IL-1β induced and p38$^{\text{MAPK}}$-dependent activation of MK2 in hepatocytes: signal transduction with robust and concentration independent signal amplification

Supplementary Information s2

Modeling of the Il-1β induced and p38 dependend MK2 activation

Contents

1 Mathematical Modeling

In the following the used mathematical model based on ordinary differential equations (ODE) is described. The model is calibrated by a maximum likelihood estimation using quantitative experimental data obtained by a western blot analysis. To obtain the real units in μM of p38 and MK2 the immunoblot data were calibrated with an internal standard. The estimation of the unknown calibration parameters of the internal standard and the dynamic ODE parameters was done simultaneously in a single multi-experiment fit. The measurement error of the data is modeled by a error model assuming a constant gaussian error on a logarithmic scale independent for each experiment. The uncertainties in data are leading to uncertainties in the estimated parameter. With the profile likelihood method it is possible to determine the uncertainty in a quantitative manner [2].
To implement the model, the experiments and to perform the maximum likelihood estimation, we used the Data2Dynamics software [3]. With this software it is also possible to perform the profile likelihood method.

The general structure of our ODE model is of the form

$$\frac{dx(t)}{dt} = f(x(t), u(t), p) \tag{1}$$

$$x(t = 0) = x_0 \tag{2}$$

$$y(t) = g(x(t), s) \tag{3}$$

Equation (1) is the ODE describing the time evolution of the vector of the dynamic variables $x(t) \in \mathbb{R}^{n_x}$ with the initial conditions $x_0 \in \mathbb{R}^{n_x}$. The ODE can depend on external inputs $u(t) \in \mathbb{R}^{n_I}$ describing i.e. the addition of the activating cytocine or inhibitors by the experimenter. The ODE also depends on a set of dynamic parameters $p \in \mathbb{R}^{n_p}$ like chemical reaction rate constants. The internal variables $x(t)$ are linked to the measured output $y(t) \in \mathbb{R}^{n_y}$ by the observation function $g(x(t), s)$ depending on the calibration parameters $s \in \mathbb{R}^{n_s}$. The vector of all model parameters $\theta = (p, x_o, s)$ is in general not known and has to be estimated from experimental data.

1.1 Dynamic variables

Our ODE model contains 5 dynamic variables:

- **Dynamic variable 1:** p38

  $$[\mathrm{p38}](\mathrm{t}=0) = \mathrm{init\_p38} \tag{4}$$

  Unit: conc. [μMol/L]

- **Dynamic variable 2:** pp38

  $$[\mathrm{pp38}](\mathrm{t}=0) = \mathrm{init\_pp38} \tag{5}$$

  Unit: conc. [μMol/L]

- **Dynamic variable 3:** MKP

  $$[\mathrm{MKP}](\mathrm{t}=0) = \mathrm{init\_MKP} \tag{6}$$

  Unit: conc. [a.u.] – not accessible

- **Dynamic variable 4:** MK2

  $$[\mathrm{MK2}](\mathrm{t}=0) = \mathrm{init\_MK2} \tag{7}$$

  Unit: conc. [μMol/L]

- **Dynamic variable 5:** pMK2

  $$[\mathrm{pMK2}](\mathrm{t}=0) = \mathrm{init\_pMK2} \tag{8}$$

  Unit: conc. [μMol/L]

1.2 Input variables

The model contains 3 external inputs variables:

- **Input variable 1:** IL1b

$$[\mathrm{IL1b}](t) = \quad \mathrm{input\_il1b} \tag{9}$$

  Unit: conc. [ng/mL]

  The p38-MK2 pathway is activated by the addition of different concentrations of IL-1β. This concentration is implemented by the parameter $input\_il1b$ which is set for each condition in each experiment.

- **Input variable 2:** SB203580

$$[\mathrm{SB203580}](t) = \quad \mathrm{input\_sb203580} \tag{10}$$

  Unit: conc. [μM]

  In some experiments we added different concentrations of SB203580 to inhibit the phosphorylation of MK2. This is modeled by the parameter $input\_sb203580$.

- **Input variable 3:** PhosphaInh

$$[\mathrm{PhosphaInh}](t) = \quad \mathrm{input\_phosphaInh} \tag{11}$$

  Unit: conc. [μM]

  Additionally we performed experiments where we inhibited all phosphatases of the system. This is described by the external input PhophoInh which is defined by the parameter $input\_phosphaInh$.

- **Input variable 3:** MK2_knockout

$$[\mathrm{MK2\_knockout}](t) = \quad \mathrm{mk2\_ko} \tag{12}$$

  Unit: bool. [1]

  To better characterize the system we performed experiments with MK2 knockout mice. This is modeled by the parameter $mk2\_ko$ which is set to zero for wild type mice and to one for MK2 knockout mice.

Unless stated otherwise we use for the external input:

$$\mathrm{input\_il1b} = 0 \tag{13}$$
$$\mathrm{input\_phosphaInh} = 0 \tag{14}$$
$$\mathrm{input\_sb203580} = 0 \tag{15}$$
$$\mathrm{mk2\_ko} = 0 \tag{16}$$

1.3 Reactions

The model contains 6 reactions, see also Figure 2 in the main part of this article:

- **Reaction 1:**

$$\mathrm{p38} \xrightarrow{\mathrm{IL1b}} \mathrm{pp38}$$

$$R_1 = \quad [\mathrm{p38}] \cdot \mathrm{p38\_act\_basal} + \frac{[\mathrm{IL1b}] \cdot [\mathrm{p38}] \cdot \mathrm{p38\_act\_il1b}}{[\mathrm{IL1b}] \cdot \mathrm{il1b\_sat} + 1} \tag{17}$$

- **Reaction 2:**

$$\text{pp38} \xrightarrow[\text{PhosphaInh}]{\text{MKP}} \text{p38}$$

$$R_2 = \frac{\text{p38\_dea\_const} \cdot [\text{pp38}]}{[\text{PhosphaInh}] \cdot \text{dePhospho\_inh} + 1} + \frac{[\text{MKP}] \cdot \text{p38\_dea\_mkp} \cdot [\text{pp38}]}{[\text{PhosphaInh}] \cdot \text{dePhospho\_inh} + 1} \tag{18}$$

- **Reaction 3:**

$$\varnothing \xrightarrow{\text{pp38}} \text{MKP}$$

$$R_3 = \text{mkp\_prod\_pp38} \cdot [\text{pp38}] \tag{19}$$

- **Reaction 4:**

$$\text{MKP} \longrightarrow \varnothing$$

$$R_4 = [\text{MKP}] \cdot \text{mkp\_deg} \tag{20}$$

- **Reaction 5:**

$$\text{MK2} \xrightarrow[\text{SB203580}]{\text{pp38}} \text{pMK2}$$

$$R_5 = -\frac{[\text{MK2}] \cdot \text{mk2\_act\_p38} \cdot [\text{pp38}] \cdot (\text{MK2\_knockout} - 1)}{[\text{SB203580}] \cdot \text{mk2\_inh\_sb} + 1} \tag{21}$$

- **Reaction 6:**

$$\text{pMK2} \xrightarrow[\text{PhosphaInh}]{} \text{MK2}$$

$$R_6 = \frac{\text{mk2\_dea} \cdot [\text{pMK2}]}{[\text{PhosphaInh}] \cdot \text{dePhospho\_inh} + 1} \tag{22}$$

1.4 ODE system

The ODE system determining the time evolution of the dynamical variables is given by:

$$\text{d[p38]/dt} = -R_1 + R_2 \tag{23}$$
$$\text{d[pp38]/dt} = +R_1 - R_2 \tag{24}$$
$$\text{d[MKP]/dt} = +R_3 - R_4 \tag{25}$$
$$\text{d[MK2]/dt} = -R_5 + R_6 \tag{26}$$
$$\text{d[pMK2]/dt} = +R_5 - R_6 \tag{27}$$

The ODE system was solved by a parallelized implementation of the CVODES algorithm [1]. It also supplies the parameter sensitivities utilized for parameter estimation.

1.5 Scaling invariances

Since MKP is not measured the concentration unit of MKP is not accessible. Mathematically this is a scaling invariance of the concentration of MKP. A transformation of the unit of MKP by a factor α

$$([\text{MKP}], \text{mkp\_prod\_pp38}, \text{p38\_dea\_mkp}) \quad \rightarrow \quad (\alpha\,[\text{MKP}], \alpha\,\text{mkp\_prod\_pp38}, \alpha^{-1}\,\text{p38\_dea\_mkp}) \tag{28}$$

does not change the output of the ODE system. This leads to a structural nonidentifiability of the parameters mkp_prod_pp38 and $p38\_dea\_mkp$. In other words, the model for the given data is over-parameterized and we can reduce it, e.g. by fixing the parameter mkp_prod_pp38 to the value of the parameter mkp_deg. With this transformation the numerical value of the initial concentration of MKP equals the initial concentration of pp38.

1.6 Initial conditions

Before treatment with IL-1β we can asume the cells to be in a stable steady state. Therefore we calculated the steady state of the system without IL-1β input and used this steady state as initial concentrations for the simulation of the ODE system. By setting eq. (23)–(27) to zero and solving them for

$$\text{input\_il1b} = \text{input\_phosphaInh} = \text{input\_sb203580} = \text{mk2\_ko} = 0 \tag{29}$$

we obtain for the steady state concentrations at timepoint 0:

$$\text{init\_MKP} = -\frac{\text{mkp\_prod\_pp38} \cdot \text{p38\_dea\_const} - \sqrt{\text{mkp\_prod\_pp38}^2 \cdot \text{p38\_dea\_const}^2 + 4 \cdot \text{init\_p38} \cdot \text{p38\_act\_basal} \cdot \text{p38\_dea\_mkp} \cdot \text{mkp\_prod\_pp38}^2}}{2 \cdot \text{mkp\_prod\_pp38} \cdot \text{p38\_dea\_mkp}} \tag{30}$$

$$\text{init\_pMK2} = -\text{init\_MK2} \cdot \text{mk2\_act\_p38} \cdot \frac{\left(\text{mkp\_prod\_pp38} \cdot \text{p38\_dea\_const} - \sqrt{\text{mkp\_prod\_pp38}^2 \cdot \text{p38\_dea\_const}^2 + 4 \cdot \text{init\_p38} \cdot \text{p38\_act\_basal} \cdot \text{p38\_dea\_mkp} \cdot \text{mkp\_prod\_pp38}^2}\right)}{2 \cdot \text{mk2\_dea} \cdot \text{mkp\_prod\_pp38} \cdot \text{p38\_dea\_mkp}} \tag{31}$$

$$\text{init\_pp38} = -\frac{\text{mkp\_prod\_pp38} \cdot \text{p38\_dea\_const} - \sqrt{\text{mkp\_prod\_pp38}^2 \cdot \text{p38\_dea\_const}^2 + 4 \cdot \text{init\_p38} \cdot \text{p38\_act\_basal} \cdot \text{p38\_dea\_mkp} \cdot \text{mkp\_prod\_pp38}^2}}{2 \cdot \text{mkp\_prod\_pp38} \cdot \text{p38\_dea\_mkp}} \tag{32}$$

The initial values of p38 and MK2 are free parameters which determine the total protein concentration

$$\text{total\_p38} = \text{init\_p38} + \text{init\_pp38} \tag{33}$$

$$\text{total\_MK2} = \text{init\_MK2} + \text{init\_pMK2}. \tag{34}$$

1.7 Summary of the model

The final model consists of 5 dynamic variables with 3 input variables and contains 10 dynamic parameters. Three initial concentrations are determined by asuming a steady state at the beginning before IL-1*beta* stimulation. 2 initial concentrations are free parameters and estimated from the experimental data.

1.8 Overview of the used calibration experiments

To obtain the unknown model parameters, the model was fitted to experimental data. The results shown in the Figures 3–5 and Figures 7–9 in the main text were obtained by a fit to all measured data, including the inhibitor experiments used for the validation showed in Figure 6 in the main part. The prediction in Figure 6 was done with a parameter set obtained by a fit where the validating inhibitor experiments were not used, see Section 2.6 for tables with the resulting parameter values of this fit.

experiment	replicates	IL-1β [ng/ml]	inhibitors or knockouts	observables	section
1	1	1, 2, 5, 10	none	pMK2, pp38	2.2.7
1	2	1, 2, 5, 10	none	pMK2, pp38	2.2.8
1	3	1, 2, 5, 10	none	pMK2, pp38	2.2.9
2	1	0.1, 0.2, 0.5, 1	none	pMK2, pp38	2.2.10
2	2	0.1, 0.2, 0.5, 1	none	pMK2, pp38	2.2.11
2	3	0.1, 0.2, 0.5, 1	none	pMK2, pp38	2.2.12
3	1	0.01, 0.05, 0.1, 0.2	none	pMK2, pp38	2.2.13
3	1	0.01, 0.05, 0.1, 0.2	none	pMK2, pp38	2.2.14
4	1	0.1, 0.2, 0.5, 1	none	pMK2, pp38	2.2.15
4	2	0.1, 0.2, 0.5, 1	none	pMK2, pp38	2.2.16
4	3	0.1, 0.2, 0.5, 1	none	pMK2, pp38	2.2.17
5	1	0.1, 0.2, 0.5, 1	MK2_KO	pMK2, pp38	2.2.18
6	1	0.1, 0.2, 0.5, 1	MK2_KO	pMK2, pp38	2.2.19
7	1	0.1, 0.2, 0.5, 1	MK2_KO	pMK2, pp38	2.2.20
7	2	0.1, 0.2, 0.5, 1	MK2_KO	pMK2, pp38	2.2.21
8	1	10	none	total MK2, total p38	2.2.22
9	1	5	none	total MK2, total p38	2.2.23
9	2	5	none	total MK2, total p38	2.2.24
10	1	1	none	total MK2, total p38	2.2.25
11	1	1	sb203580=0, 1, 2, 5 μM	pMK2, pp38	2.2.26
11	2	1	sb203580=0, 1, 2, 5 μM	pMK2, pp38	2.2.27
12	1	0, 1	phosphatase inhibitor	pMK2, pp38	2.2.28
13	1	0, 1	phosphatase inhibitor	pMK2, pp38	2.2.29
14	1	0, 1	phosphatase inhibitor	pMK2, pp38	2.2.30
15	1	0, 1	phosphatase inhibitor	pMK2, pp38	2.2.31
16	1	0, 1	phosphatase inhibitor	pMK2, pp38	2.2.32
17	1	20	none	pMK2	2.2.1
18	1	5, 10, 20, 40	none	pMK2, pp38	2.2.2
18	2	5, 10, 20, 40	none	pMK2, pp38	2.2.3
18	3	5, 10, 20, 40	none	pMK2, pp38	2.2.4
18	4	5, 10, 20, 40	none	pMK2, pp38	2.2.5
18	5	5, 10, 20, 40	none	pMK2, pp38	2.2.6

Table 1: List of all the measured time courses used for the model calibrations. The single fits are shown in the Section 2.2.

