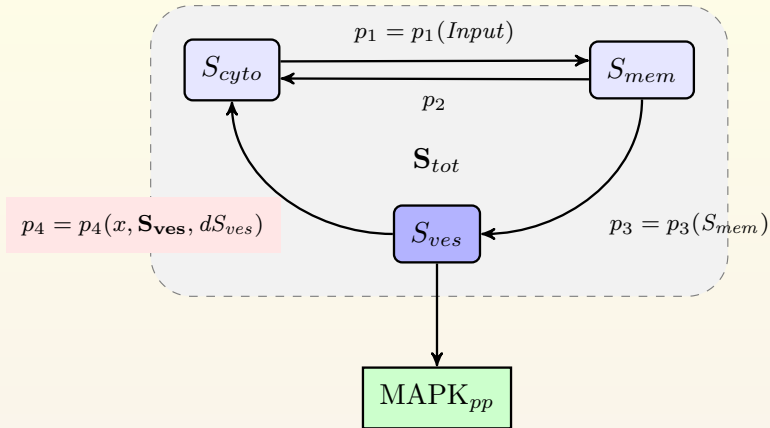
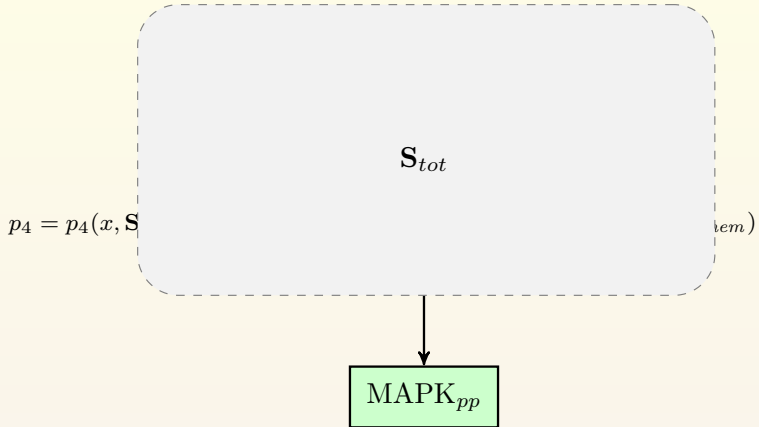


