Modular Systems Biology applied to TGFbeta and DNA Damage Response Signaling following Low Dose Radiation

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Abstract:

Modular systems biology (MSB) describes the complexity of biological systems using well defined modules that represent distinct biological response pathways or sub-systems within pathways. We review mathematical concepts from control theory that can be used to identify and construct well defined modules for describing complex biological processes. The DNA damage response and TGFbeta/Smad signaling are two important response pathways following radiation exposure that lead to a variety of cellular and tissues outcomes including apoptosis, differentiation, and the epithelial-to-mesenchymal transition (EMT). We apply the MSB approach to develop a computational description of the ATM and TGFbeta/Smad signaling pathways. Applications to low dose and dose-rate exposure to low LET radiation and space radiation are considered. Stability analysis of modular systems and the identification of pathway signals to cellular and tissue phenotypes such as EMT will be discussed.