Our experimental data consists of 1676 data points. These are measured in 18 independent biological time course experiments and 3 calibrations measurements. The biological experiments were done with 1-3 technical replicates, so that in total 35 meassurements were performed. The fit was performed simultaneously to all experiments. An overview of the experimental conditions of the performed experiments is shown in Table 1.

For each experiment we defined an observation function and set the experimental condition by defining the external input variables. We used a lognormal distributed error model. The logarithm of a lognormal distributed variable is normal distributed. For normal distributed data the maximum likelihood estimation is equivalent to the minimization of the sum of squared residuals. Therefore we compared the model simulation and the experimental data on a logarithmic scale with a constant gaussian error. In the following all experiments are described and the fit and the data are shown. The fitted parameters are shown in Section 2.3.

The experiments are falling into two groups. On the one hand we performed calibrator experiments to infer the concentrations in real units in the internal standard. This is done by calibrating the internal standard to a calibratior (Section 2.1.1), this calibrator is calibrated to BSA to obtain absolute amounts of proteins (Section 2.1.2). To obtain concentraions we also measured the volume of the used hepatocytes (Section 2.1.3). On the other hand there are the actual time course experiments which are shown in Section 2.2.

2 List of the single Experiments, Model Fits and Tables of Parameters

2.1 Calibration experiments

2.1.1 Experiment: Calibration of the internal standard to a calibrator

Comments To obtain the concentrations of p38 and MK2 in real units we measured an internal standard in most time course experiments. In this experiment this internal standard is calibrated to a calibrator. This was done for p38_total, pp38, MK2_total and pMK2.

A calibration curve with the intensity of different amounts internal standard was measured (see Section 2.1.1). On the same gel the intensity of a given volume of calibrator was measured and fitted simultaneously (see Section 2.1.1). By this one can compare the amount of internal standard with the amount of calibrator. This is done by the parameters:

- intstd_in_p38_total_calibrator
- intstd_in_pp38_calibrator
- intstd_in_MK2_total_calibrator
- intstd_in_pMK2_calibrator

E.g. corresponds 1 μL pp38 calibrator to $intstd\_in\_pp38\_calibrator$ μL pp38 internal standard.

Internal standard calibration curve The calibration curves of the internal standard are defined as

$$\begin{aligned}
\text{Y_cal_intstd_MK2_total} &= \text{offset_cal_intstd_MK2_total} + \text{scale_cal_intstd_MK2_total} \cdot \text{intstd} &(35)\\
\text{Y_cal_intstd_pMK2} &= \text{offset_cal_intstd_pMK2} + \text{scale_cal_intstd_pMK2} \cdot \text{intstd} &(36)\\
\text{Y_cal_intstd_p38_total} &= \text{offset_cal_intstd_p38_total} + \text{scale_cal_intstd_p38_total} \cdot \text{intstd} &(37)\\
\text{Y_cal_intstd_pp38} &= \text{offset_cal_intstd_pp38} + \text{scale_cal_intstd_pp38} \cdot \text{intstd}, &(38)
\end{aligned}$$

with error models

$$\begin{aligned}
\sigma\{\text{Y_cal_intstd_MK2_total}\} &= \text{sd_cal_intstd_MK2_total} &(39)\\
\sigma\{\text{Y_cal_intstd_pMK2}\} &= \text{sd_cal_intstd_pMK2} &(40)\\
\sigma\{\text{Y_cal_intstd_p38_total}\} &= \text{sd_cal_intstd_p38_total} &(41)\\
\sigma\{\text{Y_cal_intstd_pp38}\} &= \text{sd_cal_intstd_pp38}. &(42)
\end{aligned}$$

The agreement of the model observables and the experimental data, given in Table 2, yields a value of the objective function $-2\log(L) = -76.72$ for 20 data points in this data set. The model observables and the experimental data is show in Figure 1.

Measurement of the calibrator On the same gel we measured the intensity of a fixed amount of calibrator. The observation functions are defined as

$$\begin{aligned}
\text{I_MK2_total} &= \text{offset_cal_intstd_MK2_total} + \text{intstd_in_MK2_total_calibrator} \cdot \\
&\qquad \text{scale_cal_intstd_MK2_total} \cdot \text{calibrator} &(43)\\
\text{I_pMK2} &= \text{offset_cal_intstd_pMK2} + \text{intstd_in_pMK2_calibrator} \cdot \text{scale_cal_intstd_pMK2} \cdot \text{calibrator} &(44)\\
\text{I_p38_total} &= \text{offset_cal_intstd_p38_total} + \text{intstd_in_p38_total_calibrator} \cdot \\
&\qquad \text{scale_cal_intstd_p38_total} \cdot \text{calibrator} &(45)\\
\text{I_pp38} &= \text{offset_cal_intstd_pp38} + \text{intstd_in_pp38_calibrator} \cdot \text{scale_cal_intstd_pp38} \cdot \text{calibrator}, &(46)
\end{aligned}$$

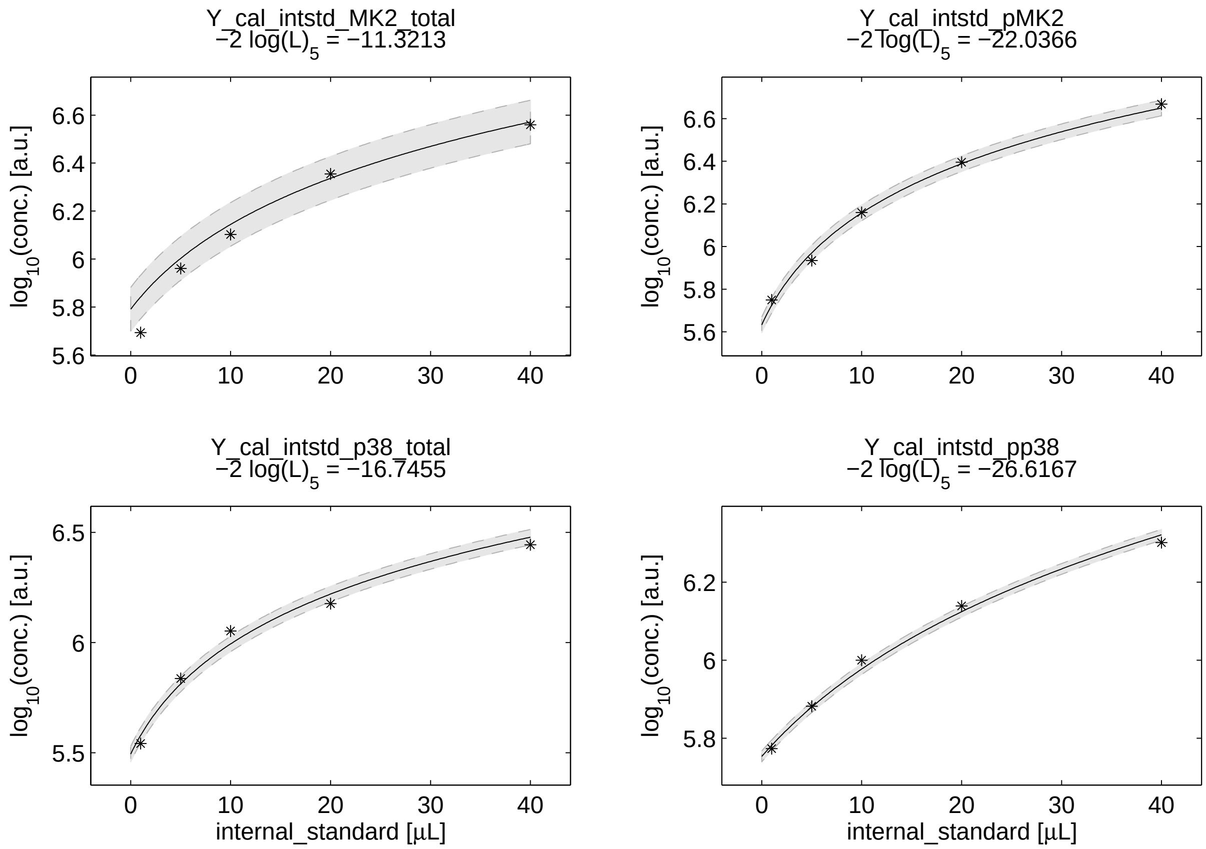

Figure 1: Observables and data for the experiment described in Section 2.1.1. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

intstd [μL]	Y_cal_intstd_MK2_total conc. [a.u.]	Y_cal_intstd_pMK2 conc. [a.u.]	Y_cal_intstd_p38_total conc.[a.u.]	Y_cal_intstd_pp38 conc. [a.u.]
1	493985	561209	348408	593590
5	913771	859077	686710	761850
10	1.26721e+06	1.4448e+06	1.12762e+06	1.00044e+06
20	2.26605e+06	2.48525e+06	1.50164e+06	1.37781e+06
40	3.63004e+06	4.64937e+06	2.77991e+06	2.00218e+06

Table 2: Experimental data for the experiment described in Section 2.1.1.

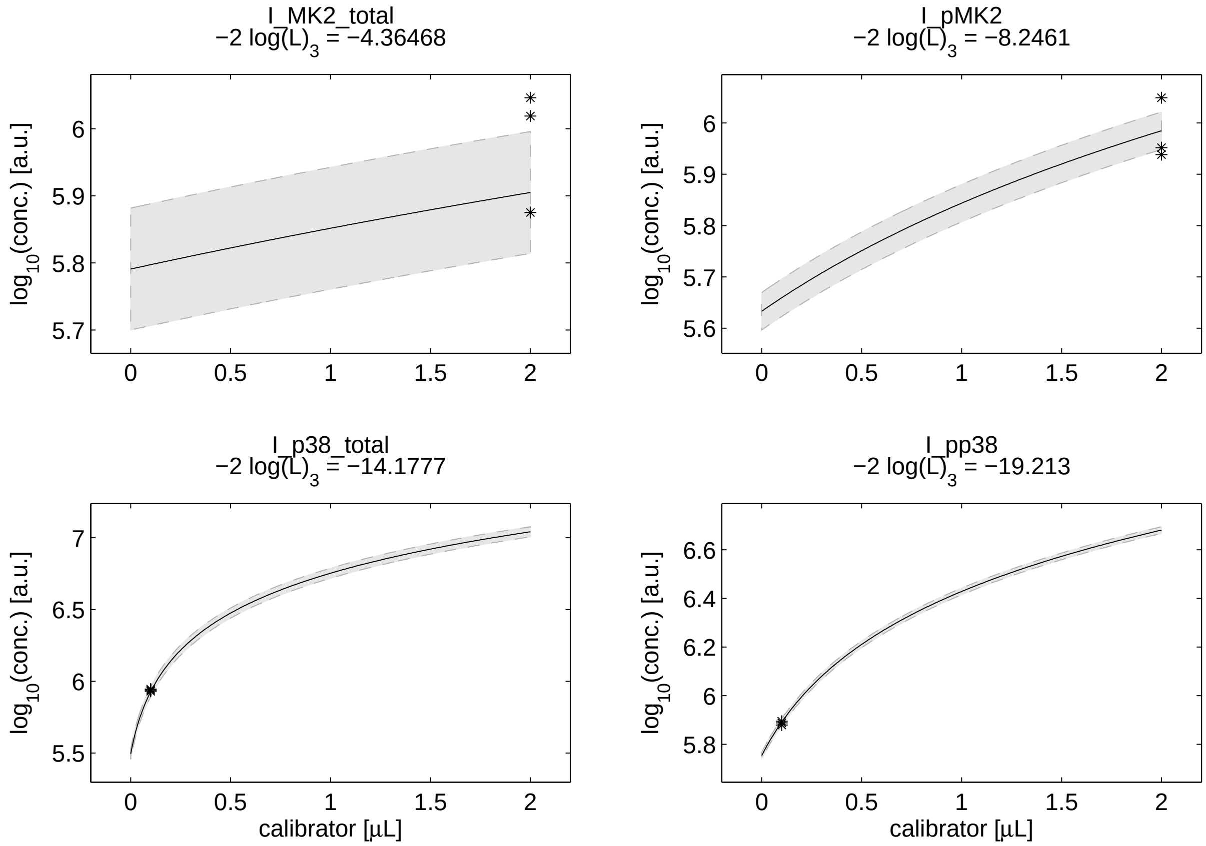

Figure 2: Observables and data for the experiment described in Section 2.1.1. The observables are displayed as solid lines.The error model that describes the measurement noise is indicated by shades.

with error models

$$\sigma\{\text{I\_MK2\_total}\} = \text{sd\_cal\_intstd\_MK2\_total} \tag{47}$$

$$\sigma\{\text{I\_pMK2}\} = \text{sd\_cal\_intstd\_pMK2} \tag{48}$$

$$\sigma\{\text{I\_p38\_total}\} = \text{sd\_cal\_intstd\_p38\_total} \tag{49}$$

$$\sigma\{\text{I\_pp38}\} = \text{sd\_cal\_intstd\_pp38}. \tag{50}$$

The agreement of the model observables and the experimental data, given in Table 3, yields a value of the objective function $-2\log(L) = -46.0015$ for 12 data points in this data set. The model observables and the experimental data is show in Figure 2.

calibrator [μL]	I_MK2_total conc. [a.u.]	I_pMK2 conc. [a.u.]	I_p38_total conc. [a.u.]	I_pp38 conc. [a.u.]
0.1			852712	784803
0.1			868880	757059
0.1			883571	772847
2	1.11195e+06	1.11984e+06		
2	750227	895231		
2	1.04461e+06	867974		

Table 3: Experimental data for the experiment described in Section 2.1.1.