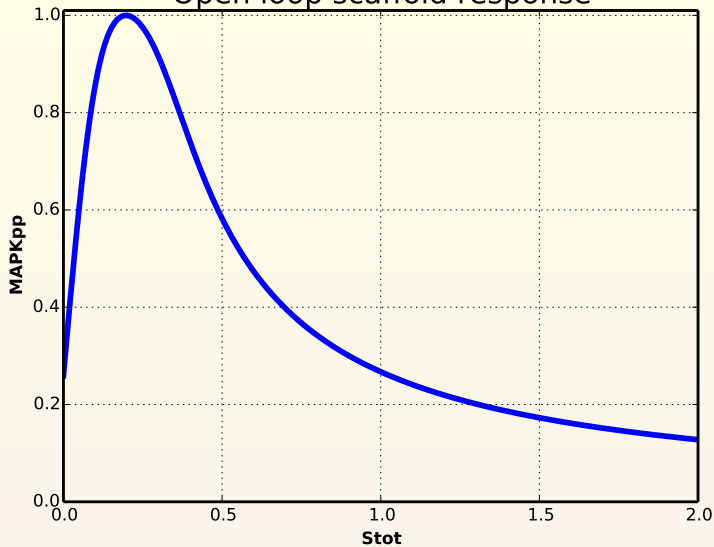
Model Schematic



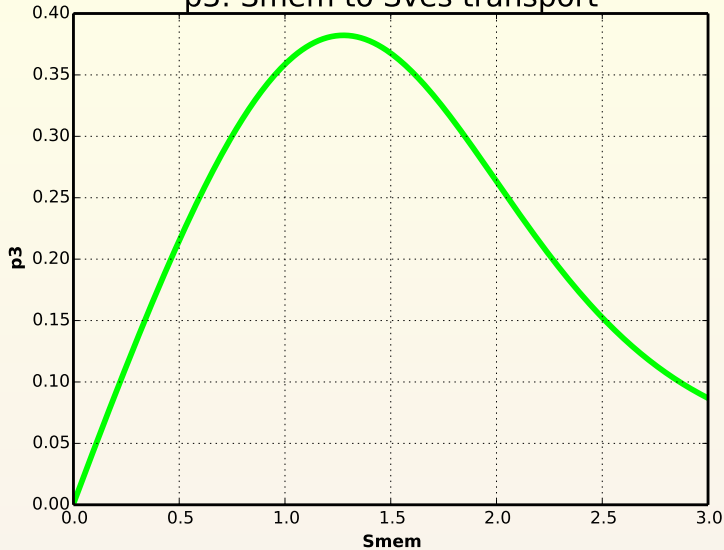
Open Loop Response



Open loop scaffold response



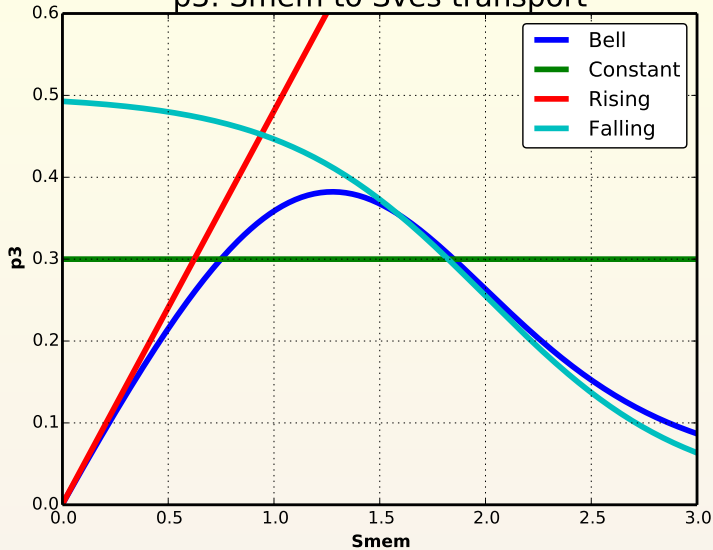
p3: Smem to Sves transport



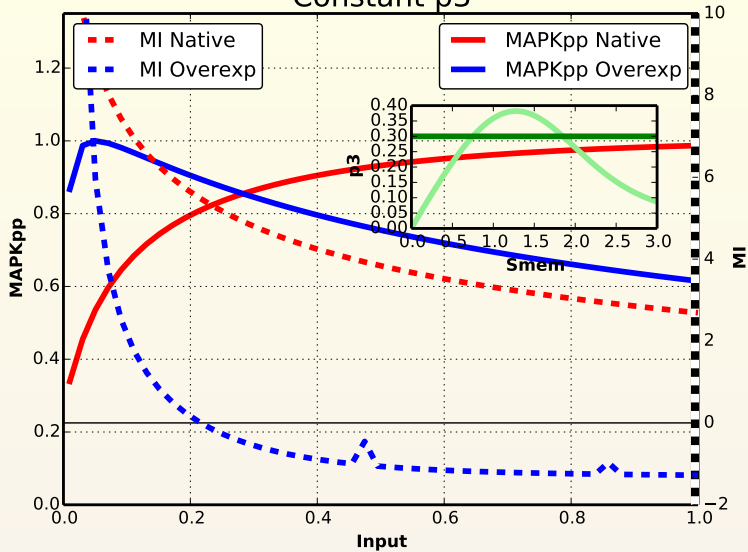
Why is p3 a bell shaped response?

