Employing a Mechanistic Model for the MAPK Pathway to Examine the Impact of Cellular All or None Behavior on Overall Tissue Response.

The mitogen activated protein kinase (MAPK) cascade is a three-tiered phosphorylation cascade that is ubiquitously expressed among eukaryotic cells. Its primary function is to propagate signals from cell surface receptors to various cytosolic and nuclear targets. Recent studies have demonstrated that the MAPK cascade exhibits an all-or-none response to graded stimuli. This study quantitatively investigates MAPK activation in Xenopus oocytes using both empirical and biologically-based mechanistic models. Empirical models can represent overall tissue MAPK activation in the oocytes. However, these models lack description of key biological processes and therefore give no insight into whether the cellular response occurs in a graded or all-or-none fashion. To examine the propagation of cellular MAPK all-or-none activation to overall tissue response, mechanistic models in conjunction with Monte Carlo simulations are employed. An adequate description of the dose response relationship of MAPK activation in Xenopus oocytes is achieved. Furthermore, application of these mechanistic models revealed that the initial receptor-ligand binding rate contributes to the cells’ ability to exhibit an all-or-none MAPK activation response. (Received August 01, 2011)