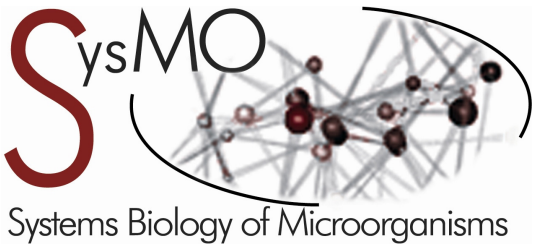
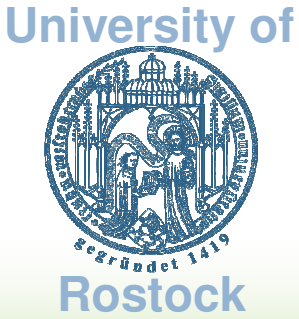
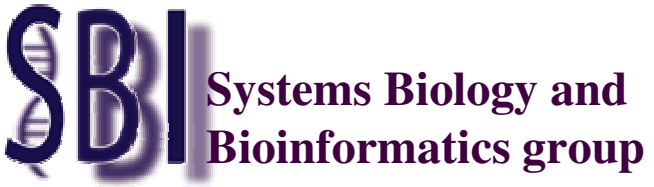
Models of the general stress response using the SBToolbox2 – can SYCAMORE substitute? –

