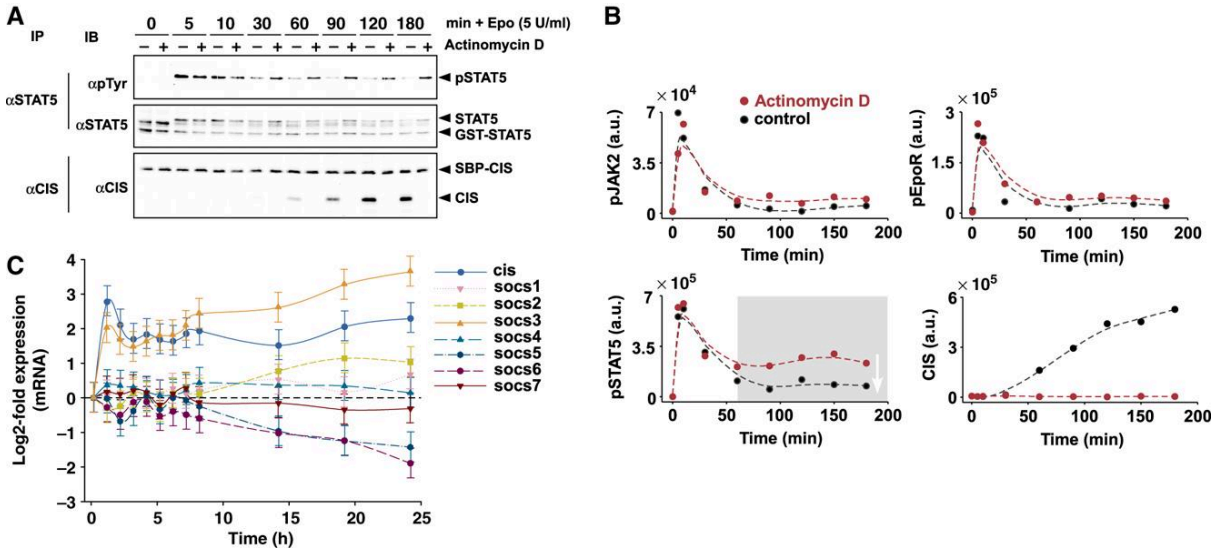
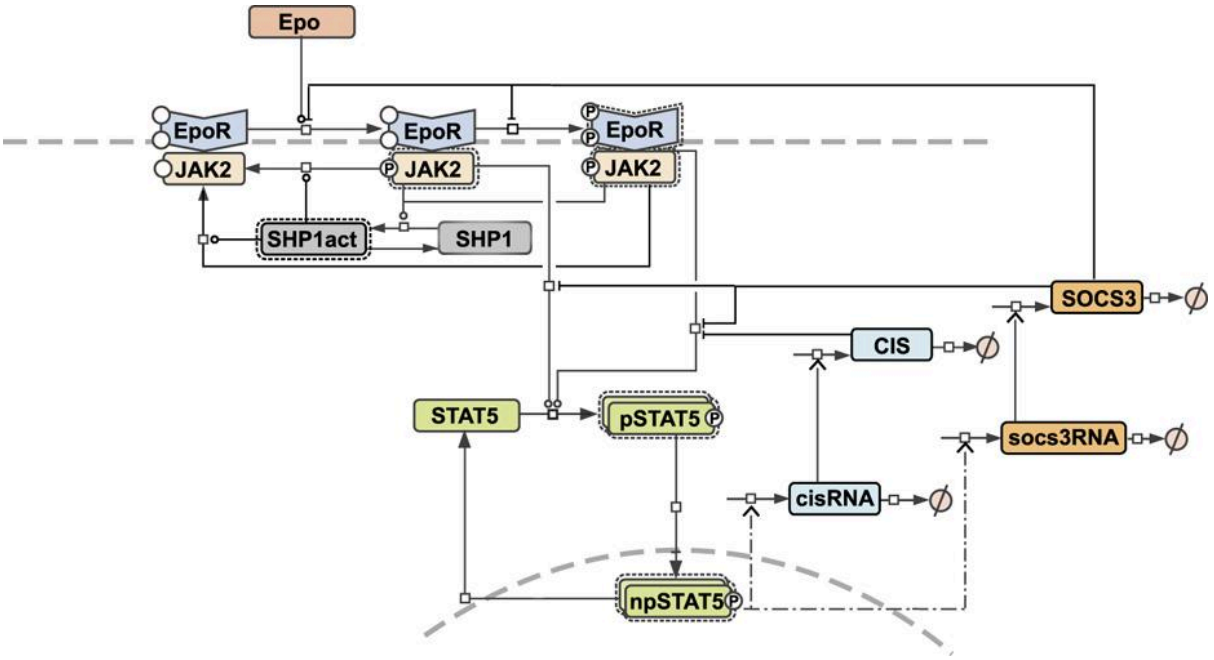
from https://www.embopress.org/doi/full/10.1038/msb.2011.50

