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Sensitivity-based approach to optimal experimental design in a receptor trafficking and down regulation model FERGAL CASEY, JOSHUA WATERFALL, RYAN GUTENKUNST, Cornell University, KEVIN BROWN, Harvard University, CHRISTOPHER MYERS, JAMES SETHNA, Cornell University — We apply the ideas of optimal experimental design to systems biology models: minimizing a design criterion based on the average variance of predictions, we suggest new experiments that need to be performed to optimally test a given biological hypothesis. The estimated variance in predictions is derived from the sensitivities of protein and chemical species in the model to changes in reaction rates. The sensitivities also allow us to determine which interactions in the biological network dominate the system behavior. To test the design principles, we have developed a differential equation model incorporating the processes of endocytosis, recycling and degradation of activated epidermal growth factor (EGF) receptor in a mammalian cell line. Recent experimental work has discovered mutant proteins that cause receptor accumulation and a prolonged growth signal. Our model is optimized to fit this mutant experimental data and wild type data for a variety of experimental conditions. Of biological interest is the effect on surface and internalized receptor levels after the overexpression or inactivation of regulator proteins in the network: the optimal design method allows us to fine tune the conditions to best predict the behavior of these unknown components of the system.

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