Ulf Liebal



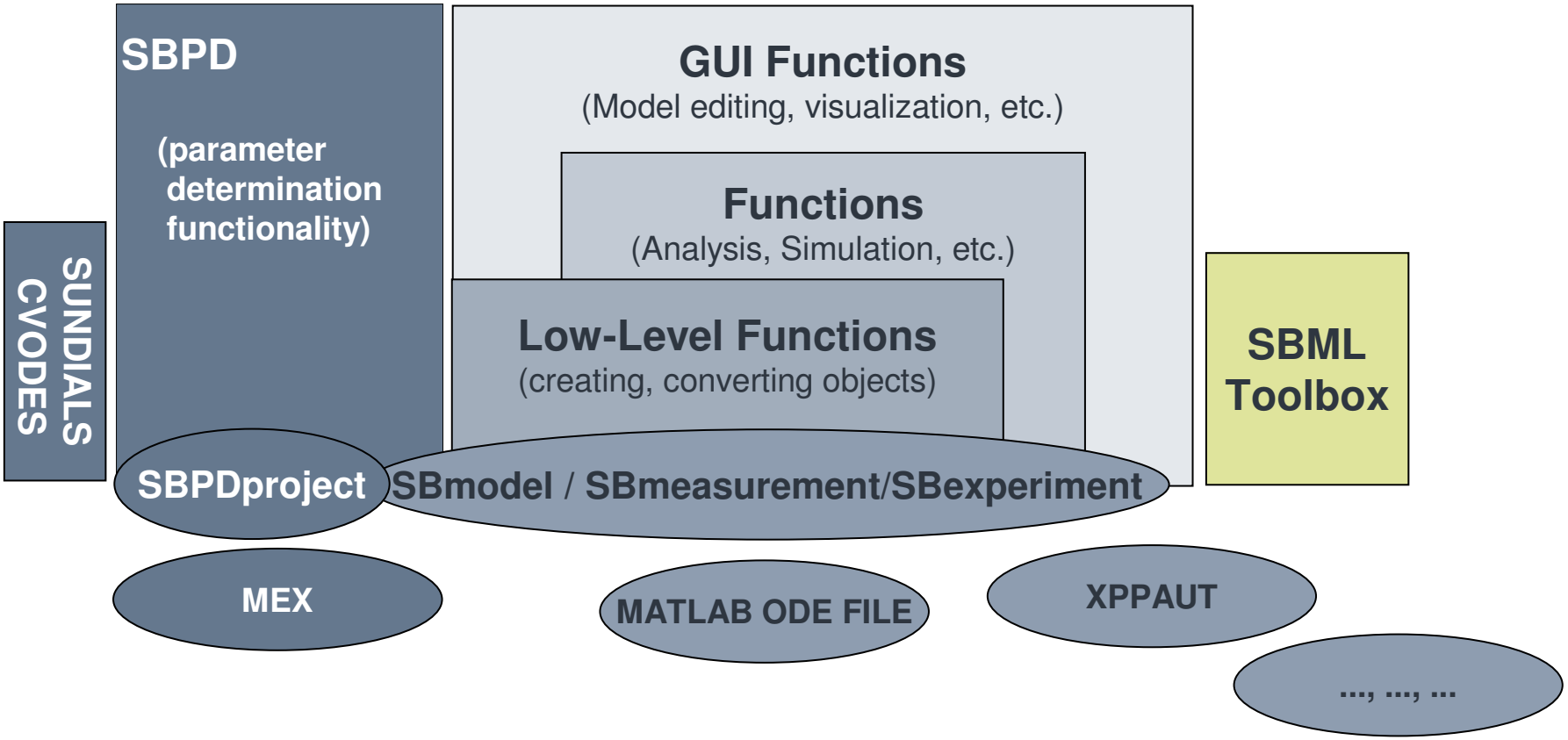




Outline

1. Introduction to the SBToolbox2
2. Biological background of the modelling target
3. Modelling procedure
    - Integration of parameter estimation
    - Loops over different parameter regimes
4. Conclusions/Questions

Introduction to the SBToolbox2



Introduction to the SBToolbox2

```
********** MODEL NAME
Simple model
********** MODEL STATES
d/dt(A) = -R
d/dt(B) = R
A(0) = 1
B(0) = 0
********** MODEL PARAMETERS
k1 = 0.5
********** MODEL REACTIONS
R = k1*A
```

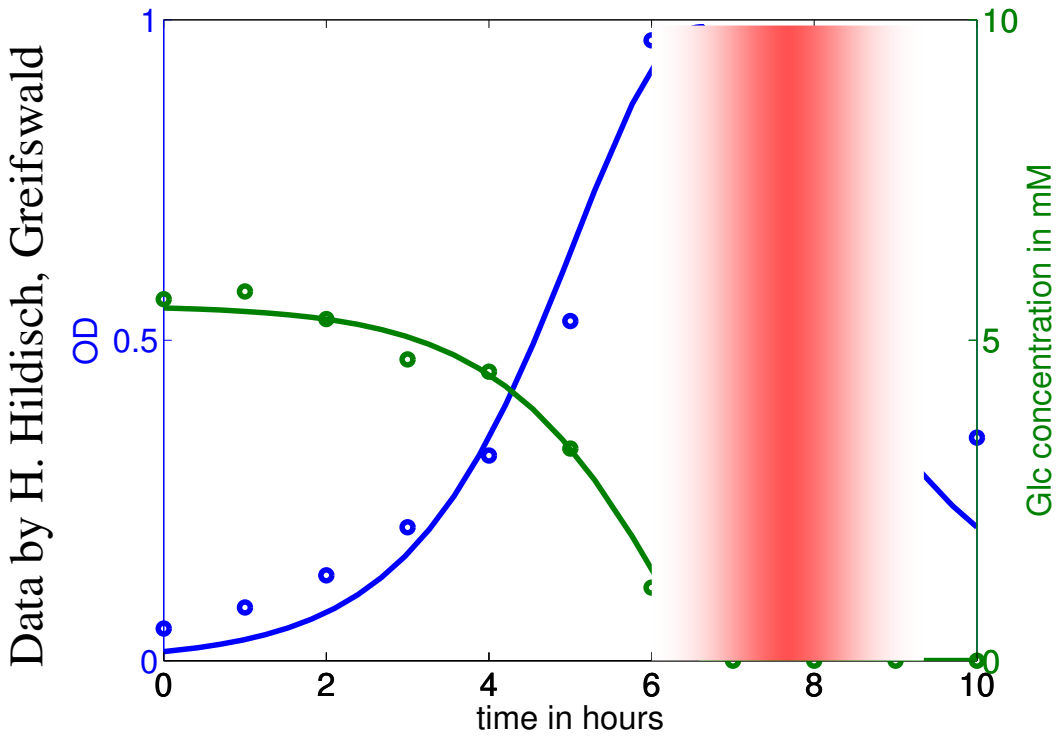
```
********** EXPERIMENT NAME
Simple Experiment for simple model
********** EXPERIMENT INITIAL PARAMETER AND STATE SETTINGS
k1 = 2
********** EXPERIMENT PARAMETER CHANGES

********** EXPERIMENT STATE CHANGES
time=10, A=1
```

```
********** MODEL NAME
Simple model
********** MODEL STATES
d/dt(A) = -R
d/dt(B) = R
A(0) = 1
B(0) = 0
********** MODEL PARAMETERS
k1 = 2
********** MODEL REACTIONS
R = k1*A
********** MODEL EVENTS
StateChange_1 = ge(time,10),A,1
```