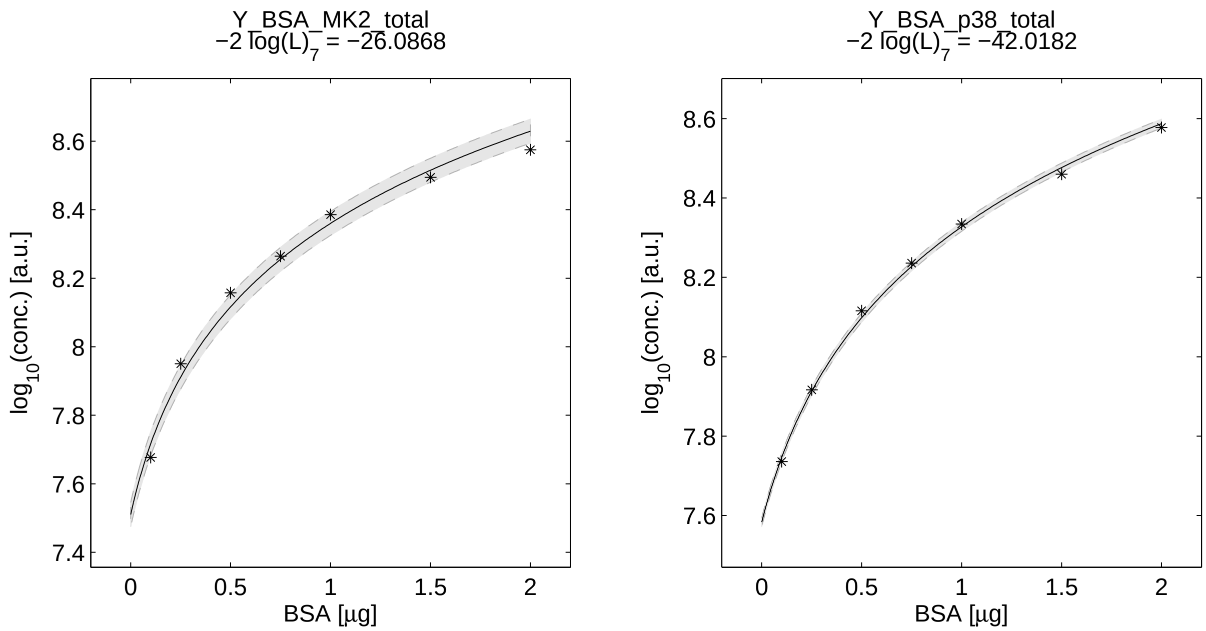

Figure 3: Observables and data for the experiment described in Section 2.1.2. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.1.2 Calibration of the calibrator to BSA

Comments To determine the amount of proteins in the calibrator we measured a BSA calibrator curve by measuring the intensity for different amounts of BSA (see Section 2.1.2). On the same gel the intensity of a given volume of calibrator was measured and fitted simultaneously (see Section 2.1.2). By this one can compare the amount of calibrator in μL with the amount of BSA in μg. With the molar mass one can calculate a concentration in μM. This was done for p38_total, MK2_total. The amount of phosphorylated p38 and MK2 in the calibrator was then determined by mass spectroscopy.

BSA calibration curve The calibration curves of BSA are defined as

$$\text{Y\_BSA\_MK2\_total} = \text{offset\_BSA\_MK2\_total} + \text{scale\_BSA\_MK2\_total} \cdot \text{BSA} \quad (51)$$

$$\text{Y\_BSA\_p38\_total} = \text{offset\_BSA\_p38\_total} + \text{scale\_BSA\_p38\_total} \cdot \text{BSA}, \quad (52)$$

with error models

$$\sigma\{\text{Y\_BSA\_MK2\_total}\} = \text{sd\_BSA\_MK2\_total} \quad (53)$$

$$\sigma\{\text{Y\_BSA\_p38\_total}\} = \text{sd\_BSA\_p38\_total}. \quad (54)$$

The agreement of the model observables and the experimental data, given in Table 4, yields a value of the objective function $-2\log(L) = -68.1049$ for 14 data points in this data set. The model observables and the experimental data is show in Figure 3.

Measurement of the calibrator On the same gel we measured the intensity of a fixed volume of calibrator. The observation functions are defined as

BSA [μg]	Y_BSA_MK2_total conc. [a.u.]	Y_BSA_p38_total conc. [a.u.]
0.1	4.75156e+07	5.4429e+07
0.25	8.92377e+07	8.25749e+07
0.5	1.43711e+08	1.30497e+08
0.75	1.83763e+08	1.72177e+08
1	2.4309e+08	2.15994e+08
1.5	3.1237e+08	2.88308e+08
2	3.75989e+08	3.7801e+08

Table 4: Experimental data for the experiment described in Section 2.1.2.

calibrator [μL]	I_MK2_total conc. [a.u.]	I_p38_total conc. [a.u.]
15		3.15027e+08
30	1.58503e+08	

Table 5: Experimental data for the experiment described in Section 2.1.3.

$$\mathrm{I\_MK2\_total} = \mathrm{offset\_BSA\_MK2\_total} + \frac{\mathrm{conc\_MK2\_total\_calibrator} \cdot \mathrm{m\_molekule\_MK2} \cdot \mathrm{scale\_BSA\_MK2\_total} \cdot \mathrm{calibrator}}{1000} \tag{55}$$

$$\mathrm{I\_p38\_total} = \mathrm{offset\_BSA\_p38\_total} + \frac{\mathrm{conc\_p38\_total\_calibrator} \cdot \mathrm{m\_molekule\_p38} \cdot \mathrm{scale\_BSA\_p38\_total} \cdot \mathrm{calibrator}}{1000} \tag{56}$$

with error models

$$\sigma\{\mathrm{I\_MK2\_total}\} = \mathrm{sd\_BSA\_MK2\_total} \tag{57}$$

$$\sigma\{\mathrm{I\_p38\_total}\} = \mathrm{sd\_BSA\_p38\_total} \tag{58}$$

For the molecular masses of p38 and MK2 we used

$$\mathrm{m\_molekule\_p38} = 67\ \mathrm{kDalton} \tag{59}$$

$$\mathrm{m\_molekule\_MK2} = 70\ \mathrm{kDalton.} \tag{60}$$

The parameter *conc_p38_total_calibrator* gives the amount of p38_total in μMol in one litre of p38_total calibrator, MK2_total respectively.

The agreement of the model observables and the experimental data, given in Table 5, yields a value of the objective function $-2\log(L) = -12.015$ for 2 data points in this data set. The model observables and the experimental data is show in Figure 4.

2.1.3 Experiment: Cell_volume

To obtain the protein concentrations in the used primary hepatocytes we need the total volume of the used cells. For this the volume of a single cells was measured ($cellvolume = (15.475 \pm 4.044)$ pL). With a measured number of cells of 59524 one can calculate the total volume of the used cells. Since the error of the measured volume is relative high (≈ 26 %), we estimated the volume simultaneously with the other experiments. As data point we used the measured volume of a single cell with the fixed error on the logarithmic scale:

$$\sigma\{\mathrm{cellvolume}\} = 0.2613 \tag{61}$$

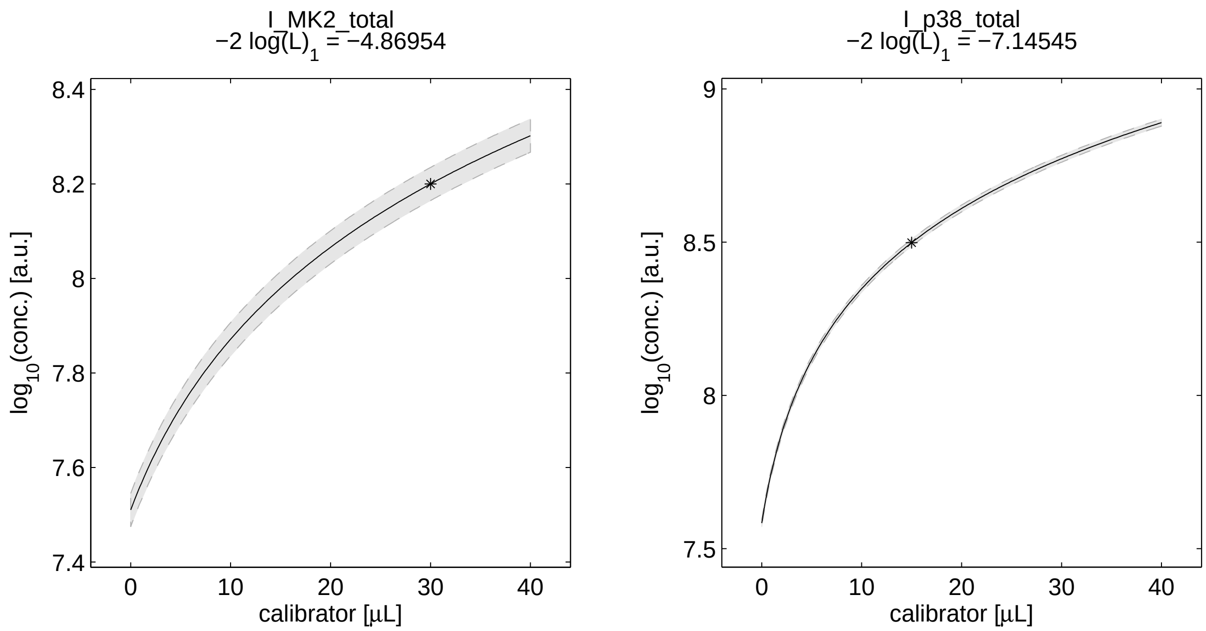

Figure 4: Observables and data for the experiment described in Section 2.1.3. Theobservables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

n_cells	cell_volume
[1]	[μL]
1	1.548e-05

Table 6: Experimental data for the experiment Cell_volume

As observation function we used

$$\text{cellvolume(n\_cells)} = \frac{\text{V} \cdot \text{n\_cells}}{59524}, \tag{62}$$

this gives the total volume V.

The agreement of the model observables and the experimental data, given in Table 6, yields a value of the objective function $-2\log(L) = -0.846295$ for 1 data points in this data set. The model observables and the experimental data is show in Figure 5.

