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Title: The frequency codification of environmental changes equip cells with a scale invariant discriminating power

Abstract: Cells continuously sense their surroundings to detect modifications and generate responses. Very often these modifications correspond to changes in the concentration of extracellular effectors that, upon binding to plasma membrane receptors, induce intracellular changes that generate the end response. The result of this signaling cascade not only depends on the presence/absence of the extracellular ligand but also on its concentration. How well cells can discriminate extracellular concentrations depends on how these concentrations are encoded in the intermediaries of the pathway. Cells use two main codification schemes: amplitude and frequency encoding in which increasing ligand concentrations yield increasing intermediary concentrations or induce a pulsatile behavior of increasing frequency, respectively. Intracellular  $\text{Ca}^{2+}$  signals are an example of the latter. Experiments showed that intracellular  $\text{Ca}^{2+}$  pulses are stochastic with a mean interpulse frequency that scales exponentially with the extracellular ligand concentration, a behavior that was also observed in the nuclear localization of transcription factors. In this talk I will show how this scaling arises in noise-driven excitable systems and how it endows cells with a scale invariant discrimination power in which extracellular concentrations can be distinguished equally well across different concentration ranges. Using the pheromone response pathway in yeast as example, I will discuss the limits to the scale invariance that the subsequent steps of the pathway impose and how the combination of frequency and (the qualitatively different) amplitude encodings can expand the range over which pheromone concentrations can be discriminated.