- Each part of the bell shaped curved is simulated to justify its use
 - ▶ Constant term
 - ▶ Linear rising term
 - ▶ Just the falling side
 - ▶ Bell shape
 - ★ by combining the rising and falling terms

p3: Smem to Sves transport



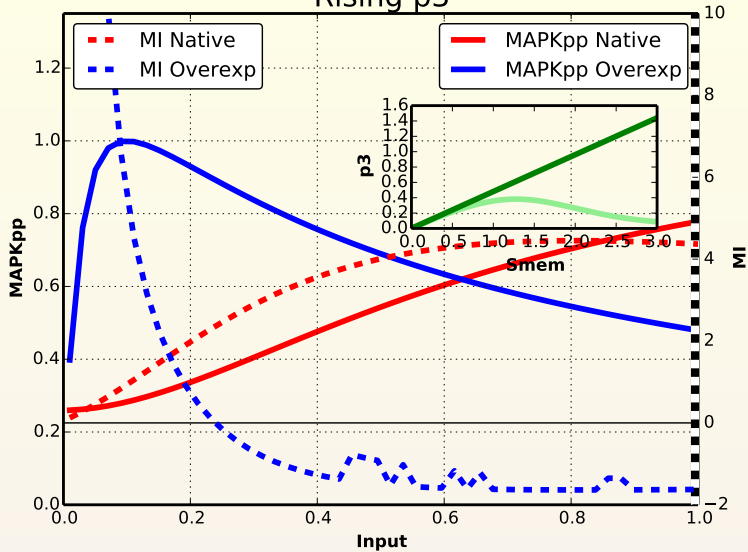
Constant p3



Results for constant p3

- At native levels, we get a saturating increase in MAPKpp, producing a negatively sloping MI curve
 - ▶ Experimentally MI is constant w.r.t. dose
- At overexpressed levels, the simulation only produces negative MI values
 - ▶ Experimentally MI goes from negative to positive

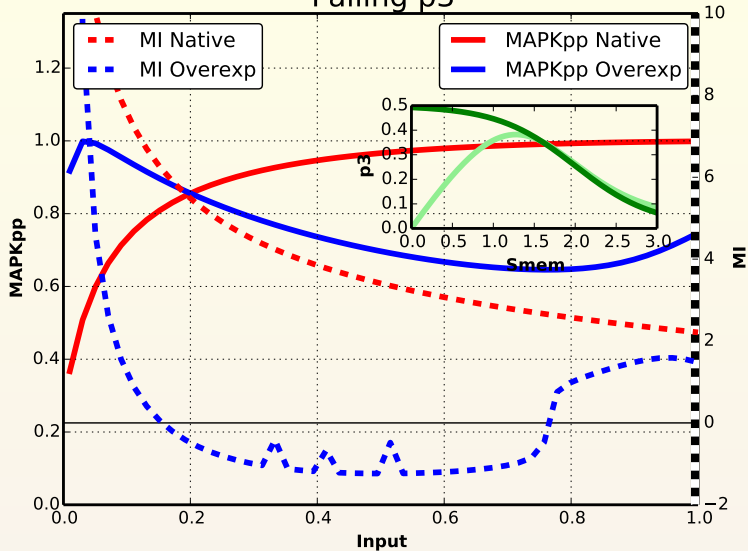
Rising p3



Results for rising p3

- At native levels, MAPKpp now rises linearly with dose, producing a flat MI response since it is the derivative
 - ▶ This is what is observed experimentally
- At overexpressed levels, the simulation still only produces negative MI values
 - ▶ Experimentally MI goes from negative to positive

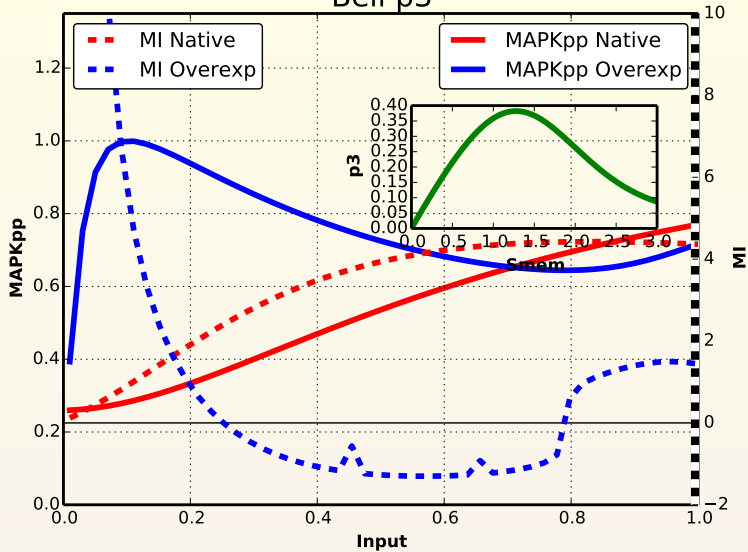
Falling p3



Results for falling p3

- At native levels, MAPKpp saturates rapidly just like the constant case, producing a decreasing MI response
 - ▶ MI should be constant
- At overexpressed levels, MAPKpp is now able to rise at high inputs after falling, producing a MI response that goes from negative to positive
 - ▶ Experimentally MI goes from negative to positive

