P39. Measuring information transfer via gonadotropin-releasing hormone receptors

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Gonadotropin-releasing hormone (GnRH) acts via G-protein coupled receptors on pituitary gonadotrophs, causing a (largely) PKC-mediated activation of ERK, and a Ca2+-mediated activation of Nuclear Factor of Activated T-cells (NFAT), both of which mediate GnRH effects on gonadotropin expression. We monitor their activation by high content imaging (fluorescence staining for ppERK and nuclear translocation of an NFAT1c-EFP reporter) in LβT2 gonadotroph cells. We also express Egr1-zsGREEN and/or NFAT-RE-asRED reporters as transcriptional readouts for ERK and NFAT activation, respectively. Single cell measures reveal high cell-to-cell variability, and information theoretical approaches can be used to explore its influence on information transfer. Here we use Mutual Information (MI) between GnRH and our single cell experimental readouts (I(response;GnRH)) as measures of information transfer via GnRH receptors. An MI of 1Bit means that the system can unambiguously distinguish two (identically distributed) inputs and we routinely provide a 3Bit input (i.e., 8=23 GnRH concentrations). However, the MI between GnRH and these readouts was always <1Bit. Joint sensing of ERK and NFAT increased MI but the effect was small and joint MI values were also <1. Information transfer could be increased by sensing response trajectory and when we tracked NFAT1c-EFP in individual cells I(NFAT-nuclear fraction;GnRH) values were maximal (~0.45Bit) at ~30min and slightly higher values (~0.65Bit) were obtained by consideration of trajectories. Thus, LβT2 cells appear to be unreliable sensors of GnRH concentration because most available information is lost through signalling and, although information transfer was increased by joint sensing and trajectory sensing, the increases seen were small.

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