansion and thus a specific amplification of the response. For Edelman, the demonstration that Darwinian principles, initially for evolution of species via selection from a repertoire of genetic traits, could also underlie complex recognition systems operating within a single individual was a turning point in his thinking. He now had his sights on the holy grail of all recognition systems: the human brain.

During those golden years of molecular and cellular immunology, important principles were also emerging in cellular neuroscience. Of notable relevance were two classic properties of neurons and their synaptic connections: (1) the organization of cortical neurons into discrete groups or columns of cells (described by Vernon Mountcastle,

Torsten Weisel, and David Hubel); and (2) the selective strengthening of a synapse as a result of its use, as initially proposed by Donald Hebb.

From this and other work, Edelman posed that the formidable recognition and processing capabilities of a complex nervous system depend fundamentally on a repertoire of cell groups that differ most specifically in their patterns of connectivity. Incoming sensory information would not only elicit a selective response that led to the strengthening of distinct cell groups, but could also be further modified by repetitive recognition (termed *re-entry*) that provided opportunity for abstraction and association. Thus, the algorithmic simplicity of repeated selection from a pre-existing (but also evolving) repertoire could account for the astonishing information-processing power of sophisticated neural systems.

It should be noted that a theory of neuronal network epigenesis had already been published in 1973 by Jean-Pierre Changeux, a contemporary and friend of Edelman's, and that this thesis involved neuronal group selection and degeneracy based on the modifiable synapse. Edelman significantly expanded those ideas in his later work, but the historical precedent of the earlier work is significant.

Edelman presented his ideas of selective brain function in several books, including "Neural Darwinism"; "Bright Air, Brilliant Fire: On the Matter of the Mind"; and "A Universe of Consciousness: How Matter Becomes Imagination," the last written with colleague Giulio Tononi. The descriptions and arguments in these books are often dense and elaborate, viewed by some readers as possessing an admirable literary quality, and by others as opaque and confusing. In any case, they represent an intermixing of artful style and probing science that derive directly from the author's substantial talents and offer a creative model for speculative science writing.

With the passing of Gerald Edelman, there remains the necessary task of testing the validity of Neural Darwinism. As with species evolution and the clonal immune response, whose initial theories were proposed prior to the knowledge of the underlying mechanism (i.e., genes, DNA, and the molecular basis of antigen recognition), his theory arrived before neuroscience could provide experimental verification, much less a reductionist explanation in cellular terms. Moreover, Edelman's selective mechanism is not as precisely defined as its predecessors in terms of functional elements and/or system outcomes.

Nevertheless, in addition to more advanced computational modeling, there have been some remarkable advances in the use of genetics and molecular reporters of synaptic activity that allow real-time evaluation of substantial groups of cells within functioning

brain tissue. Recent work on the perception of odors in the brain has, in fact, revealed a remarkably selectionist process. The advent of the federally-supported B.R.A.I.N. Initiative offers further prospects for major technical improvements in the way we perceive global brain activity. Thus, one can begin to envision a line of investigation that can address the challenge that his seminal and profoundly original work presents to neuroscience and biology in general.

Elected 1977

URS RUTISHAUSER
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Urs Rutishauser was at Rockefeller University from 1967–1983. With Edelman, he co-directed the concert series in Caspary Hall at the university for a decade.