

# Quantum-dot based Imaging Assays to Characterize and Model Signaling Pathways

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The capabilities of simultaneous application of specialized imaging techniques, advanced image analysis and computer simulation enhance our understanding of receptor and downstream signaling dynamics. We use functionalized quantum-dots to target multiple proteins in cell cultures after tyrosine kinase-linked receptor activation. A multiscale, object-oriented approach described previously [1], is used to analyze the resulting multiparametric confocal images, taking into account several color channels simultaneously. Targeting multiple species at the same time in a signaling pathway enhances our ability to develop spatio-temporal models of cellular processes. Our current systems biology computational platform, *CellSim* [2], couples a series of kinetic equations representing interactions between proteins and small molecules within a cell (or between cells) to a series of transport equations governing the motion of the various constituents through the cellular network as a function of time. This allows one to predict the dynamic changes of biological processes in response to extracellular events. As the time evolution of the heterogeneous cell is defined in totality by the parameterization of the model (diffusion constants, advection velocities and kinetic parameters), the ability to find a mathematical description that best reproduces the experimental results generated by data analysis of the images. This global optimization procedure defines confidence intervals that constrain the kinetic rate constants and diffusion constants to satisfy the experimental image based data generated. High performance computing techniques are needed for global parameter fitting for reaction-advection-diffusion models because of the wealth of data that must be processed from the resulting microscopy and the need to run multiple simulations for each test parameter set. The approach is demonstrated for age related alterations of the EGF/MAPK pathway in human fibroblasts.

1) Kriete A.; Papazoglou E.; Edrissi, B.; Pais, H.; Pourrezaei, K.(2006) Automated quantification of quantum-dot-labelled epidermal growth factor receptor internalization via multiscale image segmentation. *J Microscopy* 2006 Apr; 222(Pt 1), pp 22-27

2) <http://bio.physics.drexel.edu/research.html>