The result is a new model where the experimental settings have been added

Biological background of modelling



Glucose starvation

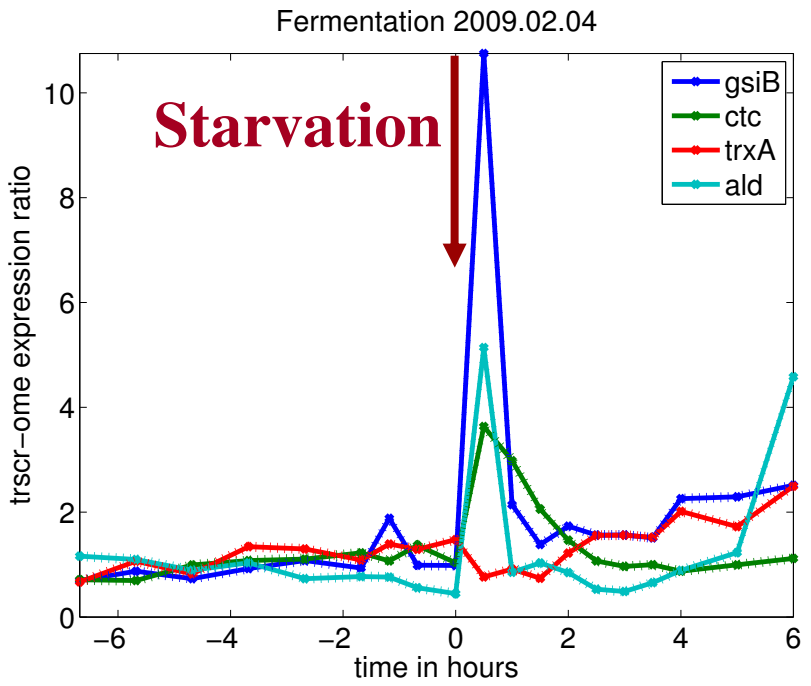
↓

Reorganisation of metabolism and of protein expression

Glc starvation heralds possible future stress incidents.
Diversification of phenotypes to maximise survival. (Chemotaxis, Competence, Sporulation, General Stress Response, etc.)

Biological background of modelling

sigB mediated General Stress Response:
sensing of the cellular energy level
control of ~150 genes
adaptive response



