

# Sum-of-squares methods for analyzing G-protein signaling

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# [ Parameter Estimation ]

- ODE model of G-protein signaling
- Describe the feasible parameter space

# [ G-proteins ]

- Important in cell signal transduction
- Heterotrimers
- Found associated with seven-transmembrane-spanning receptors
- Examples in our photoreception, taste, and olfaction, and in yeast conjugation.

# G-proteins

[http://stke.sciencemag.org/content/vol2004/issue218/images/data/re3/DC1/G\\_Protein-Cycle\\_STKE.swfh](http://stke.sciencemag.org/content/vol2004/issue218/images/data/re3/DC1/G_Protein-Cycle_STKE.swfh)

- How they work
- ODE model

$$\dot{x}_1 = -k_1 x_1 u + k_2 x_2 - k_3 x_1 + k_5$$

$$\dot{x}_2 = k_1 x_1 u - k_2 x_2 - k_4 x_2$$

$$\dot{x}_3 = -k_6 x_2 x_3 + k_8 (G_{total} - x_3 - x_4)(G_{total} - x_3)$$

$$\dot{x}_4 = k_6 x_2 x_3 - k_7 x_4$$

$$y = (G_{total} - x_3) / G_{total}$$

where:

input,  $u$ =[Ligand],

$x_1$ =[Receptor],  $x_2$ =[Receptor:Ligand],

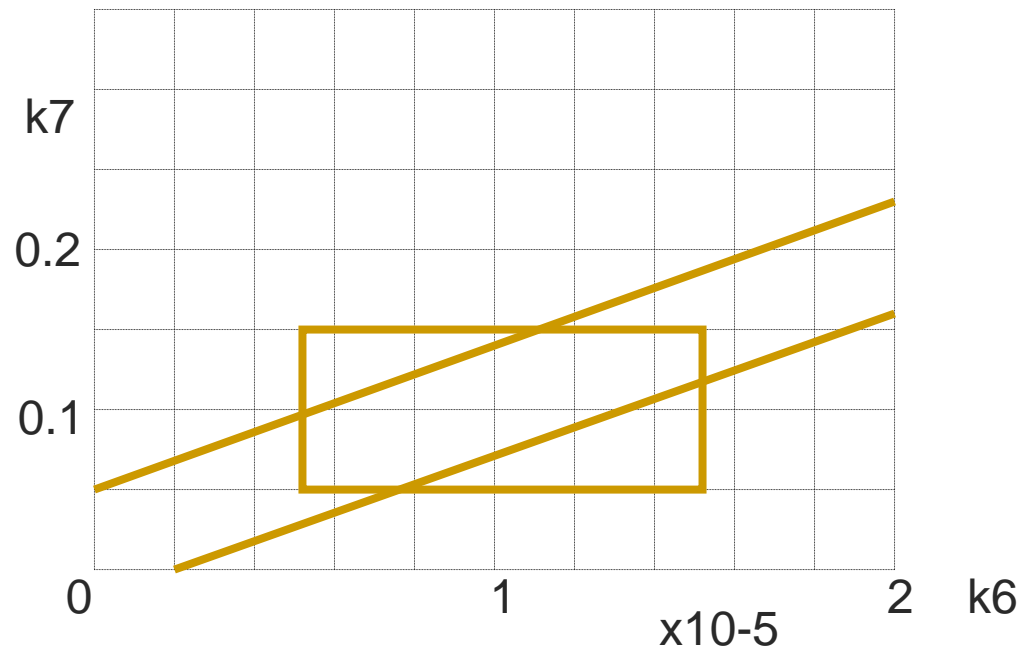
$x_3$ =[ $G_{undissociated}$ ],  $x_4$ =[ $G_{active}$ ] or  $G_{\alpha}$ -GTP

# [ Methodology ]

- Dose response data
- Model, quadratic surrogate model
- Find bounds on feasible parameter space using SOS optimization toolbox
- Bounding ellipsoids could point to correlations between parameters

# [ Results ]

- Studying k6 and k7 with all other parameters fixed
- Superimposed bounds: diagonal strip on rectangle



# [ Are $k_6$ and $k_7$ correlated? ]

- The G-protein activation and deactivation rates are correlated
- Is this true throughout feasible parameter space?

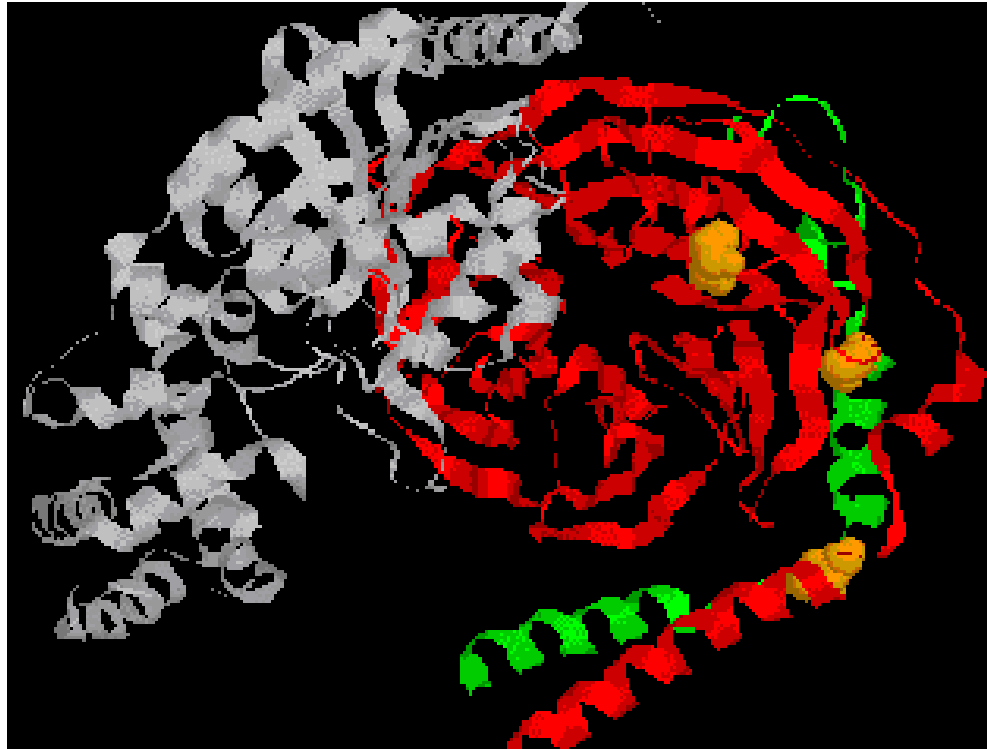
# [ Conclusion ]

- We described a **subspace** of parameters consistent with data, the given ODE, and a-priori constraints
- We need to extend the size and range of well-conditioned SOS problems
- Future research includes probing the fragility of SOS

# [ FOSBE Paper, People ]

- Application of Robust Model Validation Using SOSTOOLS to the Study of G-protein signaling in yeast
- Tau-Mu Yi, Maryam Fazel, Jorge Goncalves, Xin Liu, Tosin Otitoju, Stephen Prajna, Antonis Papachristodoulou, John C. Doyle

# [ The End ]



[http://www.urmc.rochester.edu/phph/graduate/IND447/gprotein\\_receptors.html](http://www.urmc.rochester.edu/phph/graduate/IND447/gprotein_receptors.html)

- Thank you for listening!

Structure of a trimeric G protein:

alpha (grey),  
beta (red),  
gamma (green)