# Figure 1



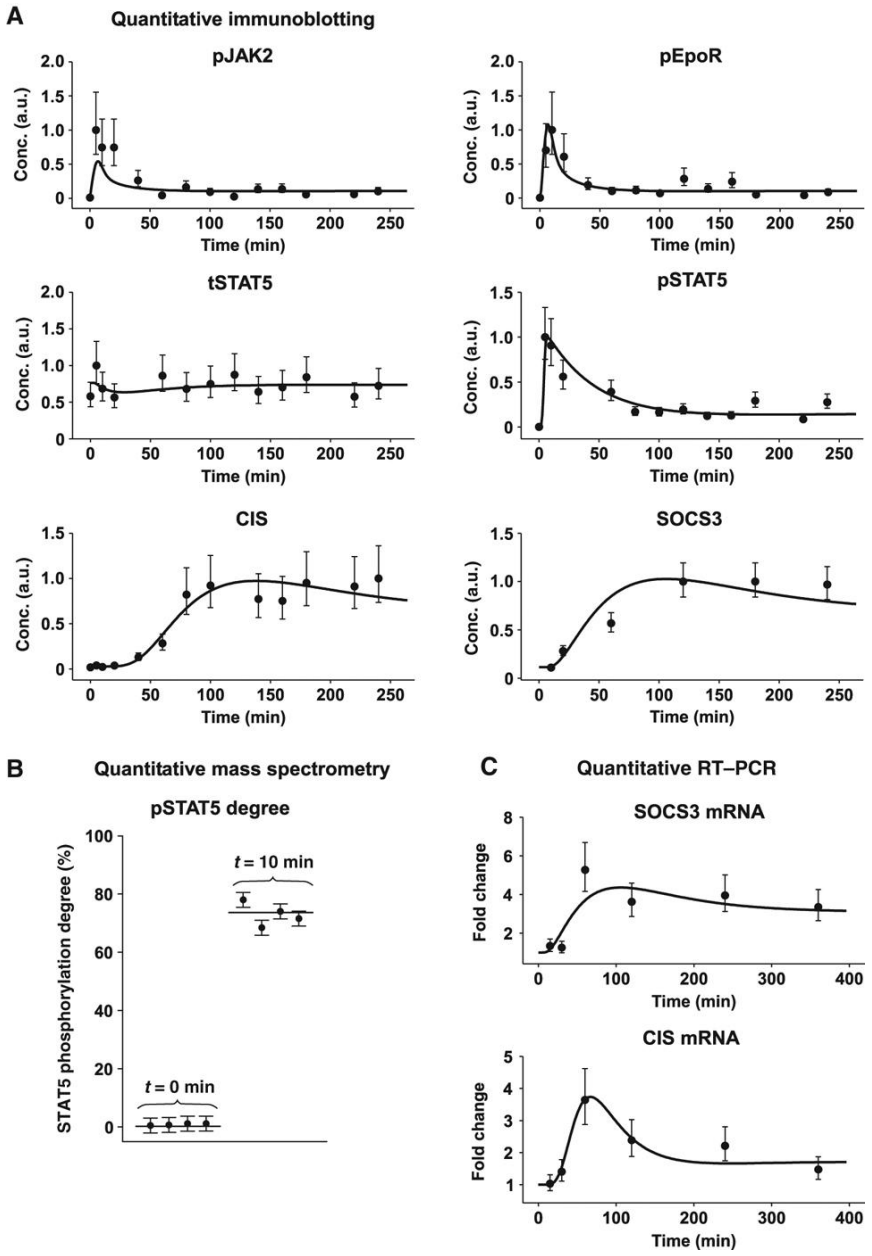

→ nein, nur experimentelle Daten (Western Blot, Microarray)

# Figure 2




→ nein, nur graphische Darstellung Modell

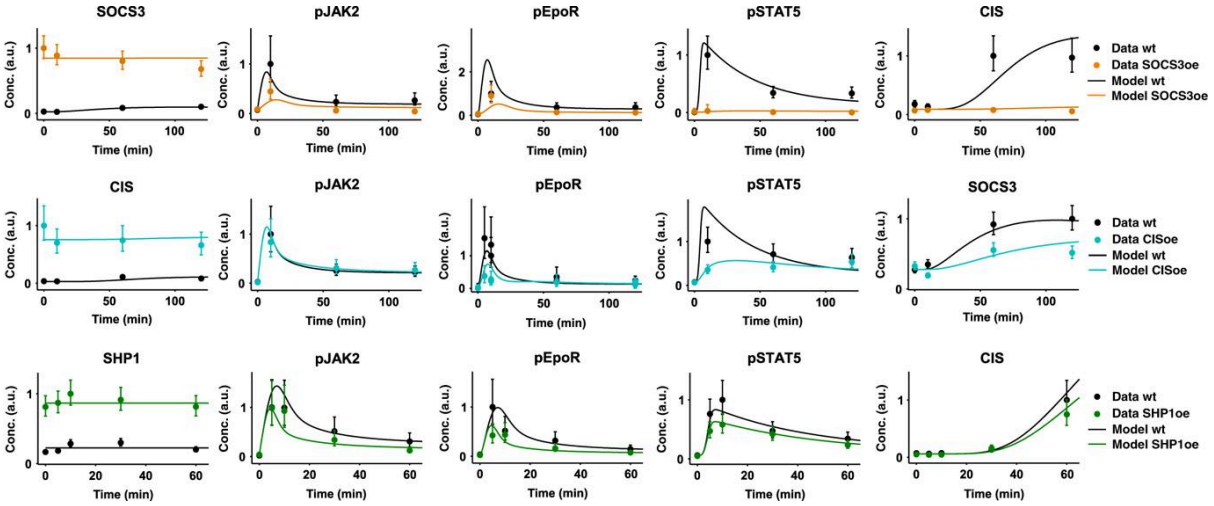
# Figure 3




*Model calibration with experimental data of JAK2-STAT5 signaling obtained by different experimental techniques. For all experiments, primary CFU-E cells were starved and stimulated with 5 U/ml Epo. At the indicated time points, samples were subjected to (A) quantitative immunoblotting, (B) mass spectrometry analysis or (C) qRT–PCR. Experimental data (black circles) with estimated standard errors and trajectories of the best fit (solid lines) are represented. Mass spectrometry data represent replicates of four independent experiments. (For additional experimental data used for the model calibration, see Figure 4 and Supplementary Figures S11–S23.) In total, 531 data points representing 18 different experimental conditions were used for model calibration. Source data is available for this figure at www.nature.com/msb.*