Data by P. Kumar Sappa, Greifswald

Biological background of modelling

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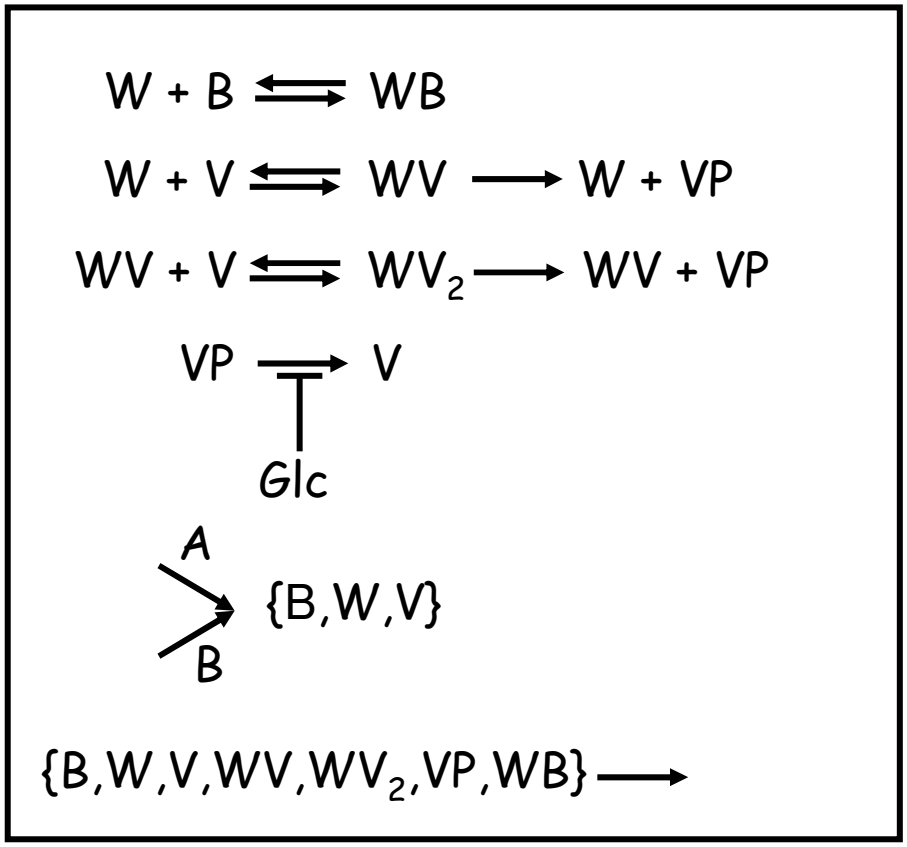
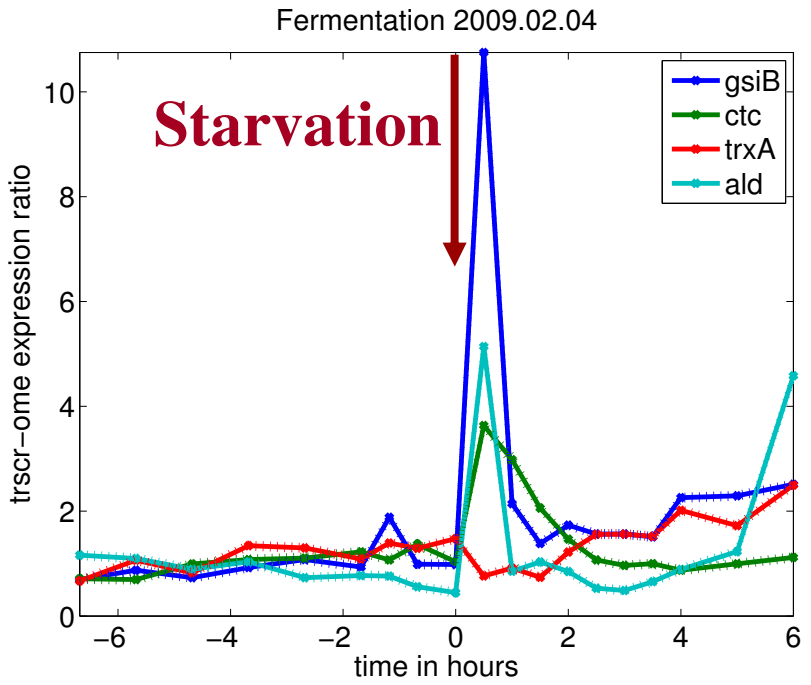
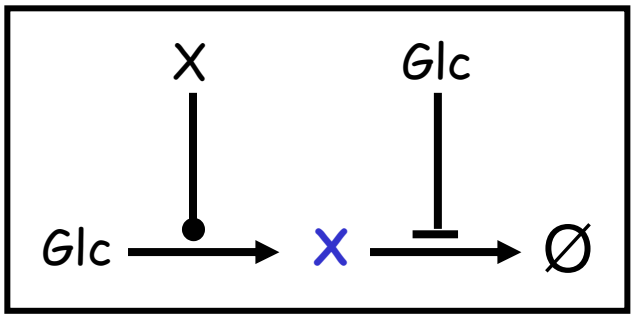




