Modeling the Notch Signaling System

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Notch signaling is an important developmental pathway used to affect metazoan cellular differentiation. Stimulation of the pathway results from activated Notch, a membrane bound receptor that interacts with ligands of the DSL (Delta/Serrate/Jagged) family found on adjacent cells. Activation of Notch results in its proteolytic cleavage and nuclear localization, upon which the cleaved Notch acts as a transcriptional activator to stimulate expression of target genes. In the past ten years, researchers have better mapped the temporal events leading to Notch cleavage, activation, and target gene expression. However, a quantitative framework that gauges the level of cleavage, activation, or target gene expression is still lacking. Additionally, it is not clear how Notch signaling affects the differentiation process. Although different levels of Notch are observed between different tissue types, and it has been proposed that Notch signaling leads to an imbalance in the expression levels of Notch using some form of feedback regulation, it is not known if this results from Notch signaling by itself or is due to a combination with other developmental cues. A statistical mechanics treatment of the data gathered by research groups in the Notch field as well as results accumulated from a rotation project will being new insights to the processes leading to cellular differentiation, Notch cleavage, and target gene activation.