https://jjj.biochem.sun.ac.za/models/bachmann/
SED-ML file to reproduce Figure 3

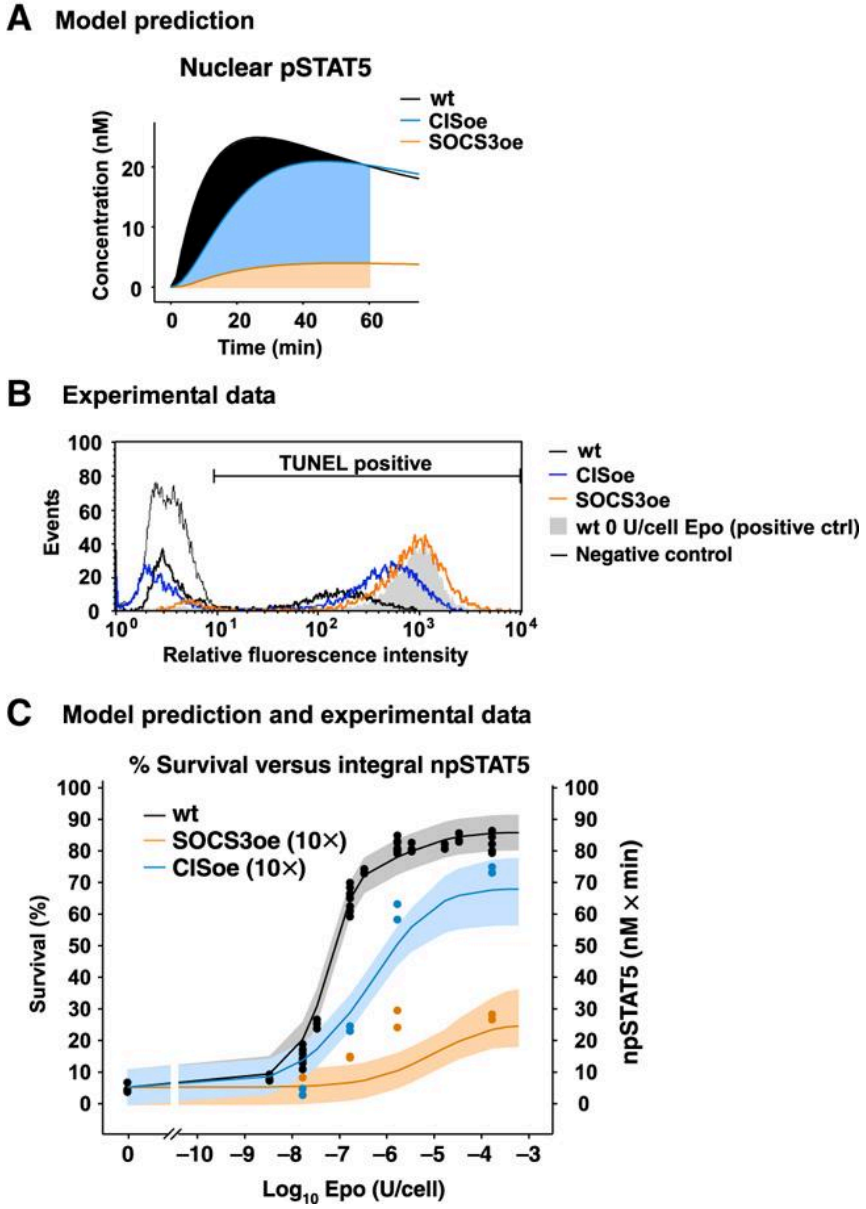
# Figure 4




*Experimental data of JAK2-STAT5 signaling under perturbed conditions used for model calibration. CFU-E cells were retrovirally transduced with SHP-1 (SHP1oe), SOCS3 (SOCS3oe) or CIS (CISoe). Positively transduced cells were starved and stimulated with 5 U/ml Epo for 60 or 120 min, respectively. Cellular lysates were subjected to immunoprecipitation and immunoblotting to determine activation profiles of JAK2-STAT5 pathway components for overexpression conditions compared with control cells. Trajectories of the best fit are indicated (solid lines) with experimental data (circles) and estimated standard errors. For pEpoR in the CIS overexpression experiment, two data sets were combined. (For further information and additional experimental data used for the model calibration, see Figure 3 and Supplementary Figures S11–S23.) Source data is available for this figure at www.nature.com/msb.*