Bell p3

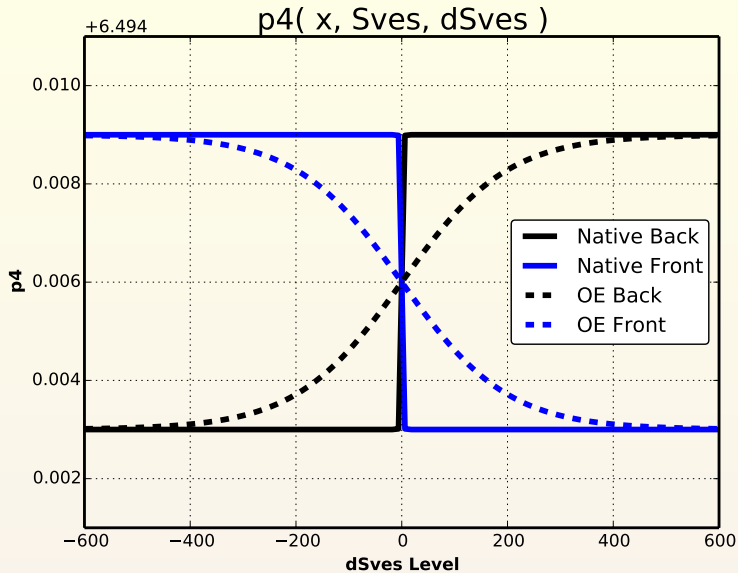


Results for bell shaped p3

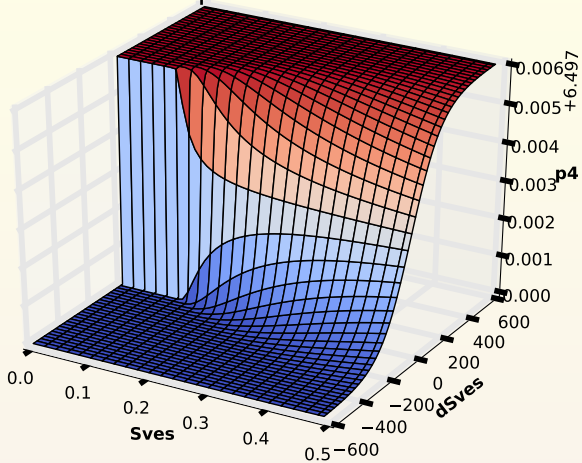
- Now the experimental results can be satisfied at both expression levels
- At native levels, MAPKpp rises linearly, producing constant MI
- At overexpressed levels, MAPKpp has an inverted bell response, producing a MI curve that changes sign

p4 as a function of Sves and dSves

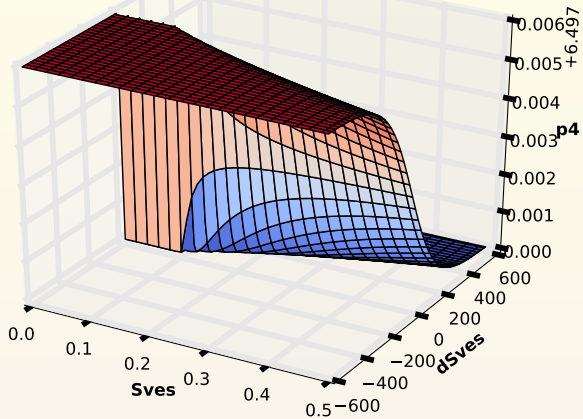
- Previously I've demonstrated why p4 had to be a function of dSves
- dSves serves as the polarity compass btw front and back of the cell
- Now I'm demonstrating why p4 needs to be a function of Sves as well
- Sves serves as sigmoidal strength factor
 - ▶ Low Sves: short transition range
 - ▶ High Sves: long transition range



