A Statement of the Problem: How to Bring Quantitative Methods to the Messy Biology of Alzheimer's Disease

Karl Herrup

Division of Life Science, The Hong Kong University of Science and Technology, Hong Kong.

Alzheimer's disease (AD) is arguably the most complex disease that afflicts the human nervous system. It is also one of the most prevalent; by some estimates the risk of being affected over the age of 85 is nearly 50%. This presents a substantial number of challenges to our current disease-related research models – problems to which computational methods may well be productively applied. As one example, our algorithms of gene discovery are mostly based on models of an uncommon mutation; in modeling AD, with 50% prevalence, concepts such as 'wild type' largely break down. Compounding this difficulty is the issue of diagnosis. The risk of AD is estimated to double every five years beginning at age 65 (when it is 2-3%). This means that with high prevalence and advanced age-of-onset, for most cross-sectional studies today's control will be tomorrow's case. Are our current models up to this challenge? Epidemiological studies have identified environmental factors associated with reduced life-time risk of AD; yet prospective clinical trials have largely failed to validate the efficacy of these agents. Can a systems-level approach to disease modeling expose the basis of this paradox? No answers to these and other equally knotty questions are currently apparent. The challenge for researchers with computational skills is to approach this 'messy biology' with a fresh eye and offer guidance to the next generation of clinical researchers so that AD, and many other conditions like it, can be effectively brought under control in our lifetime.