*https://www.embopress.org/action/downloadSupplement?doi=10.1038%2Fmsb.2011.50&file=msb201150-sup-0006-SourceData-S6.xls*

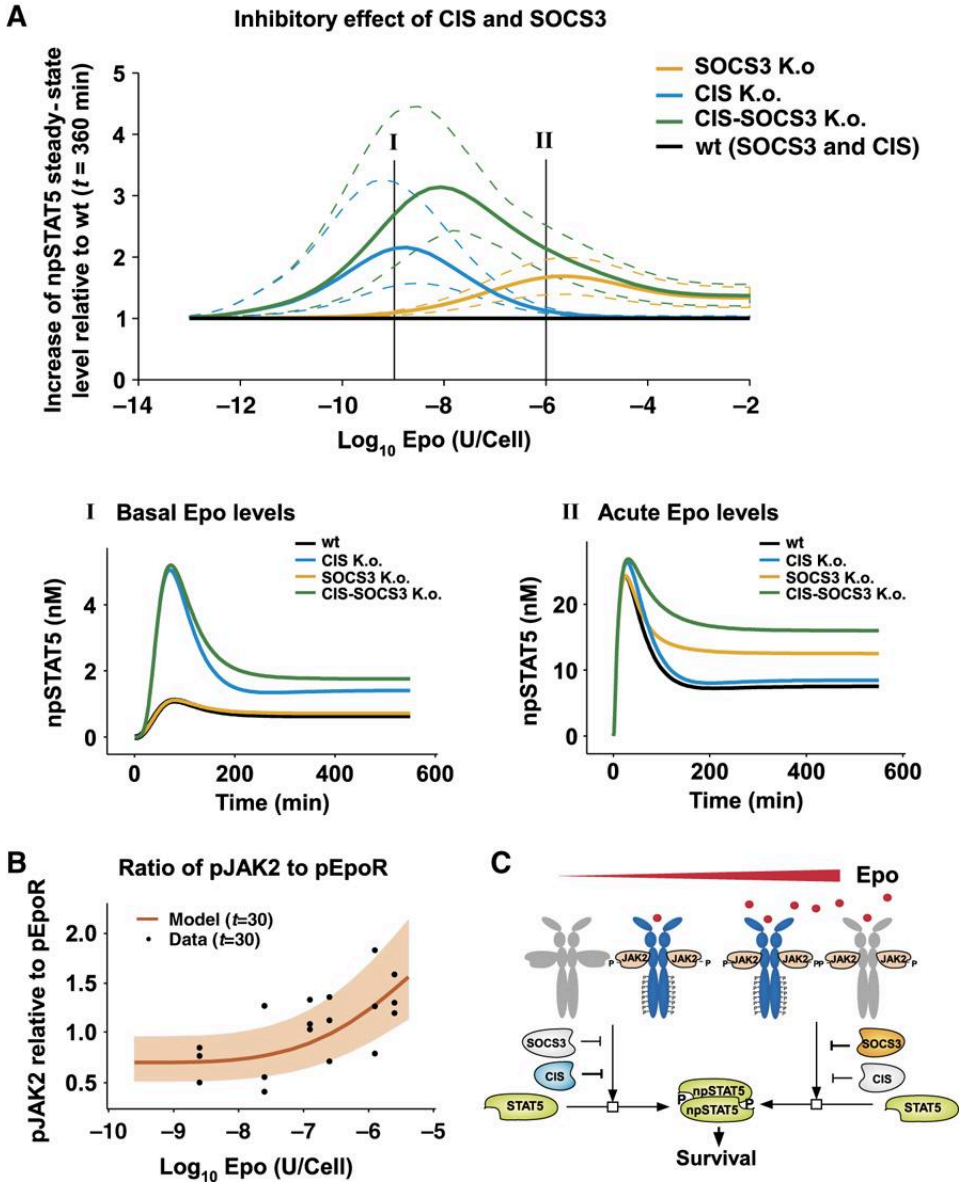
# Figure 5




*Linking the integral response of phosphorylated STAT5 in the nucleus to the survival rate of CFU-E cells. (A) The calibrated model was used to simulate the integral response of phosphorylated STAT5 in the nucleus (npSTAT5) over the broad physiological range of Epo concentrations in wild-type, CIS and SOCS3 overexpressing (oe) cells. A representative example at Epo=10−6.78 U/cell is depicted. (B) TUNEL assay to determine the fraction of apoptotic cells. Wild-type CFU-E cells and cells overexpressing SHP-1, CIS or SOCS3 were cultured 24 h in various Epo concentrations. Histograms show the representative result of a TUNEL assay with Epo=10−6.78 U/cell. Cells for positive control were treated with DNaseI for 10 min. (C) Overlay of scaled integral response of npSTAT5 (60 min) including 95% confidence bands (shades) and experimentally determined survival rates of CFU-E cells for wild-type cells, CIS and SOCS3 overexpressing cells (circles). Source data is available for this figure at [www.nature.com/msb](www.nature.com/msb).*

*https://www.embopress.org/action/downloadSupplement?doi=10.1038%2Fmsb.2011.50&file=msb201150-sup-0007-SourceData-S7.xls*

