

A spatial model of ERK nuclear translocation

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The extracellular signal-regulated kinase (ERK) is involved in many important cellular processes such as gene expression, cell spreading and tumor growth. In the final steps of the ERK cascade, phosphorylated ERK dissociates from MEK and goes into the nucleus.

Various experiments have shown that MEK guides the localization of ERK. When ERK is overexpressed in a cell and it saturates MEK, the nuclear concentration of ERK increases and their diffusion coefficient decreases. Although this suggests that there is an agent which immobilizes ERK in the nucleus previous models of ERK nuclear translocation do not include this factor. In our simulations we tried to reproduce experiments of ERK nuclear translocation and we did not have a sustained nuclear accumulation until we added an anchor molecule.

We constructed a spatial PDE-based model from a previous ODE model made by Fujioka et al. with the VirtualCell software. Our goal was explore two different theories explaining MEK's control over ERK localization in the MAP kinase pathway and to reproduce ERK nuclear translocation experiments done by Costa et al. We found that Raf concentration is cell-type specific and that in order to reproduce the Costa experiments we had to add an anchor molecule in the nucleus, increase the nucleus-to- cytoplasm ratio, and increase the cRaf concentration.