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**Lae Un Kim, Maria D'Orsogna and Tom Chou\*** (tomchou@ucla.edu), Dept. of Biomathematics, UCLA, LSB 5209, Los Angeles, CA 90095-1766. *Onset, timing, and exposure therapy of stress disorders: mechanistic insight from a mathematical model of oscillating neuroendocrine dynamics.*

The hypothalamic-pituitary-adrenal (HPA) axis is a neuroendocrine system that regulates stress response. Disruptions in the activity of the HPA axis are correlated with stress-related diseases such as post-traumatic stress disorder (PTSD) and major depressive disorder. In this talk, we characterize "normal" and "diseased" states of the HPA axis as basins of attraction of a dynamical system describing the inhibition of peptide hormones such as corticotropin-releasing hormone (CRH) and adrenocorticotrophic hormone (ACTH) by circulating glucocorticoids such as cortisol (CORT). Our model distinguishes the relatively slow process of cortisol-mediated CRH biosynthesis from rapid trans-synaptic effects that regulate the CRH secretion process. We show that the slow component of the negative feedback allows external stress-induced reversible transitions between "normal" and "diseased" states in novel intensity-, duration-, and timing-dependent ways. Our two-step negative feedback model suggests a mechanism whereby exposure therapy of stress disorders such as PTSD may act to normalize downstream dysregulation of the HPA axis. (Received February 04, 2018)