Functional Analysis of Molecular Networks by Fault Diagnosis Engineering: A Novel Technology in Systems Biology

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One of the most challenging questions in understanding the molecular basis of complex human disorders is how much different genes can contribute to the development of the disease and which molecules are the most critical ones in pathogenesis. Advances in technology, including high-throughput methods such as microarrays, allow the screening of tens of thousands of genes in humans, in a relatively short period of time. Therefore, we are now capable to measure the "expression levels" of thousands of genes in normal and disease conditions. We now need to develop technologies for measuring the "functionality levels" of thousands of molecules that interact with each other to deliver a specific function and measure the vulnerability of the molecular systems to the dysfunction of each molecular components. In the area of electronic engineering, there are a variety of methods to identify the defective or vulnerable components of complex digital electronic circuits. Recently, we have been able to use some basic concepts of electrical engineering and develop novel technologies to address this challenging question. We have shown before that by developing proper biologically-driven digital vulnerability assessment methods, the vulnerability of complex signaling networks to the possible dysfunction of a single faulty molecule can be determined (Abdi et al, 2008, Abdi & Emamian, 2009, Abdi and Emamian, 2010). We have been able to collect experimental data that confirm the biological relevance of this approach. Following these studies, we tried to test this technology on larger networks, with multiple inputs and multiple end nodes. Examining such networks confirmed the utility of this technology for correct prediction of critically important molecules in multi-input, multi-output networks as well. We have also obtained data showing how the vulnerability of molecular networks to the simultaneous dysfunction of multiple molecules can be computed by this novel technology. We conclude that biologically relevant vulnerable molecules in complex cellular networks involved in complex human disorders can be identified, by developing biologically-oriented engineering techniques. We anticipate this cross-disciplinary study to have a major impact on our understanding of biological systems, due to its capability of discovering the key molecules that have causative effects in disease development. Such molecules are promising targets for drug discovery.