An Information Theoretic Approach to Gonadotropin-Releasing Hormone (GnRH) Signalling

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Introduction

Most work on cell signalling mechanisms involves measurement of average responses from large populations of cells. Single cell measurements typically exhibit high cell-to-cell variability (fig. 1) due to intrinsic differences in amount of protein expressed, amount activated and relative compartmentalisation. Signalling pathways can be considered to be 'noisy' information channels; information can be defined as the uncertainty about the environment that is removed by signalling. It is crucial that each cell is able to sense the environment and react appropriately (to survive or die, to proliferate or differentiate, to express or not express a particular gene). Here we apply information theory (Mutual Information (MI)) (ref. 1) to GnRH sensing (fig. 2) and explore how this reliability might be regulated.

Results

Fig. 4: Measuring MI for GnRH signalling. GnRH caused the expected concentration and time-dependent increases in ppERK (A), NFAT1-EFP nuclear fraction (C) and ERK-driven gene expression (B) in LBT2 cells. MI values between GnRH and these responses had similar time-courses to the population averages (D, E, F).

Fig. 6: GnRH sensing via parallel pathways. When ppERK (A) and NFAT translocation (B) responses were measured in the same cells, joint MI values exceeded those for either response alone (C). Similarly, when transresponsiveness responses were measured in the same cells (Eg1-1x-ZS GREEN (D), and NFAT-RE asRED (E)) joint MI values exceeded those for either response alone (F).

Conclusions

- GnRH signalling pathways can be thought of as noisy communication channels.
- MI can be used to measure the reliability of hormone sensing via these channels.
- Single pathways in single cells do not sense GnRH reliably (MI < 1 bit).
- GnRH sensing is improved by increasing GnRH number and by use of convergent pathways.

References


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