p4 Back



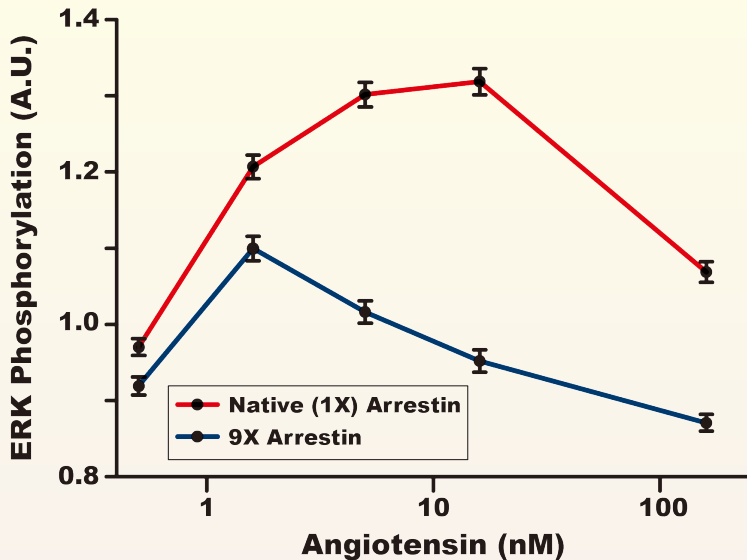
p4 Front



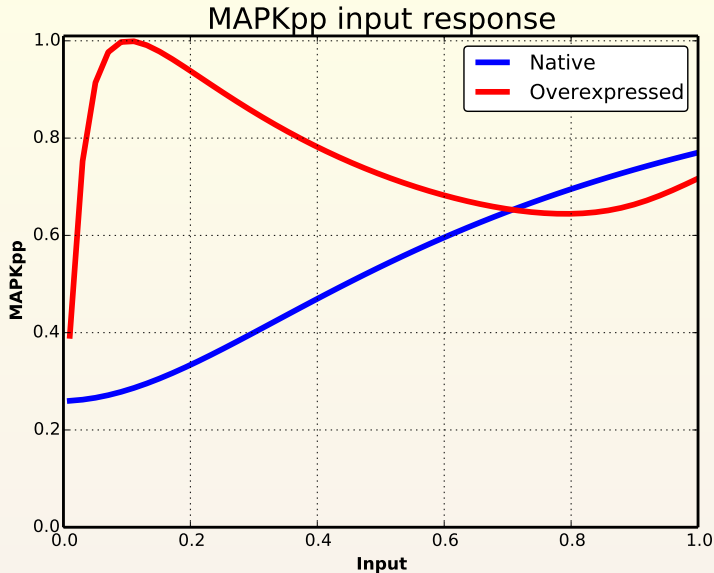
Comparison with experiments

MAPKpp Dose Response

D

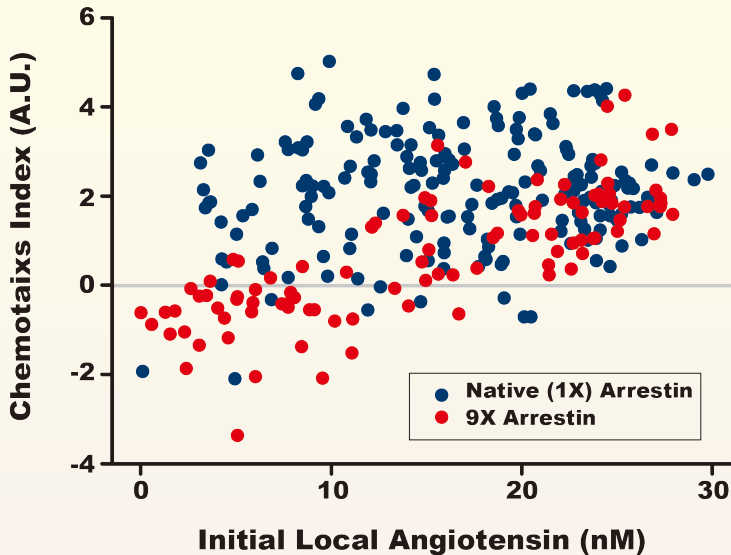


