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Laura F. Strube* (strube@math.utah.edu) and **Frederick R. Adler**. *A Mathematical Model of Translational Regulation by the Integrated Stress Response*. Preliminary report.

The Integrated Stress Response (ISR) is a protective mechanism that is activated in response to a wide variety of intracellular stresses. Cells use the ISR to temporarily attenuate canonical translation while simultaneously upregulating the translation of stress response genes via a non-canonical pathway. The key proteins in this system are the eukaryotic initiation factor eIF2 α , its recycler eIF2B, a stress-detecting eIF2 α kinase, and the transcription factor ATF4. We describe a non-linear ODE model of ISR-induced translation regulation incorporating stochastically derived reaction rates that describes translation as a function of stress level. We show that the model exhibits three qualitative behaviors corresponding to degree of stress. When stress levels are low, the system acts as a filter and maintains general translation while exhibiting minimal translation of ATF4. Under intermediate levels of stress, the system produces ATF4 protein while reducing general translation. When stress levels are high both general translation and ATF4 translation fail. This model demonstrates that the stochastic mechanism underlying ATF4 translation allows the cell to differentially regulate two translation mechanisms despite their reliance on the same initiation factors. (Received September 20, 2016)