# Figure 6




*Dual negative feedback with divided function in JAK2-STAT5 signaling. (A) The steady-state level of phosphorylated STAT5 in the nucleus was simulated in the presence of only one transcriptional negative regulator, CIS or SOCS3, and in the absence of both. The increase of pSTAT5 steady-state levels was calculated relative to wild-type cells (black line) at t=360 min. Dashed lines indicate upper and lower 95% confidence bands for the prediction. For two exemplary Epo concentrations, (I) Epo=10−9 U/cell and (II) Epo=10−6 U/cell, the time profiles of npSTAT5 are shown. (B) Model prediction and experimental data for the increase of phosphorylated JAK2 relative to phosphorylated Epo receptor with rising Epo concentrations at t=30 min. (C) Mechanistic scheme explaining dual negative feedback with divided function in JAK2-STAT5 signaling for different Epo concentration ranges. The concentration dependency of the inhibitory effects of CIS and SOCS3 is caused by the increasing fraction of phosphorylated JAK2 compared with phosphorylated EpoR. At low Epo levels, CIS mostly impacts pEpoR-dependent STAT5 activation by preventing binding of STAT5 via its SH2 domain to the specific phosphotyrosine sites on the EpoR receptor. At high Epo concentrations, SOCS3 mostly impacts pJAK2-dependent STAT5 phosphorylation by inhibiting the activation of JAK2 via its kinase inhibitory region (KIR)*