MAPKpp Dose Response

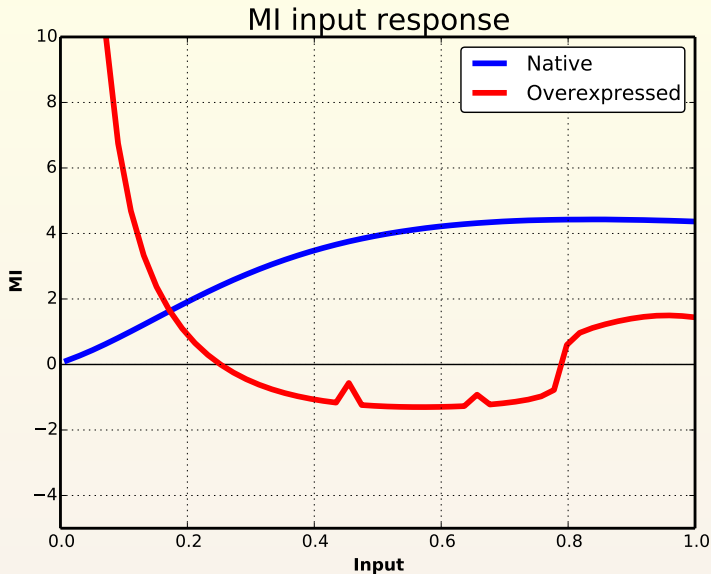


MI Dose Response

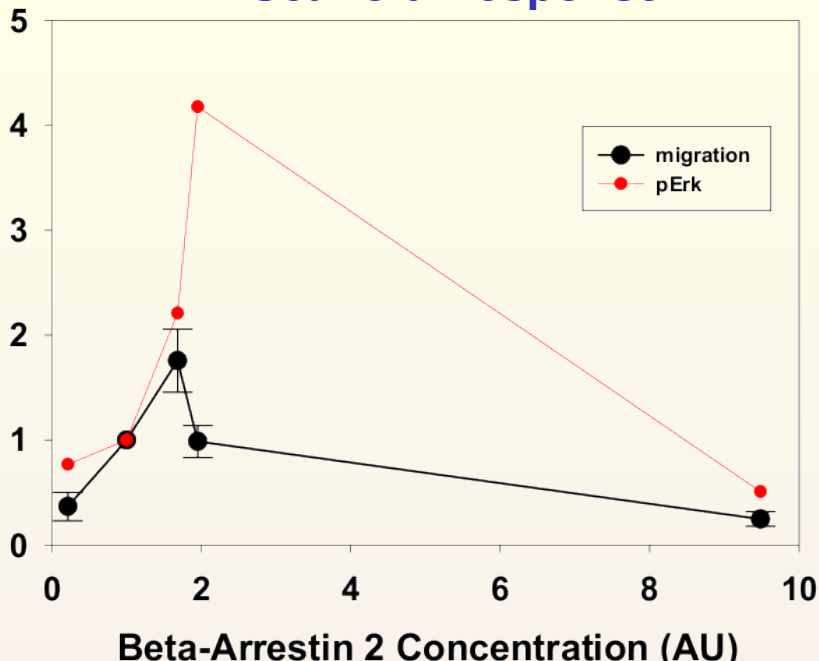
B



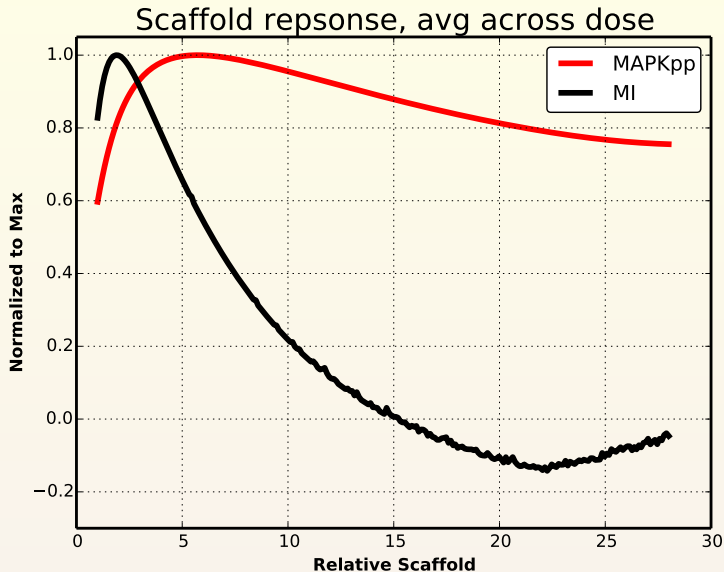
MI Dose Response



