Curing Cancer, Part 1 – Reductionism versus Complexity
8 December 2020

In 1971, President Richard M. Nixon announced the beginning of the US "war on cancer" (see President Nixon's 1971 State of the Union at 15:03). Despite massive government expenditures (Kolata: Grant System Leads Cancer Researchers to Play It Safe, New York Times, 27Jun09) and testimonials that the war on cancer "did everything it was supposed to do" (NCI: National Cancer Act of 1971, accessed 10Nov20), cancer is still a leading cause of death (Centers for Disease Control and Prevention 2016, Cancer Statistics 2020), with high mortality from cancer of the lung, colon, pancreas and breast (Cancer Facts & Figures 2020).

Our war on cancer has failed because our basic approach to biology is wrong. Biologic thinking has traditionally relied on reductionism, the theory that the behavior of the whole is equal to the sum of the behavior of the parts. Based on this theory, sophisticated systems are presumed to be combinations of simpler systems that themselves can be reduced to simpler parts (Mazzocchi 2008), disease is due to flawed parts and treatment needs to merely identify and repair the damaged parts. Although logical and rational, reductionism does not actually describe how complex systems function.

In complex systems, the properties of the entire system are greater than the sum of the properties of each part due to interactions between the parts (Kane 2015). Novel properties emerge from the parts and their interactions if one views the entire system as a whole. For example, start with a large number of biological molecules (proteins and other organic compounds), each relatively inert by itself, but capable of interacting in different ways with each other. Then confine them to a small space to promote these interactions. The result may be a living system, a self-sustaining web of reactions that can reproduce and evolve, properties that could not be even imagined by studying each part (Kauffman 1993, Pernick 2017).

Other examples of complex systems include communities formed by individuals and electric grids composed of individual power plants. In each complex system, the result is more dynamic and intricate than could be predicted from studying each component.

Complex systems often exhibit self-organized criticality, the tendency of large systems with many components to evolve to a critical state or "tipping point" (Bak, How Nature Works 1999). When dropping individual grains of sand onto a surface, each grain typically just adds to a growing sandpile. Occasionally, it triggers a small avalanche of the sandpile. Less frequently, it triggers a larger avalanche, and rarely, it causes the entire sandpile to collapse. What is different about the grain of sand that triggers an avalanche from the grain of sand that just sits there? Surprisingly, there is no difference. The grain that appears to do nothing causes subtle structural changes in the sandpile, promoting an eventual collapse after enough grains are dropped. Although we focus on each grain as being important to the outcome, the functional unit is the sandpile itself.

Similarly, cellular networks composed of biologic molecules, cells, tissues and organs are poised at a critical state in which small perturbations typically cause no change but occasionally cause small network changes. Rarely, a trivial event sets in motion a large systemic response, leading to a major reconfiguration of the system (Bak, How Nature Works 1999), such as initial steps towards malignancy. Although cancer scientists tend to focus on initial or "driver" mutations, complexity theory suggests that we should focus on the cellular networks as the functional units.

The human body is composed of a myriad of interacting networks positioned at critical states, which is required for network flexibility to enable embryonic development, the inflammatory response to trauma and infection and the capability for our species to evolve to a changing environment. However, the tradeoff for maintaining these critical states is that cancer, a type of catastrophic systemic failure, is inevitable. We can reduce its incidence, we can detect it earlier and we can treat it more effectively but attaining a "world without cancer" (American Cancer Society, accessed 13Nov20) is not possible.