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Protein activation by calcium oscillations and Jensen's Inequality

Oscillating concentrations of cellular Ca^{2+}-ions are of great importance for the signalling in the cell. It is widely believed that the information of extracellular stimuli is encoded into an oscillating Ca^{2+} pattern, which subsequently is decoded by the activation of Ca^{2+}-sensitive proteins. Besides this advantage of an oscillating Ca^{2+} signal, we here show that oscillations additionally lead to a better activation of the target proteins compared to a constant signal. In two asymptotic cases we can analytically prove this for arbitrary oscillation shapes and a very general decoding model, which comprises most previous models of Ca^{2+}-sensitive proteins. For this we use Jensen's inequality that relates the value of a convex function of an average to the average of the convex function. Moreover, numerical simulations indicate that oscillations lead to a better activation not only in the two asymptotic cases. The results underline the importance of the cooperativity of the binding of Ca^{2+} and of zero-order ultrasensitivity, which are two properties that are often observed in experiments on the activation of Ca^{2+}-sensitive target proteins. We compare our theoretical predictions with data from experimental studies investigating the activation of NFAT and Ras by oscillatory and constant signals.

References

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