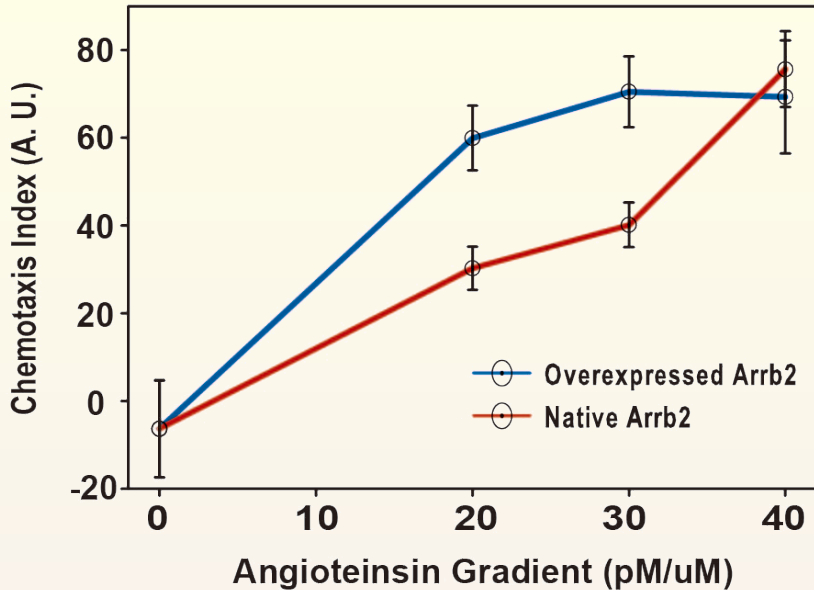
Scaffold Response



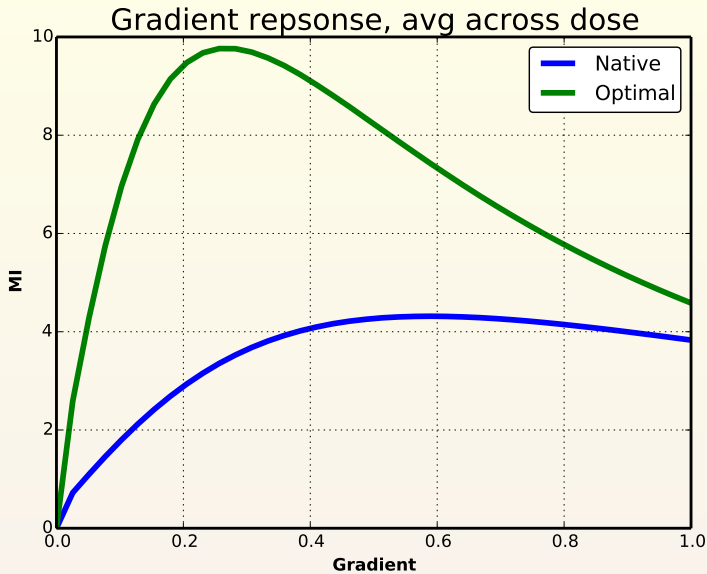
Scaffold Response



Gradient Response

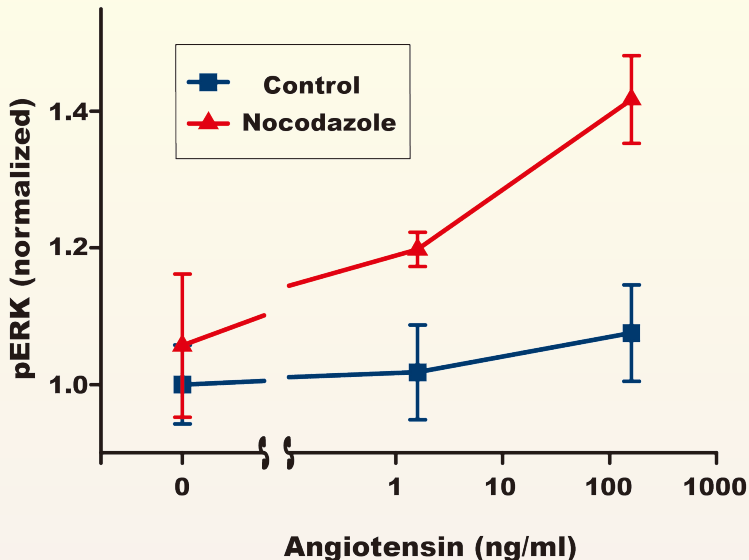


