Dec 22, 2022

**Outline**

**Introduction:**

- EGFR pathway

- Previous models and short term signaling experimental data:

1- Kholodenko

2- Blinov

Describing the strengths and weaknesses of these models.

- Rule-based modeling

- Energy Modeling

- Scope of this paper: Presenting an eBNG model for EGFR pathway that, in

contrast to the previous models, is fitted to the data and address the problem of regulatory

complexity brought on by the cooperative interactions between different sites in the EGFR

signaling pathway.

**Methods:**

- Building the rule-based model

- Building the energy-based model in 5 steps

- Model fitting

1- Parameter estimation using PEtab format and pyPESTO

2- MCMC sampling using pyPESTO

- Sensitivity Analysis

- ...

**Results:**

- Blinov model violates detailed balance (Detailed balance proof) ??

- Fitting the rule-based version of the Kholodenko’s model to the data

1- pyPESTO results for parameter estimation and comparsion to the original

Kholodenko’s model fit

2 - MCMC sampling and convergence diagnostics of the fitted Kholodenko’s model

3- Showing that the presented model by Kholodenko is able to describe the EGFR

transient behavior (identifiability of all the parameters in the model) but in the

original paper, they have not using a systematic approach which has been addressed

in this paper

- Energy-based model of EGFR pathway

1- Step by step energy modeling of EGFR signaling pathway

2- EGFR eBNG model in step 4 recovers the Kholodenko’s original output

3- Expanding the energy-based model using multiple binding partners on EGFR in step 5

- Fitting the energy-based version of the EGFR model to the data

1- Parameter estimation results

2- MCMC sampling results

3 - ...

- Sensitivity analysis results

**Discussion:**

**References:**

**Tables:**

**Figures:**