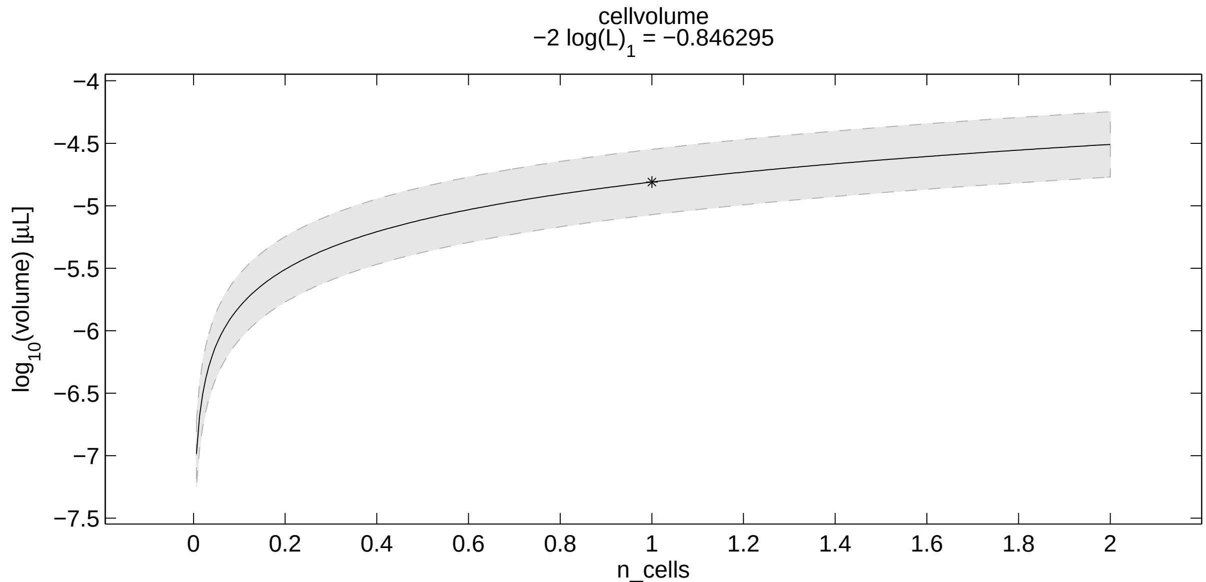

Figure 5: Cell_volume observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.1.4 Summary of the calibration

With the calibration we can set the scaling parameters

$$\text{scale\_p38\_total} = \frac{\text{conc\_p38\_total\_calibrator}}{\text{intstd\_in\_p38\_total\_calibrator}} \quad (63)$$

$$\text{scale\_MK2\_total} = \frac{\text{conc\_MK2\_total\_calibrator}}{\text{intstd\_in\_MK2\_total\_calibrator}} \quad (64)$$

$$\text{scale\_pp38} = \frac{\text{frac\_massspec\_pp38} \cdot \text{conc\_p38\_total\_calibrator}}{\text{intstd\_in\_pp38\_calibrator}} \quad (65)$$

$$\text{scale\_pMK2} = \frac{\text{frac\_massspec\_pp38} \cdot \text{conc\_MK2\_total\_calibrator}}{\text{intstd\_in\_pMK2\_calibrator}}. \quad (66)$$

These are defining the amount of the corresponding protein in μMol in one litre internal standard. As mentioned above the ratio of pp38 and pMK2 in the calibrator was measured by mass spectroscopy:

$$\text{frac\_massspec\_pp38} = 7.2\ \% \quad (67)$$

$$\text{frac\_massspec\_pp38} = 59\ \% \quad (68)$$

With this, typical observation functions for an experiment with measured internal standard, e. g. for pp38, are looking like

$$\text{p\_p38\_au(t)} = \text{offset\_gel\_pp38\_ExpID} + [\text{pp38}](\text{t}) \cdot \text{scale\_pp38\_ExpID} \quad (69)$$

$$\text{int\_p\_p38\_au(intstd)} = \text{offset\_gel\_pp38\_ExpID} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_ExpID} \cdot \text{intstd}}{\text{V}}. \quad (70)$$

p_p38_au is the simulated value of the measured protein. The intensity background of the gel is modeled by the gel specific offset parameter $offset\_gel\_pp38\_ExpID$. $[pp38](t)$ is the by the ODE simulated concentration of pp38 in μM which is scaled by the scaling parameter $scale\_pp38\_ExpID$ with the unit

Intensity/μM. This scaling parameter is determined by the internal standard $int\_p\_p38\_au$, for which a calibration curve for different volumes $intstd$ of internal standard is measured. The parameter $scale\_pp38$ is determined in the previous calibration experiments (Section 2.1.1 and 2.1.2) and defines the amount of pp38 in the internal standard. This means the product $scale\_pp38 \cdot intstd$ is the total amount of measured pp38 in the internal standard. To obtain the corresponding amount of pp38 in the measured cells one has to divide this by the total cell volume V:

$$\frac{\text{scale\_pp38} \cdot \text{intstd}}{\text{V}} \tag{71}$$

With this the parameter $scale\_pp38\_ExpID$ has the correct unit and determines the correct scale of pp38 in μM.

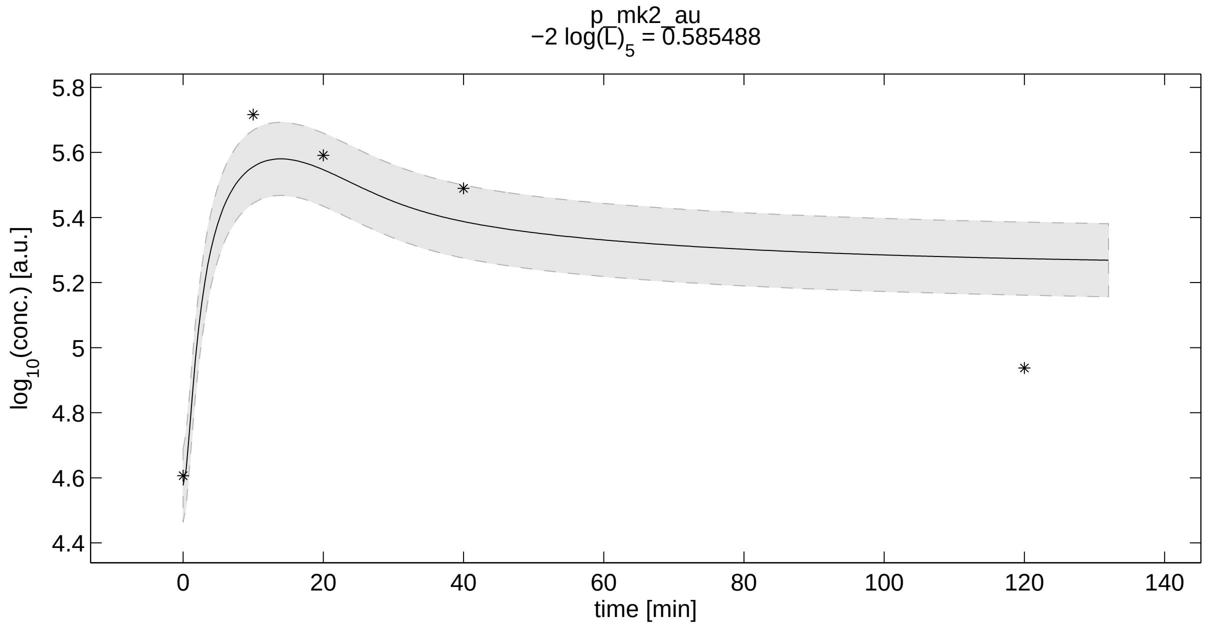

Figure 6: 090102_page090116_wt_il1_20_pmk2 observables and experimental data for the experiment. The observables are displayed as solid lines.The error model that describes the measurement noise is indicated by shades.

time [min]	input_il1b [ng · ml^{-1}]	p_mk2_au conc. [a.u.]
0	20	40431
10	20	519999
20	20	389767
40	20	308655
120	20	86614

Table 7: Experimental data for the experiment 090102_page090116_wt_il1_20_pmk2

2.2 Time course experiments for different IL-1β doses and inhibitors

2.2.1 Experiment: 090102_page090116_wt_il1_20_pmk2

Comments In this experiment the primary hepatocytes were treated with 20 ng/ml IL-1β.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 7, yields a value of the objective function $-2\log(L) = 0.585488$ for 5 data points in this data set. The model observables and the experimental data is show in Figure 6.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \quad \text{offset\_gel\_pMK2\_090102} + [\text{pMK2}] \cdot \text{scale\_pMK2\_090102} \tag{72}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \quad \text{sd\_pMK2\_au} \tag{73}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \rightarrow 20$$

$$\text{scale\_pMK2\_090102} \rightarrow \frac{\text{scale\_pMK2\_090102}}{\text{init\_MK2}}$$

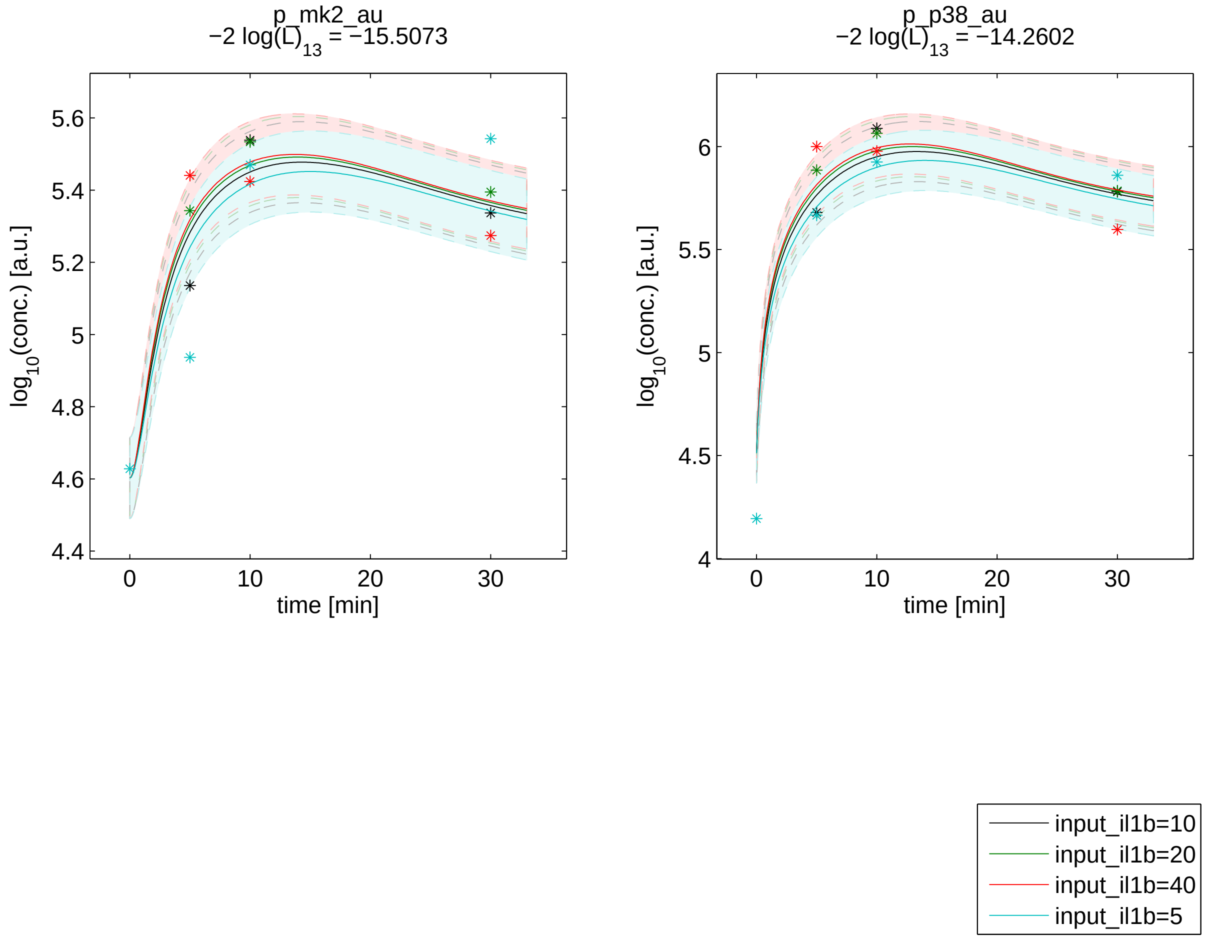

Figure 7: 090615d_page090922a_wt_il1_0u5u10u20u40_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.2 Experiment: 090615d_page090922a_wt_il1_0u5u10u20u40_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 5–40 ng/ml.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 8, yields a value of the objective function $-2\log(L) = -29.7675$ for 26 data points in this data set. The model observables and the experimental data is show in Figure 7.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \quad \text{offset\_gel\_pMK2\_090615d\_090922a} + [\text{pMK2}] \cdot \text{scale\_pMK2\_090615d\_090922a} \tag{74}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \quad \text{sd\_pMK2\_au} \tag{75}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au(t)} = \quad \text{offset\_gel\_pp38\_090615d\_090922a} + [\text{pp38}] \cdot \text{scale\_pp38\_090615d\_090922a} \tag{76}$$

time [min]	input_il1b [$ng \cdot ml^{-1}$]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	5	463621	86479
5	10	478366	136670
5	20	767973	220230
5	40	998747	275795
10	5	841383	294867
10	10	1.22359e+06	345405
10	20	1.15988e+06	341760
10	40	949109	265298
30	5	725408	348571
30	10	603405	217098
30	20	609009	248117
30	40	395657	188015
0	5	15634	42469

Table 8: Experimental data for the experiment 090615d_page090922a_wt_il1_0u5u10u20u40_pmk2_pp38

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(t) = \text{sd\_pp38\_au} \quad (77)$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \rightarrow 10 \mid 20 \mid 40 \mid 5$$

$$\text{scale\_pMK2\_090615d\_090922a} \rightarrow \frac{\text{scale\_pMK2\_090615d\_090922a}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_090615d\_090922a} \rightarrow \frac{\text{scale\_pp38\_090615d\_090922a}}{\text{init\_p38}}$$

