seemingly contradictory interactions among Bcl-2 proteins and their contributions to mitochondrial outer membrane permeabilization as inhibitors, promoters, or sensitizers of apoptosis.

906-Pos Board B706 Robustness Portraits of Diverse Biological Networks Conserved Despite Order-Of-Magnitude Parameter Variation
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Many biological networks are robust to a wide variety of internal and external perturbations, yet fragile to a select group of uncommon perturbations. Because fragile system modes are highly sensitive to certain biochemical parameters, it is unclear how precisely biochemical parameters must be known to predict in order to accurately predict the robustness portrait of a system. Here, we examined a previously well-characterized model of the cardiac beta-adrenergic signaling network. Our findings show how the robustness portrait was well conserved, even when parameters were rounded to their nearest 1-2 orders of magnitude ($r = 0.82$ and 0.63, respectively). This analysis was then extended to 10 additional networks of diverse biological processes, including E. Coli chemotaxis, stem cell differentiation, and cytokine signaling. Nine out of 10 of these networks exhibited conserved robustness portraits ($r > 0.75$) despite systematic order-of-magnitude variations in their biochemical parameters. These results illustrate the ability to predict both fragile and robust aspects of diverse biological networks despite imprecise biochemical parameters. Additionally, this work suggests a strategy from which approximate models can be used to prioritize experiments towards fragile system modes, leading to efficient model validation and revision.

907-Pos Board B707 A mathematical Model of Signaling in Podocyte Foot Processes
Cible V. Falkenberg, Michael L. Blinov, Leslie M. Loew.

The first stage of blood filtration occurs in the glomerulus, where water and other small sized molecules are freely filtered into the urinary space while albumin and larger proteins are retained in the blood capillaries. Maintenance of this size-selective glomerular filtration barrier is regulated by differently differentiated cells, podocytes, their cell-cell interactions in the slit diaphragm and the cell-GBM (glomerular basement membrane) interaction of the podocyte foot processes. Mutations of the nephrin gene (NPHS1) triggers actin reorganization, loss of the podocyte functional morphology and massive proteinuria. The glomerular tissue is challenging to study in vitro, because podocytes from isolated glomeruli undergo de-differentiation within hours, while cultures of stabilized cell lines never complete differentiation. Therefore, to provide insight into how the integrity of the filtration barrier is dynamically maintained, we have developed a mathematical model of the podocyte that preserves the spatial organization found in the intact glomerulus, focusing on the nephrin pathway. Nephrin has four binding sites phosphorylated by the same mechanism (nephrin clustering and Fyn phosphorylation) that can trigger the formation of actin branches via Arp2/3. Importantly, Nck (a scaffold that coordinates F-actin nucleation), PLCY1 (an enzyme that hydrolyzes PIP2) and podocin (important for nephrin localization) all compete for one of the phosphorylation sites on nephrin. The model includes complex formation around nephrin and several proteins involved in actin cytoskeleton remodeling, such as P13K and Fyn. We use rule-based modeling to explore the transition from the pseudopodia actin depolymerization to the urinary space.

908-Pos Board B708 Is Intracellular pH a Master Clock for the Events of Mitosis?
Lucian J. Gagliardi.

Experiments have shown that the intracellular pH of many cell types rises to a maximum at the onset of mitosis, subsequently decreasing 0.3 to 0.5 pH units from typical peak values of 7.3 to 7.5 measured during prophase [1]. This result, and observations that tubulin net charge depends strongly on pH, varying quite linearly from −12 to −28 (electron charges) between pH 5.5 and 8.0 [2,3], could be significant for microtubule (MT) dynamics during mitosis. Studies have shown that MT dynamics is sensitive to pH, with MT growth favored by higher intracellular pH values [4-6]. Given the above observations collectively, it seems reasonable to assume that the shift from the dominance of MT growth during prophase, and to a lesser extent during prometaphase, to a parity between MT polymerization and depolymerization during metaphase chromosome oscillations could be attributed to the gradual downward intracellular pH shift during mitosis that is observed in many cells. Thus the timing and sequencing of prophase, prometaphase, and metaphase chromosome motions may be understood as an increase in the MT disassembly to assembly probability ratio resulting from a continuously falling intracellular pH [7,8].