Gradient Response

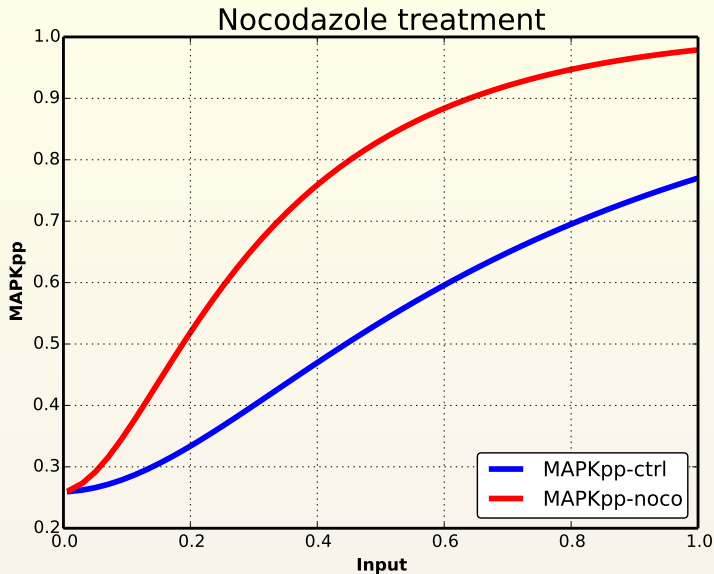


Nocodazole treatment

E

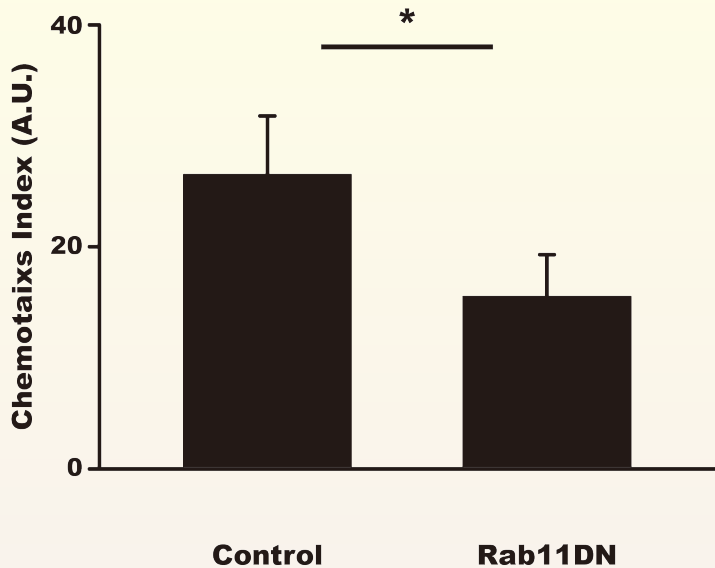


$$S_{ves} \rightarrow S_{cyto}, 20\%p_4$$



Rab11-DN

F



Rab11-DN