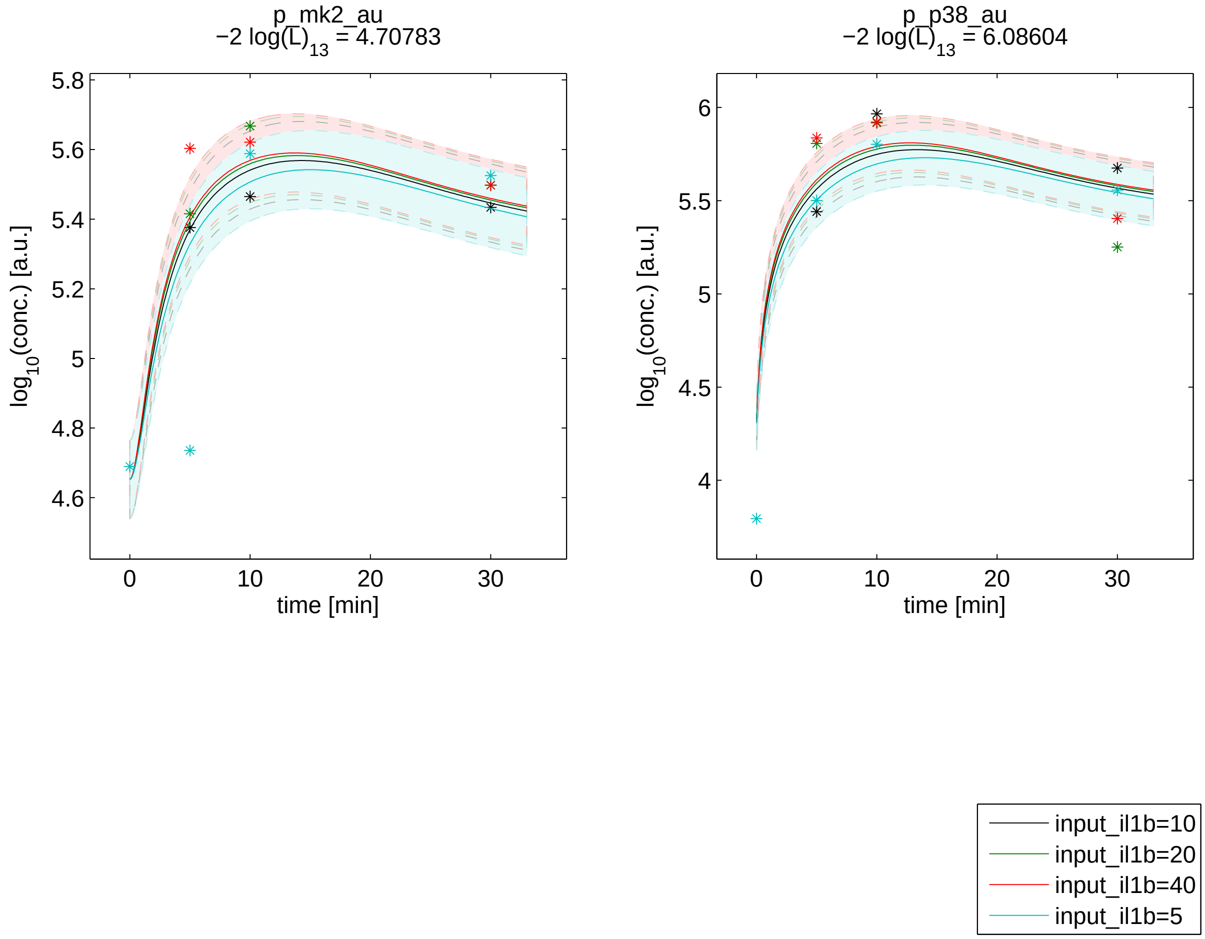

Figure 8: 090615d_page090922b_wt_il1_0u5u10u20u40_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.3 Experiment: 090615d_page090922b_wt_il1_0u5u10u20u40_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 5–40 ng/ml.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 9, yields a value of the objective function $-2\log(L) = 10.7939$ for 26 data points in this data set. The model observables and the experimental data is show in Figure 8.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \quad \text{offset\_gel\_pMK2\_090615d\_090922b} + [\text{pMK2}] \cdot \text{scale\_pMK2\_090615d\_090922b} \tag{78}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \quad \text{sd\_pMK2\_au} \tag{79}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au(t)} = \quad \text{offset\_gel\_pp38\_090615d\_090922b} + [\text{pp38}] \cdot \text{scale\_pp38\_090615d\_090922b} \tag{80}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	5	316559	54389
5	10	276372	237636
5	20	640375	260276
5	40	686666	400926
10	5	633892	387492
10	10	923556	291766
10	20	826173	464694
10	40	832909	418138
30	5	360133	335219
30	10	472570	271549
30	20	178493	314745
30	40	253719	314434
0	5	6238	48922

Table 9: Experimental data for the experiment 090615d_page090922b_wt_il1_0u5u10u20u40_pmk2_pp38

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(t) = \quad \text{sd\_pp38\_au} \tag{81}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \quad \rightarrow \quad 10 \mid 20 \mid 40 \mid 5$$

$$\text{scale\_pMK2\_090615d\_090922b} \quad \rightarrow \quad \frac{\text{scale\_pMK2\_090615d\_090922b}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_090615d\_090922b} \quad \rightarrow \quad \frac{\text{scale\_pp38\_090615d\_090922b}}{\text{init\_p38}}$$

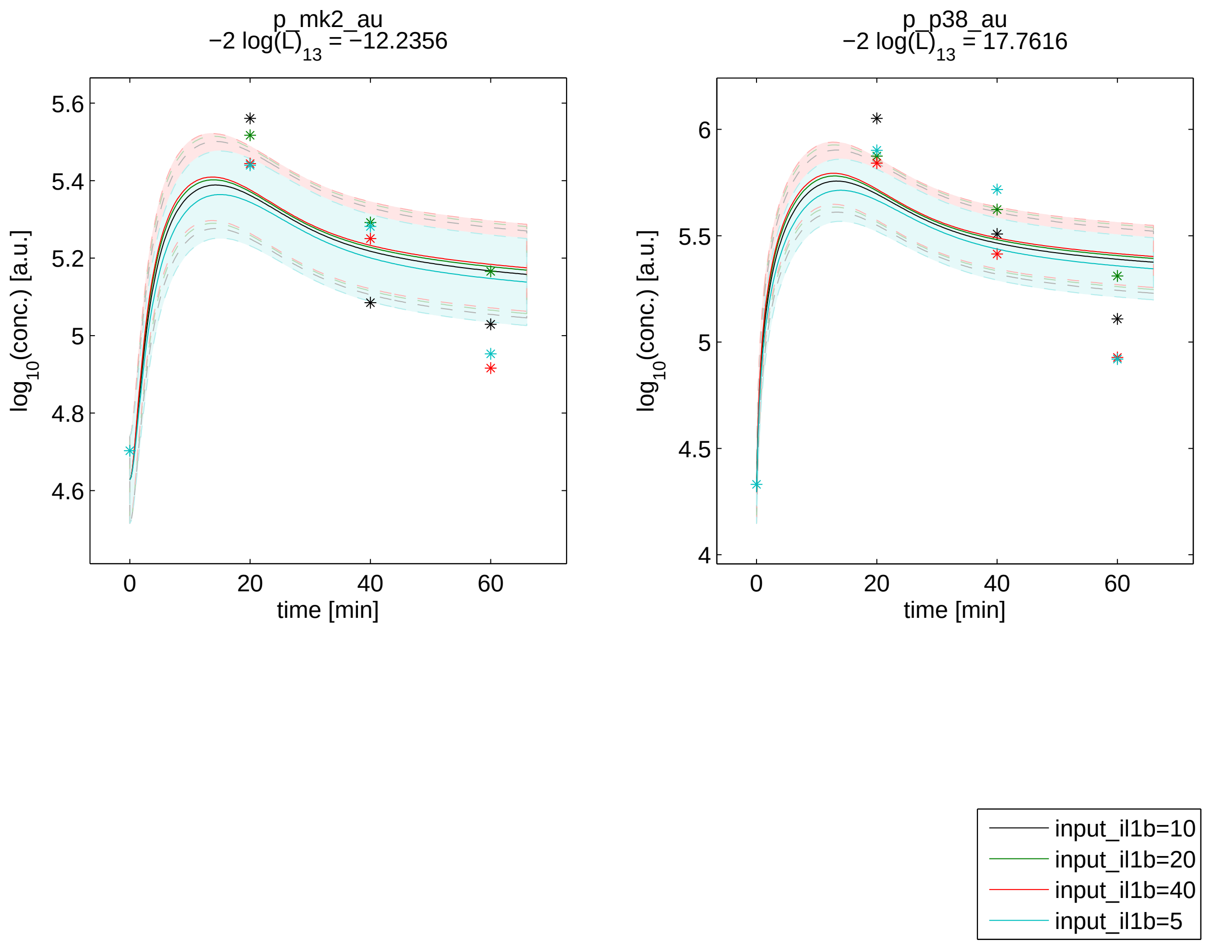

Figure 9: 090615d_page090922d_wt_il1_0u5u10u20u40_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.4 Experiment: 090615d_page090922d_wt_il1_0u5u10u20u40_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 5–40 ng/ml.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 10, yields a value of the objective function $-2\log(L) = 5.52599$ for 26 data points in this data set. The model observables and the experimental data is show in Figure 9.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \quad \text{offset\_gel\_pMK2\_090615d\_090922d} + [\text{pMK2}] \cdot \text{scale\_pMK2\_090615d\_090922d} \tag{82}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \quad \text{sd\_pMK2\_au} \tag{83}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au(t)} = \quad \text{offset\_gel\_pp38\_090615d\_090922d} + [\text{pp38}] \cdot \text{scale\_pp38\_090615d\_090922d} \tag{84}$$

time [min]	input_il1b [$ng \cdot ml^{-1}$]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
20	5	797129	275248
20	10	1.12635e+06	363543
20	20	749117	329073
20	40	694659	277874
40	5	521691	191276
40	10	322413	121595
40	20	419944	195814
40	40	259587	178017
60	5	83158	89755
60	10	128606	106983
60	20	204702	146477
60	40	84661	82470
0	5	21421	50438

Table 10: Experimental data for the experiment 090615d_page090922d_wt_il1_0u5u10u20u40_pmk2_pp38

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(t) = \quad \text{sd\_pp38\_au} \tag{85}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \quad \rightarrow \quad 10 \mid 20 \mid 40 \mid 5$$

$$\text{scale\_pMK2\_090615d\_090922d} \quad \rightarrow \quad \frac{\text{scale\_pMK2\_090615d\_090922d}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_090615d\_090922d} \quad \rightarrow \quad \frac{\text{scale\_pp38\_090615d\_090922d}}{\text{init\_p38}}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	5	3.85704e+06	832129
5	10	5.45230e+06	1.06561e+06
5	20	6.11666e+06	1.10801e+06
5	40	7.34388e+06	1.39979e+06
10	5	7.20263e+06	1.30066e+06
10	10	9.92429e+06	1.51536e+06
10	20	1.07679e+07	1.72398e+06
10	40	1.00502e+07	1.84325e+06
15	5	7.51519e+06	1.50596e+06
15	10	7.96418e+06	1.67580e+06
15	20	8.55007e+06	1.75636e+06
15	40	8.41126e+06	1.62515e+06
20	5	9.04304e+06	1.31570e+06
20	10	9.95753e+06	1.85173e+06
20	20	5.73780e+06	1.35735e+06
20	40	6.56592e+06	1.42385e+06
30	5	7.49298e+06	1.34872e+06
30	10	3.68589e+06	1.07438e+06
30	20	5.10401e+06	1.20820e+06
30	40	3.81070e+06	1.13802e+06
40	5	6.04455e+06	1.09083e+06
40	10	4.28244e+06	1.06774e+06
40	20	3.88159e+06	881711
40	40	3.05142e+06	792293
60	5	2.53057e+06	666561
60	10	2.06356e+06	610114
60	20	2.47781e+06	349859
60	40	1.68575e+06	400739
0	5	701946	131368
0	5	741466	120531

Table 11: Experimental data for the experiment 090615d_page100416_wt_il1_0u5u10u20u40_pmk2_pp38

2.2.5 Experiment: 090615d_page100416_wt_il1_0u5u10u20u40_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 5–40 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 11 and 12 yields a value of the objective function $-2\log(L) = -15.7179$ for 70 data points in this data set. The model observables and the experimental data is show in Figure 10.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \quad \text{offset\_gel\_pMK2\_090615d\_100416} + [\text{pMK2}] \cdot \text{scale\_pMK2\_090615d\_100416} \tag{86}$$

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	16635	113502
5	215793	1.52989e+06
10	845957	4.52694e+06
20	2.0123e+06	1.07057e+07
40	4.2294e+06	1.09304e+07

Table 12: Internal standard for the experiment 090615d_page100416_wt_il1_0u5u10u20u40_pmk2_pp38

