1080-92-155 **Guanyu Wang*** (gwang@gwu.edu), 725 21st Street, N.W., Department of Physics, Washington, DC 20052. *Singularity analysis of cell signaling networks reveals connections between complex diseases.*

Connections between cancer and metabolic diseases may consist in the complex network of interactions among a common set of biomolecules. By applying singularity and bifurcation analysis, the phenotypes constrained by the AKT signaling pathway are identified and mapped onto the parameter space, which include cancer and certain metabolic diseases. By considering physiologic properties (sensitivity, robustness and adaptivity) the AKT pathway must possess in order to efficiently sense growth factors and nutrients, the region of normal responses is located. To optimize these properties, the intracellular concentration of the AKT protein must be sufficiently high to saturate its enzymes; the strength of the positive feedback must be stronger than that of the negative feedback. The analysis illuminates the parameter space and reveals system-level mechanisms in regulating biological functions (cell growth, survival, proliferation and metabolism) and how their deregulation may lead to the development of diseases. The analytical expressions summarize the synergistic interactions among many molecules, which provides valuable insights into therapeutic interventions. In particular, a strategy for overcoming the limitations of mTOR inhibition is proposed for cancer therapy. (Received January 23, 2012)