# Supplementary Figure 9

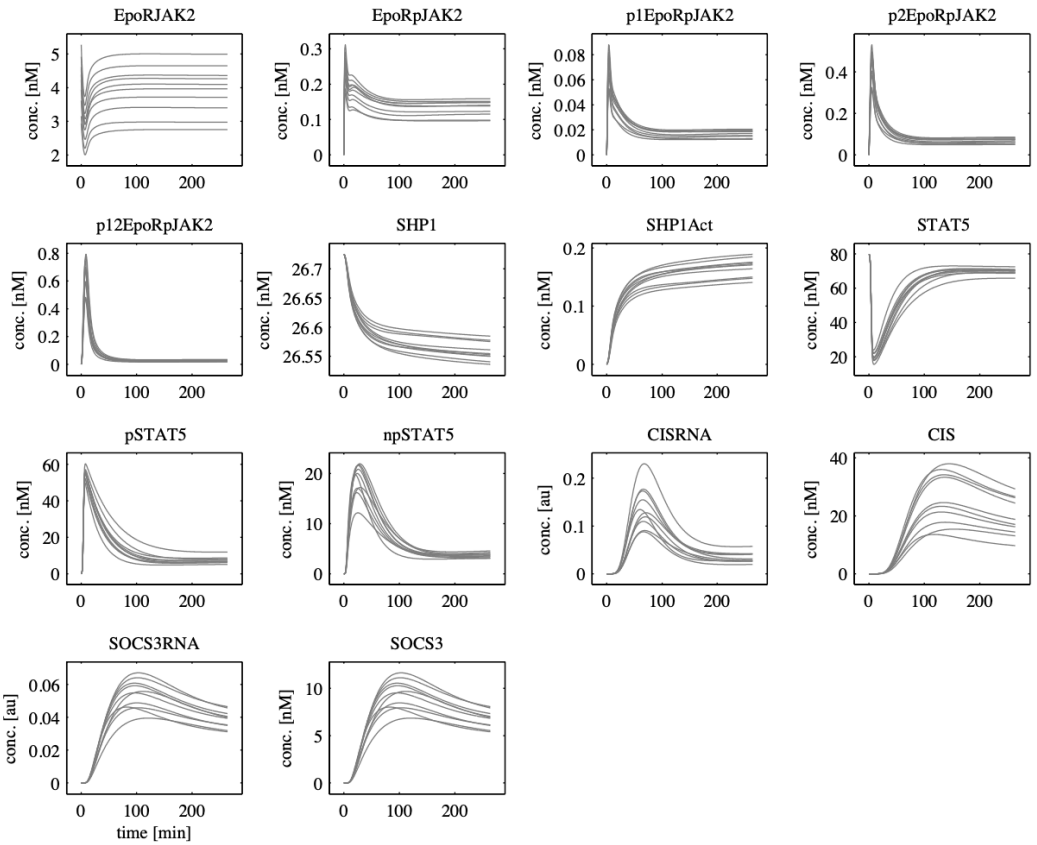



**Figure S9: Simulation of the effect of extrinsic noise on the model dynamics.**
The figure shows the effect of extrinsic noise on the model dynamics. For the computation, the parameters accounting for the concentration level of the modeled components, CISEqc, CISRNAEqc, SOCS3Eqc, SOCS3RNAEqc, init_EpoRJAK2, init_SHP1 and init_STAT5 where varied by 10% in logarithmic space around their estimated values. Ten realizations are displayed. The qualitative behaviour of the model dynamics, especially the STAT5 activation, is not affected by extrinsic noise, e.g. bi-stability does not occur in the parameter ranges that are determined by the experimental data.

https://www.ebi.ac.uk/biomodels/BIOMD0000000347
https://jjj.biochem.sun.ac.za/models/bachmann2/
SED-ML file to reproduce Supplementary Figure 9

# Notes

in den Figures sind oft Modelldaten & experimentelle Daten enthalten - mit SED-ML können wir dann aber nur die Modelldaten reproduzieren (außer man hat irgendwie Zugriff auf die experimentellen Daten)

Beispiel: https://www.ebi.ac.uk/biomodels/BIOMD0000000861#Curation

es gibt auch noch viele Supplementary Figures mit detaillierteren Infos zu den Experimenten
https://www.embopress.org/action/downloadSupplement?doi=10.1038%2Fmsb.2011.50&file=msb201150-sup-0001.pdf

noch ein paar Quellen - keine Ahnung wie hilfreich
https://github.com/Benchmarking-Initiative/Benchmark-Models/tree/master/Benchmark-Models/Bachmann_MSB2011
https://fairdomhub.org/models/185
https://jjj.bio.vu.nl/models/experiments/?id=bachmann&model=