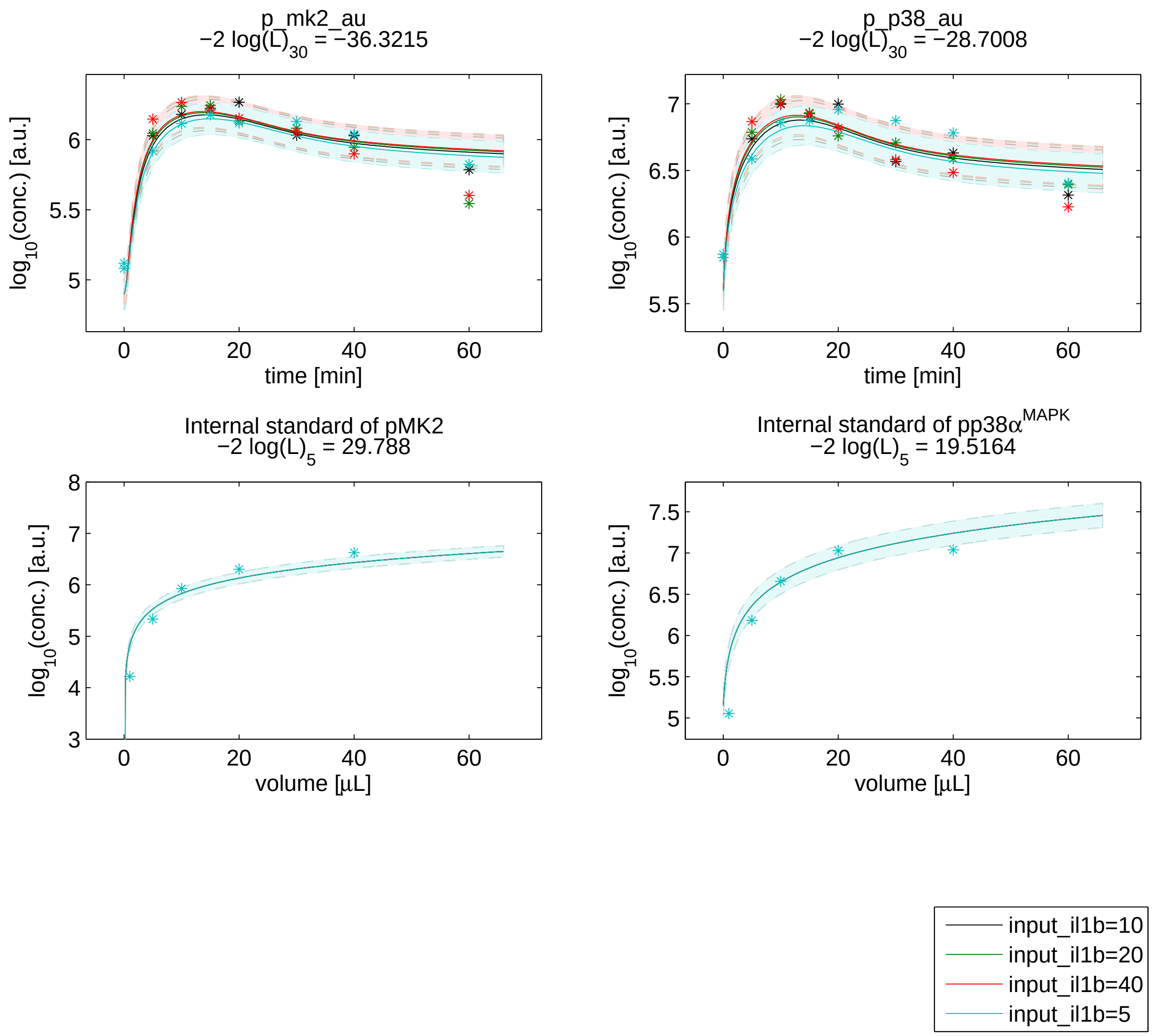

Figure 10: 090615d_page100416_wt_il1_0u5u10u20u40_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \quad \text{sd\_pMK2\_au} \tag{87}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au}(\text{t}) = \quad \text{offset\_gel\_pp38\_090615d\_100416} + [\text{pp38}] \cdot \text{scale\_pp38\_090615d\_100416} \tag{88}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \quad \text{sd\_pp38\_au} \tag{89}$$

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au}(\text{intstd}) = \quad \text{offset\_gel\_pMK2\_090615d\_100416} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_090615d\_100416} \cdot \text{intstd}}{\text{V}} \tag{90}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \quad \text{sd\_pMK2\_au} \tag{91}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au}(\text{intstd}) = \quad \text{offset\_gel\_pp38\_090615d\_100416} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_090615d\_100416} \cdot \text{intstd}}{\text{V}} \tag{92}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_au} \tag{93}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \quad \rightarrow \quad 10 \mid 20 \mid 40 \mid 5$$

$$\text{scale\_090615d\_100416} \quad \rightarrow \quad \frac{\text{scale\_090615d\_100416}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_090615d\_100416} \quad \rightarrow \quad \frac{\text{scale\_pp38\_090615d\_100416}}{\text{init\_p38}}$$

time [min]	input_il1b [$ng \cdot ml^{-1}$]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	5	441436	222497
5	10	824574	269158
5	20	637912	177187
5	40	620782	348341
10	5	1.55456e+06	414908
10	10	1.66948e+06	506620
10	20	1.74006e+06	462302
10	40	1.60241e+06	458197
15	5	1.01049e+06	427271
15	10	1.83170e+06	531053
15	20	1.56507e+06	409766
15	40	1.50000e+06	404697
20	5	1.26182e+06	399013
20	10	1.45601e+06	332797
20	20	614984	352496
20	40	1.31569e+06	393247
30	5	840187	324738
30	10	471757	257150
30	20	424028	195467
30	40	502516	226108
40	5	708126	357230
40	10	736960	267618
40	20	545801	235957
40	40	172379	176232
60	5	349761	135355
60	10	290272	159155
60	20	387787	168381
60	40	175167	88950
0	5	44235	12126
0	5	50732	26077

Table 13: Experimental data for the experiment 090615d_page100419_wt_il1_0u5u10u20u40_pmk2_pp38

2.2.6 Experiment: 090615d_page100419_wt_il1_0u5u10u20u40_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 5–40 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 13 and 14, yields a value of the objective function $-2\log(L) = 37.2513$ for 70 data points in this data set. The model observables and the experimental data is show in Figure 11.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \text{offset\_gel\_pMK2\_090615d\_110419} + [\text{pMK2}] \cdot \text{scale\_pMK2\_090615d\_110419} \quad (94)$$

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	12501	2456
5	227332	75620
10	687776	177162
20	920562	444395
40	2.80949e+06	1.27738e+06

Table 14: Internal standard for the experiment 090615d_page100419_wt_il1_0u5u10u20u40_pmk2_pp38

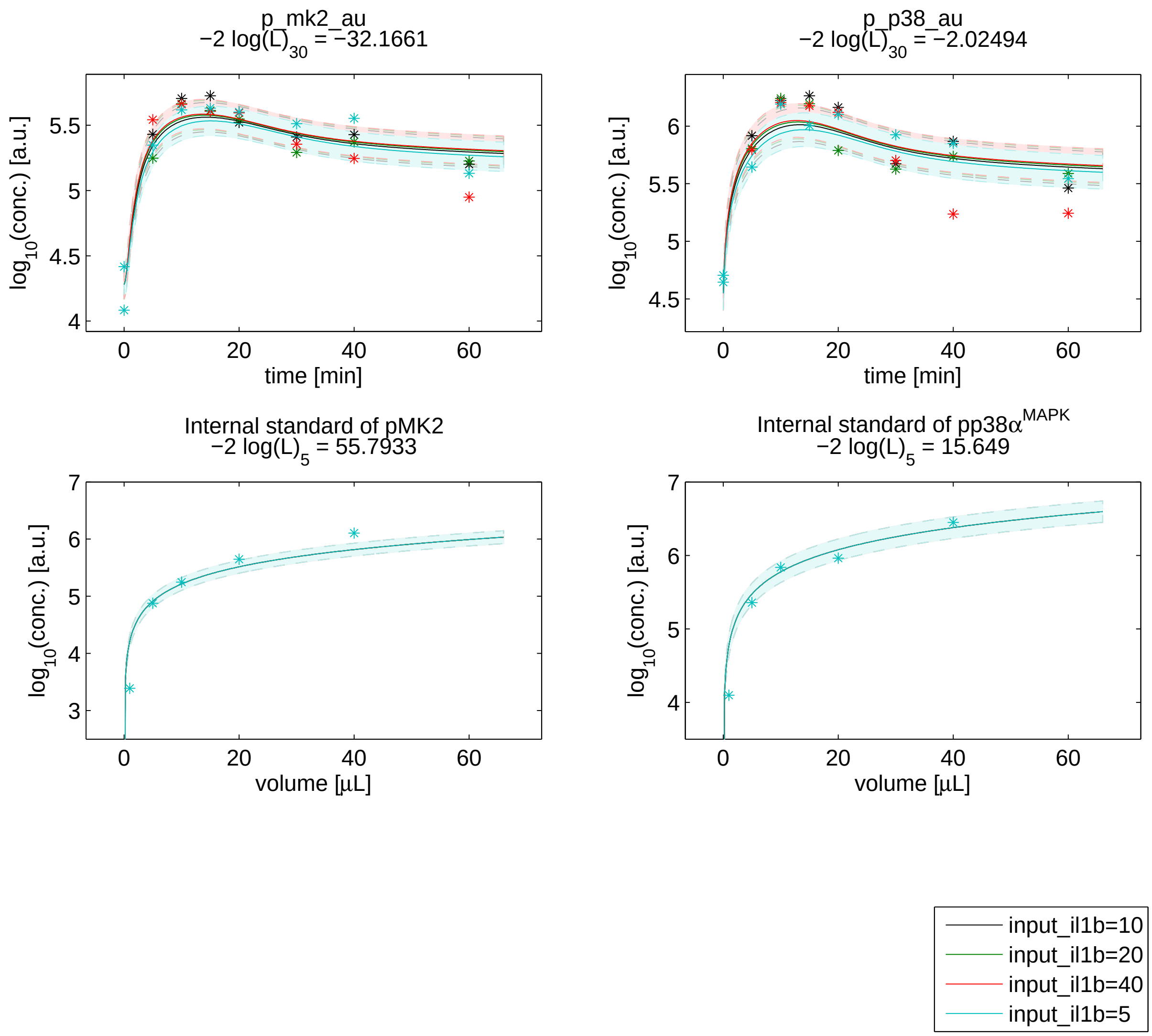

Figure 11: 090615d_page100419_wt_il1_0u5u10u20u40_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \quad \text{sd\_pMK2\_au} \tag{95}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au}(\text{t}) = \quad \text{offset\_gel\_pp38\_090615d\_110419} + [\text{pp38}] \cdot \text{scale\_pp38\_090615d\_110419} \tag{96}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \quad \text{sd\_pp38\_au} \tag{97}$$

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au}(\text{intstd}) = \quad \text{offset\_gel\_pMK2\_090615d\_110419} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_090615d\_110419} \cdot \text{intstd}}{\text{V}} \tag{98}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \quad \text{sd\_pMK2\_au} \tag{99}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au}(\text{intstd}) = \quad \text{offset\_gel\_pp38\_090615d\_110419} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_090615d\_110419} \cdot \text{intstd}}{\text{V}} \tag{100}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_au} \tag{101}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \quad \rightarrow \quad 10 \mid 20 \mid 40 \mid 5$$

$$\text{scale\_pMK2\_090615d\_110419} \quad \rightarrow \quad \frac{\text{scale\_pMK2\_090615d\_110419}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_090615d\_110419} \quad \rightarrow \quad \frac{\text{scale\_pp38\_090615d\_110419}}{\text{init\_p38}}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	1	1.50187e+06	1.11242e+06
5	2	1.71921e+06	1.30618e+06
5	5	1.89156e+06	1.06816e+06
5	10	1.48687e+06	1.03857e+06
10	1	2.18956e+06	982099
10	2	2.88284e+06	1.52456e+06
10	5	3.32338e+06	1.56689e+06
10	10	1.70111e+06	1.19469e+06
15	1	2.57455e+06	1.17143e+06
15	2	3.01582e+06	1.63693e+06
15	5	2.35668e+06	1.02704e+06
15	10	2.74691e+06	1.47736e+06
20	1	3.34091e+06	1.55023e+06
20	2	3.02110e+06	1.21861e+06
20	5	3.11033e+06	1.49846e+06
20	10	2.96366e+06	1.28430e+06
30	1	2.88188e+06	1.65872e+06
30	2	2.10930e+06	1.56836e+06
30	5	2.51228e+06	1.42122e+06
30	10	1.74290e+06	1.02397e+06
40	1	2.35449e+06	1.51809e+06
40	2	1.27989e+06	1.01723e+06
40	5	1.35202e+06	1.07519e+06
40	10	1.75703e+06	1.29907e+06
60	1	903187	1.01064e+06
60	2	847397	842638
60	5	1.49937e+06	1.16036e+06
60	10	1.14342e+06	1.04137e+06
0	1	612490	684038
0	1	717948	751458
0	1	629607	676409
0	1	698580	755642

Table 15: Experimental data for the experiment 100421_page100428_wt_il1_0u1u2u5u10_pmk2_pp38

2.2.7 Experiment: 100421_page100428_wt_il1_0u1u2u5u10_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 1–10 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 15 and 15, yields a value of the objective function $-2\log(L) = -121.552$ for 74 data points in this data set. The model observables and the experimental data is show in Figure 12.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \text{offset\_gel\_pMK2\_100241\_100428} + [\text{pMK2}] \cdot \text{scale\_pMK2\_100241\_100428} \tag{102}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \text{sd\_pMK2\_au} \tag{103}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au(t)} = \text{offset\_gel\_pp38\_100241\_100428} + [\text{pp38}] \cdot \text{scale\_pp38\_100241\_100428} \tag{104}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \text{sd\_pp38\_au} \tag{105}$$