Data by P. Kumar Sappa, Greifswald

Integration of parameter estimation

Glc-Biomass model



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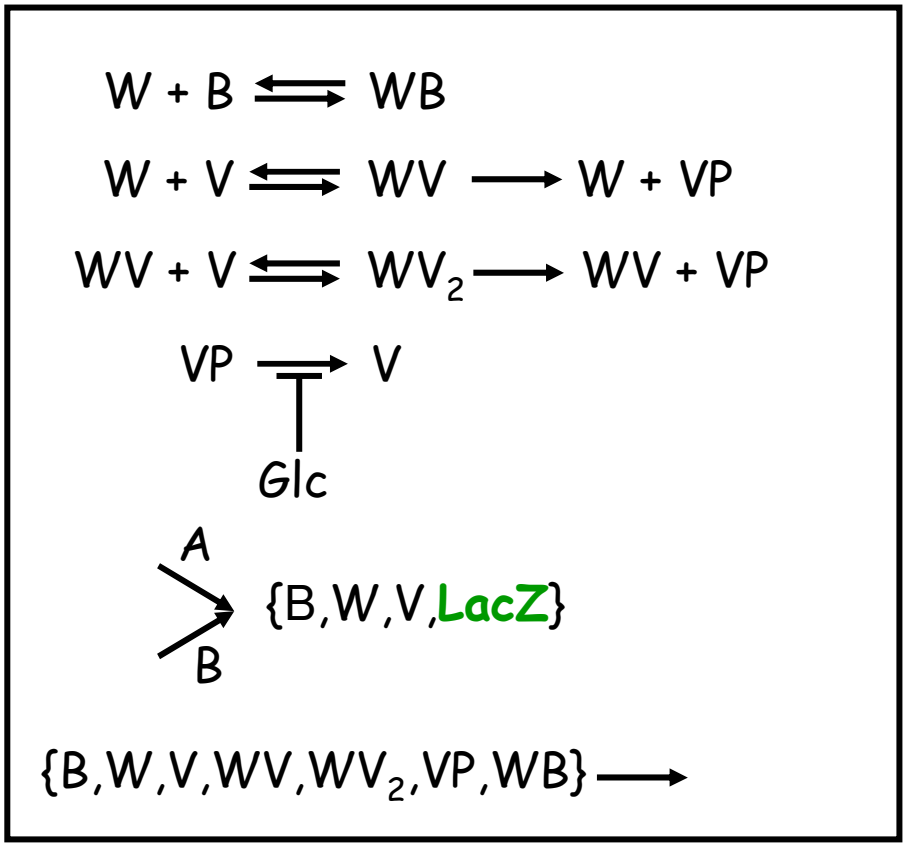
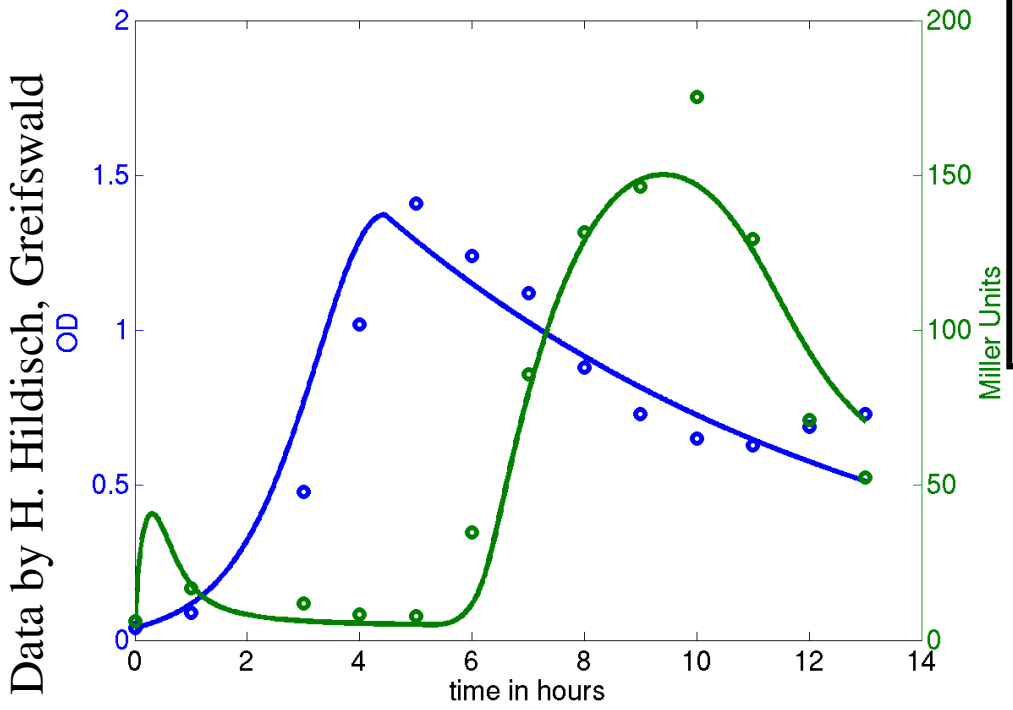
sigB-model





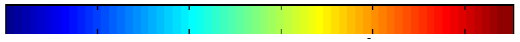
Problem: Identifiability

Loops over different parameter regimes

How do the **reactions cooperate** to establish high fitness **before starvation**?