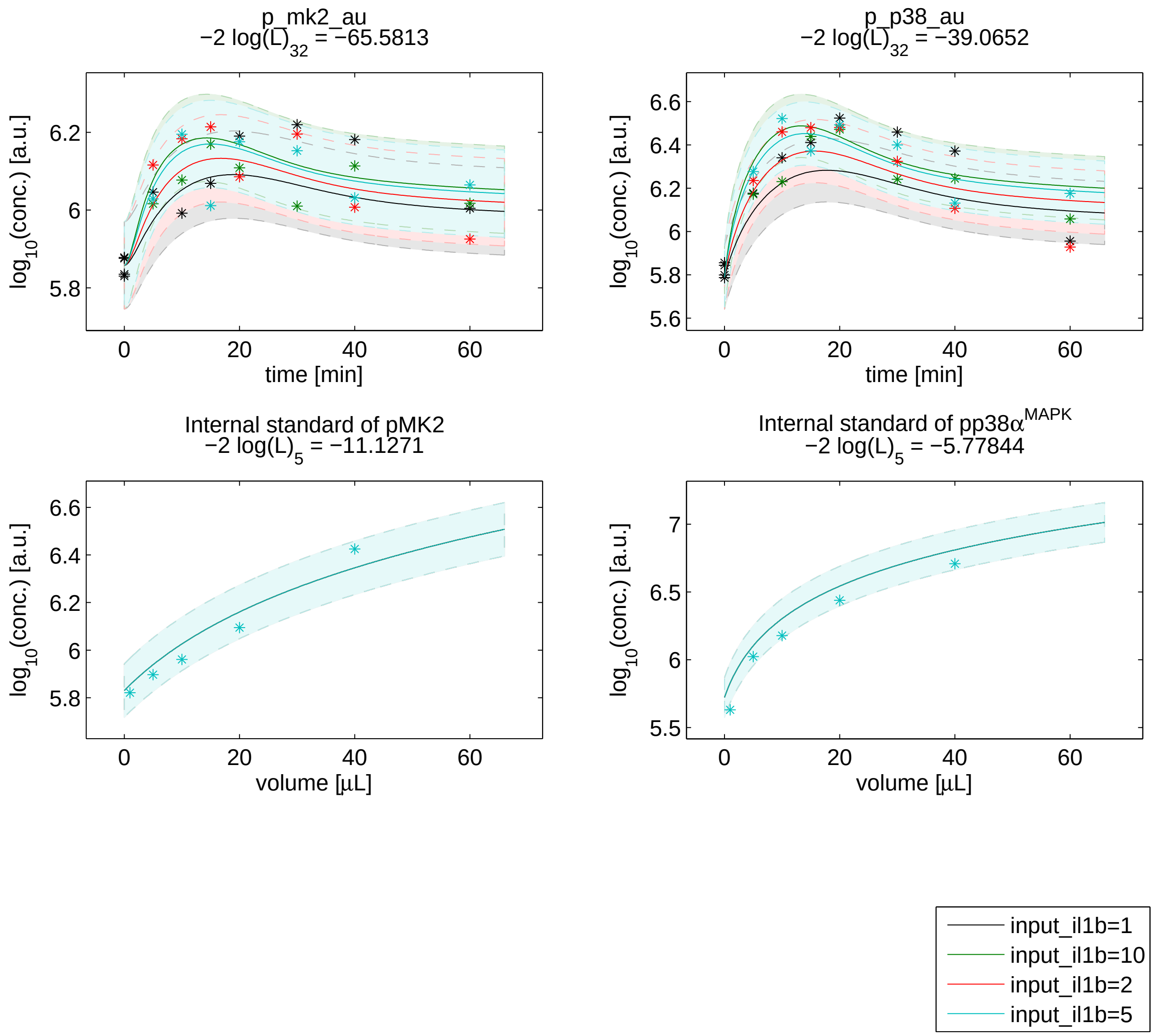

Figure 12: 100421_page100428_wt_il1_0u1u2u5u10_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	427058	662529
5	1.05384e+06	788116
10	1.50544e+06	913120
20	2.74532e+06	1.24266e+06
40	5.11046e+06	2.66121e+06

Table 16: Internal standard for the experiment 100421_page100428_wt_il1_0u1u2u5u10_pmk2_pp38

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au(intstd)} = \quad \text{offset\_gel\_pMK2\_100241\_100428} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_100241\_100428} \cdot \text{intstd}}{\text{V}} \tag{106}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \quad \text{sd\_pMK2\_au} \tag{107}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au(intstd)} = \quad \text{offset\_gel\_pp38\_100241\_100428} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_100241\_100428} \cdot \text{intstd}}{\text{V}} \tag{108}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_au} \tag{109}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \quad \rightarrow \quad 1 \mid 10 \mid 2 \mid 5$$

$$\text{scale\_pMK2\_100241\_100428} \quad \rightarrow \quad \frac{\text{scale\_pMK2\_100241\_100428}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_100241\_100428} \quad \rightarrow \quad \frac{\text{scale\_pp38\_100241\_100428}}{\text{init\_p38}}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	1	925339	79748
5	2	934619	89586
5	5	1.07770e+06	122261
5	10	1.38406e+06	137162
10	1	1.28419e+06	151815
10	2	1.48179e+06	158137
10	5	1.39311e+06	190807
10	10	1.47578e+06	173884
15	1	1.80453e+06	194760
15	2	1.51348e+06	210006
15	5	1.47673e+06	204830
15	10	1.60325e+06	236763
20	1	1.21865e+06	130650
20	2	1.63203e+06	243140
20	5	1.90430e+06	226179
20	10	1.77121e+06	217254
30	1	1.39577e+06	164699
30	2	1.27977e+06	133866
30	5	1.08711e+06	189901
30	10	1.18237e+06	122531
40	1	965871	106761
40	2	1.01813e+06	168894
40	5	1.10041e+06	105705
40	10	882114	134872
60	1	892197	96343
60	2	768930	116729
60	5	742301	61663
60	10	861305	73937
0	1	612099	14804
0	1	654480	5236
0	1	592011	20906
0	1	609305	6756

Table 17: Experimental data for the experiment 100421_page100430_wt_il1_0u1u2u5u10_pmk2_pp38

2.2.8 Experiment: 100421_page100430_wt_il1_0u1u2u5u10_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 1–10 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 17 and 18, yields a value of the objective function $-2\log(L) = -96.9426$ for 74 data points in this data set. The model observables and the experimental data is show in Figure 13.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \text{offset\_gel\_pMK2\_100241\_100430} + [\text{pMK2}] \cdot \text{scale\_pMK2\_100241\_100430} \tag{110}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \text{sd\_pMK2\_au} \tag{111}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au(t)} = \text{offset\_gel\_pp38\_100241\_100430} + [\text{pp38}] \cdot \text{scale\_pp38\_100241\_100430} \tag{112}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \text{sd\_pp38\_au} \tag{113}$$

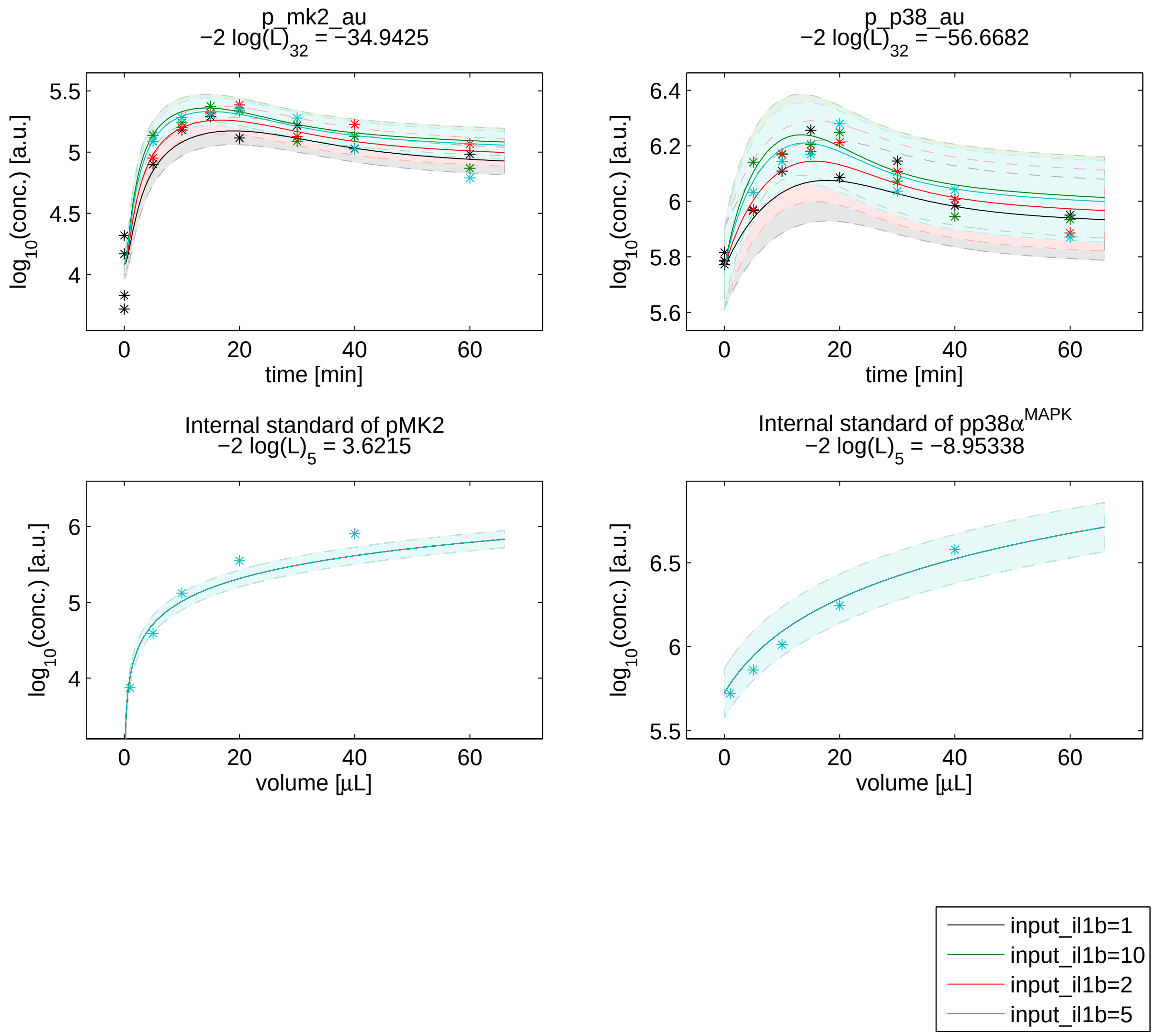

Figure 13: 100421_page100430_wt_il1_0u1u2u5u10_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	526196	7486
5	727135	38881
10	1.02843e+06	132803
20	1.75768e+06	354564
40	3.78369e+06	805892

Table 18: Internal standard for the experiment 100421_page100430_wt_il1_0u1u2u5u10_pmk2_pp38

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au}(\text{intstd}) = \quad \text{offset\_gel\_pMK2\_100241\_100430} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_100241\_100430} \cdot \text{intstd}}{\text{V}} \tag{114}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \quad \text{sd\_pMK2\_au} \tag{115}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au}(\text{intstd}) = \quad \text{offset\_gel\_pp38\_100241\_100430} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_100241\_100430} \cdot \text{intstd}}{\text{V}} \tag{116}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_au} \tag{117}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \quad \rightarrow \quad 1 \mid 10 \mid 2 \mid 5$$

$$\text{scale\_pMK2\_100241\_100430} \quad \rightarrow \quad \frac{\text{scale\_pMK2\_100241\_100430}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_100241\_100430} \quad \rightarrow \quad \frac{\text{scale\_pp38\_100241\_100430}}{\text{init\_p38}}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	1	759356	1.62877e+06
5	2	911797	1.32369e+06
5	5	1.10082e+06	1.49914e+06
5	10	1.29946e+06	1.75591e+06
10	1	1.52933e+06	1.55353e+06
10	2	1.63557e+06	1.53194e+06
10	5	1.98894e+06	751224
10	10	1.97715e+06	1.72726e+06
15	1	1.71820e+06	1.07659e+06
15	2	1.87097e+06	2.14204e+06
15	5	2.20478e+06	1.04897e+06
15	10	2.01690e+06	2.22913e+06
20	1	2.02467e+06	1.46725e+06
20	2	1.35225e+06	1.76359e+06
20	5	1.93808e+06	2.09011e+06
20	10	1.90135e+06	2.04503e+06
30	1	1.58485e+06	1.79597e+06
30	2	1.37374e+06	2.00700e+06
30	5	1.55227e+06	1.66012e+06
30	10	1.45740e+06	1.73791e+06
40	1	1.14096e+06	849242
40	2	1.11313e+06	1.25292e+06
40	5	1.06826e+06	1.59457e+06
40	10	1.12252e+06	1.23639e+06
60	1	1.03999e+06	702862
60	2	1.05752e+06	1.42231e+06
60	5	893271	2.00756e+06
60	10	792604	1.13760e+06
0	1	594037	792582
0	1	560650	1.17330e+06
0	1	585123	801775
0	1	607990	1.07508e+06

Table 19: Experimental data for the experiment 100421_page100505_wt_il1_0u1u2u5u10_pmk2_pp38

2.2.9 Experiment: 100421_page100505_wt_il1_0u1u2u5u10_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 1–10 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 19 and 20, yields a value of the objective function $-2\log(L) = -96.2628$ for 74 data points in this data set. The model observables and the experimental data is show in Figure 14.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au}(t) = \text{offset\_gel\_pMK2\_100241\_100505} + [\text{pMK2}] \cdot \text{scale\_pMK2\_100241\_100505} \quad (118)$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(t) = \text{sd\_pMK2\_au} \quad (119)$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au}(t) = \text{offset\_gel\_pp38\_100241\_100505} + [\text{pp38}] \cdot \text{scale\_pp38\_100241\_100505} \quad (120)$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(t) = \text{sd\_pp38\_au} \quad (121)$$