Strategy:

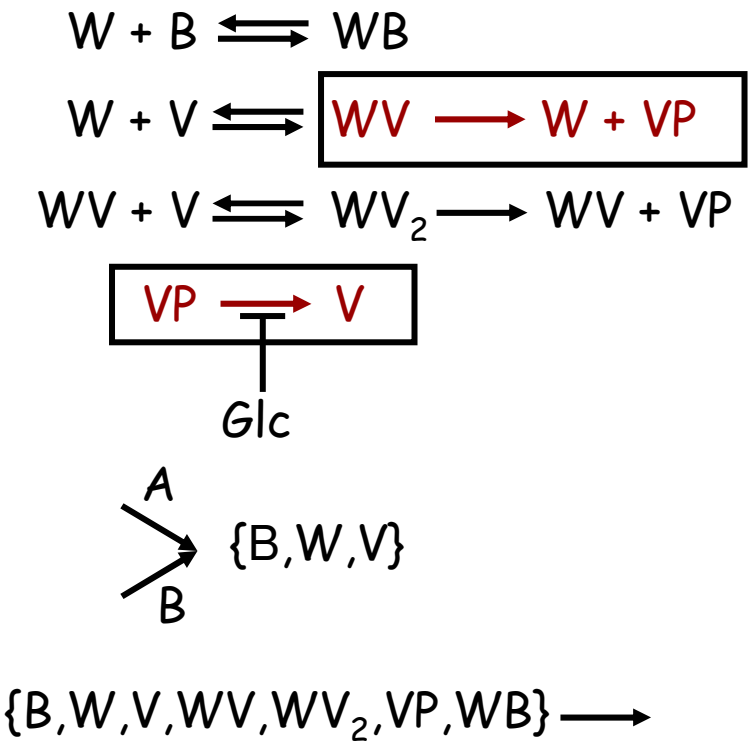
1. Select two parameters;
2. Defining magnitudes for parameter changes;
3. Randomly combining parameter values;
4. Evaluating their steady state fitness.

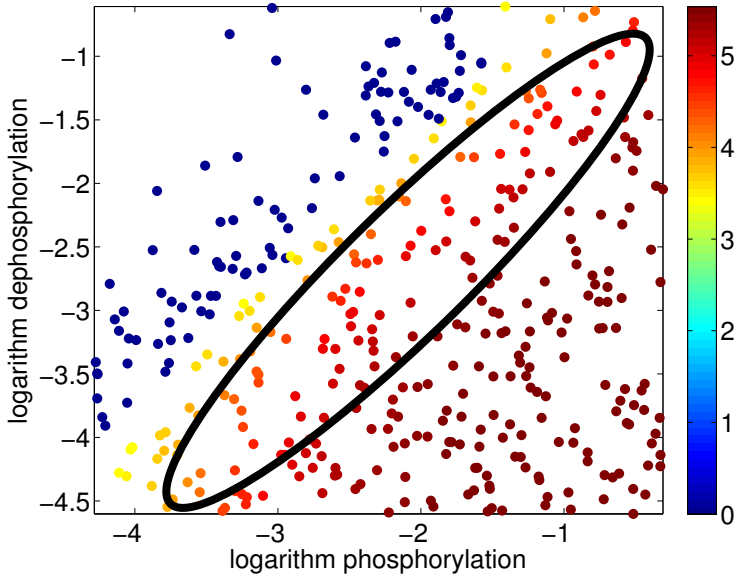


high ratio low ratio

of B/WB

Loops over different parameter regimes





- Determining the minimum value of phosphorylation.
- Fitness must be sensitive to dephosphorylation.

Conclusions/Questions

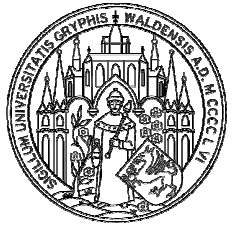
1. Evaluating model results based on user defined fitness functions.
2. allowing for loops with arbitrary distributions of parameter values.
3. Close contact interfaces of the programs with each other, such that models are easily imported to Matlab, Mathematica or Octave/Scilab.
4. Standard schemes for experimental data.

Acknowlegdements

Praveen Kumar Sappa, Greifswald
Hendrikje Hildisch, Greifswald
Thomas Millat, Rostock
Leif Steil, Greifswald
Uwe Völker, Greifswald
Olaf Wolkenhauer, Rostock

Thank you!

EMA Uni. Greifswald



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