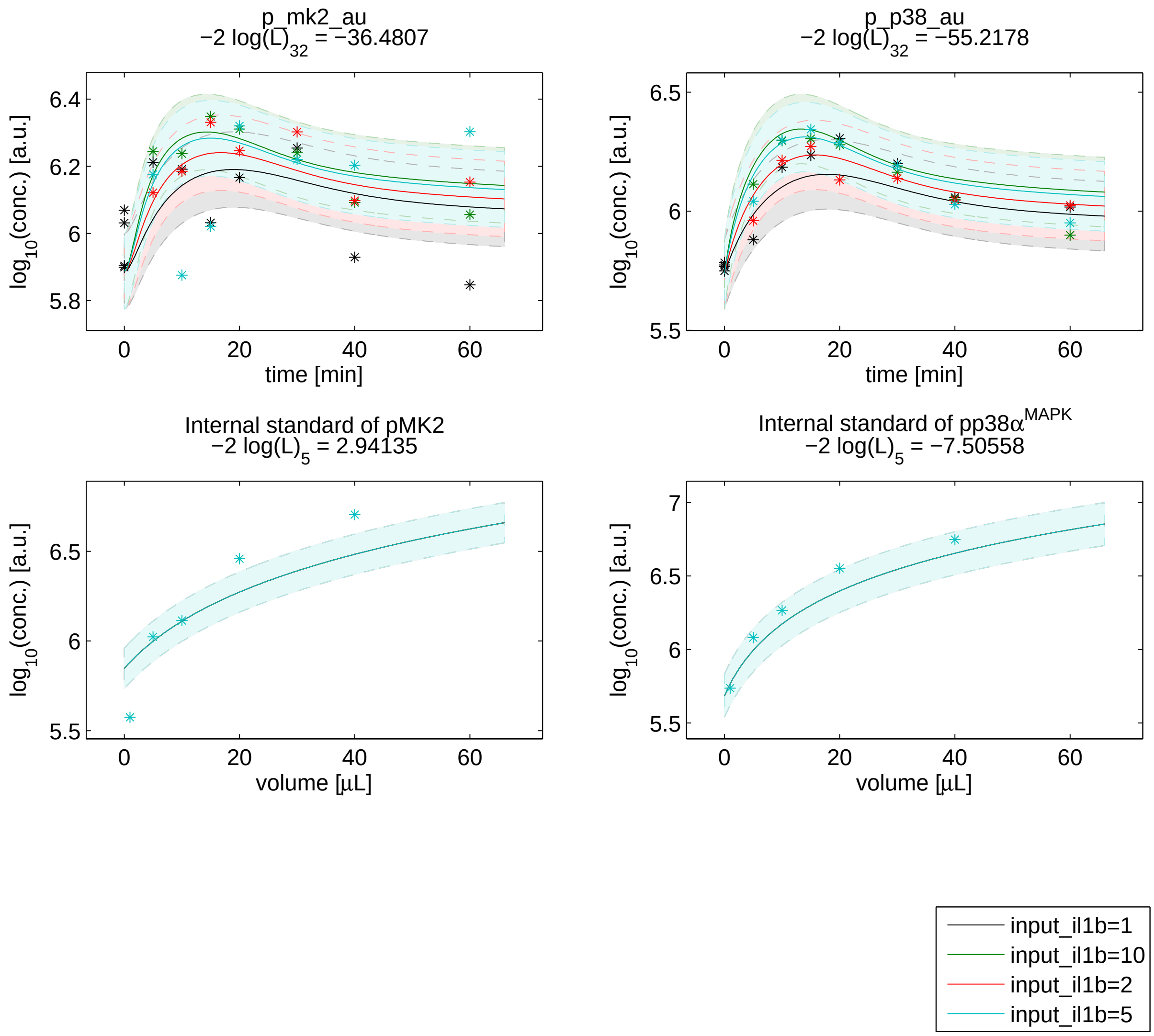

Figure 14: 100421_page100505_wt_il1_0u1u2u5u10_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	546004	375348
5	1.20220e+06	1.05445e+06
10	1.84295e+06	1.29914e+06
20	3.56130e+06	2.87569e+06
40	5.58367e+06	5.06114e+06

Table 20: Internal standard for the experiment 100421_page100505_wt_il1_0u1u2u5u10_pmk2_pp38

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au(intstd)} = \text{offset\_gel\_pMK2\_100241\_100505} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_100241\_100505} \cdot \text{intstd}}{\text{V}} \tag{122}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}\text{(intstd)} = \text{sd\_pMK2\_au} \tag{123}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au(intstd)} = \text{offset\_gel\_pp38\_100241\_100505} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_100241\_100505} \cdot \text{intstd}}{\text{V}} \tag{124}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}\text{(intstd)} = \text{sd\_pp38\_au} \tag{125}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \rightarrow 1 \mid 10 \mid 2 \mid 5$$

$$\text{scale\_pMK2\_100241\_100505} \rightarrow \frac{\text{scale\_pMK2\_100241\_100505}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_100241\_100505} \rightarrow \frac{\text{scale\_pp38\_100241\_100505}}{\text{init\_p38}}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	0.1	655788	1.23377e+06
5	0.2	680181	1.20598e+06
5	0.5	670694	1.39637e+06
5	1	902767	1.39392e+06
10	0.1	743838	1.24324e+06
10	0.2	803710	1.63004e+06
10	0.5	976969	1.91712e+06
10	1	1.14049e+06	2.02172e+06
15	0.1	886648	1.34560e+06
15	0.2	833157	1.68593e+06
15	0.5	927728	1.87098e+06
15	1	1.16055e+06	2.08684e+06
20	0.1	795094	1.33514e+06
20	0.2	933583	1.73856e+06
20	0.5	1.06691e+06	2.20341e+06
20	1	1.12970e+06	2.11432e+06
30	0.1	707073	1.59443e+06
30	0.2	881612	1.57580e+06
30	0.5	1.05158e+06	2.46336e+06
30	1	1.02165e+06	2.21556e+06
40	0.1	743265	1.37064e+06
40	0.2	829158	1.79449e+06
40	0.5	871513	2.14972e+06
40	1	747174	1.85104e+06
60	0.1	844785	1.32768e+06
60	0.2	736592	1.36100e+06
60	0.5	745767	1.44543e+06
60	1	726370	1.66707e+06
0	0.1	640530	980406
0	0.1	637960	863996
0	0.1	712929	942422
0	0.1	591955	780806

Table 21: Experimental data for the experiment 100504_page100527_wt_il1_0u01u02u05u1_pmk2_pp38

2.2.10 Experiment: 100504_page100527_wt_il1_0u01u02u05u1_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 0.1–1 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 21 and 21, yields a value of the objective function $-2\log(L) = -150.792$for 74 data points in this data set. The model observables and the experimental data is show in Figure 15.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au}(t) = \quad \text{offset\_gel\_pMK2\_100504\_100527} + [\text{pMK2}] \cdot \text{scale\_pMK2\_100504\_100527} \tag{126}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(t) = \quad \text{sd\_pMK2\_au} \tag{127}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au}(t) = \quad \text{offset\_gel\_pp38\_100504\_100527} + [\text{pp38}] \cdot \text{scale\_pp38\_100504\_100527} \tag{128}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(t) = \quad \text{sd\_pp38\_au} \tag{129}$$

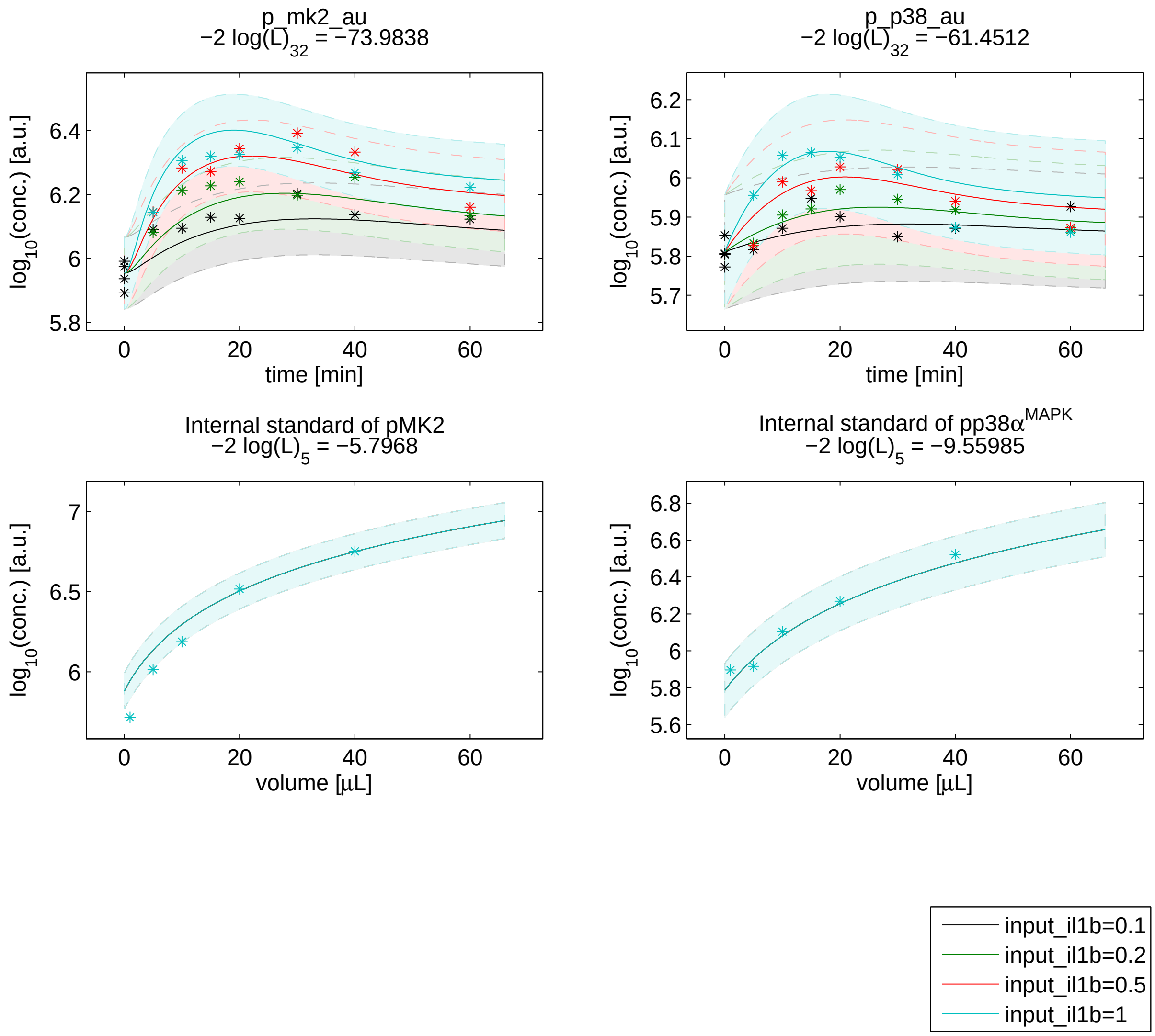

Figure 15: 100504_page100527_wt_il1_0u01u02u05u1_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	788202	520015
5	823964	1.03403e+06
10	1.26961e+06	1.53923e+06
20	1.85502e+06	3.28215e+06
40	3.32714e+06	5.64156e+06

Table 22: Internal standard for the experiment 100504_page100527_wt_il1_0u01u02u05u1_pmk2_pp38

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au}(\text{intstd}) = \quad \text{offset\_gel\_pMK2\_100504\_100527} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_100504\_100527} \cdot \text{intstd}}{\text{V}} \tag{130}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \quad \text{sd\_pMK2\_au} \tag{131}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au}(\text{intstd}) = \quad \text{offset\_gel\_pp38\_100504\_100527} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_100504\_100527} \cdot \text{intstd}}{\text{V}} \tag{132}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_au} \tag{133}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \quad \rightarrow \quad 0.1 \mid 0.2 \mid 0.5 \mid 1$$

$$\text{scale\_pMK2\_100504\_100527} \quad \rightarrow \quad \frac{\text{scale\_pMK2\_100504\_100527}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_100504\_100527} \quad \rightarrow \quad \frac{\text{scale\_pp38\_100504\_100527}}{\text{init\_p38}}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	0.1	550897	646582
5	0.2	593221	954446
5	0.5	779551	923157
5	1	848287	938554
10	0.1	754585	922032
10	0.2	866653	628859
10	0.5	1.27894e+06	1.20937e+06
10	1	1.57159e+06	1.46954e+06
15	0.1	777535	710791
15	0.2	1.06002e+06	1.17807e+06
15	0.5	1.53187e+06	1.33487e+06
15	1	1.95532e+06	1.80957e+06
20	0.1	807512	916207
20	0.2	1.47264e+06	1.27341e+06
20	0.5	1.86917e+06	1.61236e+06
20	1	2.07454e+06	1.80864e+06
30	0.1	966461	1.07429e+06
30	0.2	1.08517e+06	1.45219e+06
30	0.5	1.83886e+06	1.61689e+06
30	1	1.72210e+06	1.46825e+06
40	0.1	788372	1.08898e+06
40	0.2	968676	1.18565e+06
40	0.5	1.21770e+06	1.28502e+06
40	1	1.03184e+06	1.16326e+06
60	0.1	672987	1.00642e+06
60	0.2	837162	1.18775e+06
60	0.5	852687	1.10349e+06
60	1	767548	1.22126e+06
0	0.1	444955	695275
0	0.1	438132	618163
0	0.1	484372	861630
0	0.1	479522	745207

Table 23: Experimental data for the experiment 100504_pagedate100512_wt_il1_0u01u02u05u1_pmk2_pp38

2.2.11 Experiment: 100504_pagedate100512_wt_il1_0u01u02u05u1_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 0.1–1 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 23 and 24, yields a value of the objective function $-2\log(L) = -126.257$ for 74 data points in this data set. The model observables and the experimental data is show in Figure 16.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au}(t) = \quad \text{offset\_gel\_pMK2\_100504\_100512} + [\text{pMK2}] \cdot \text{scale\_pMK2\_100504\_100512} \tag{134}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(t) = \quad \text{sd\_pMK2\_au} \tag{135}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au}(t) = \quad \text{offset\_gel\_pp38\_100504\_100512} + [\text{pp38}] \cdot \text{scale\_pp38\_100504\_100512} \tag{136}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(t) = \quad \text{sd\_pp38\_au} \tag{137}$$

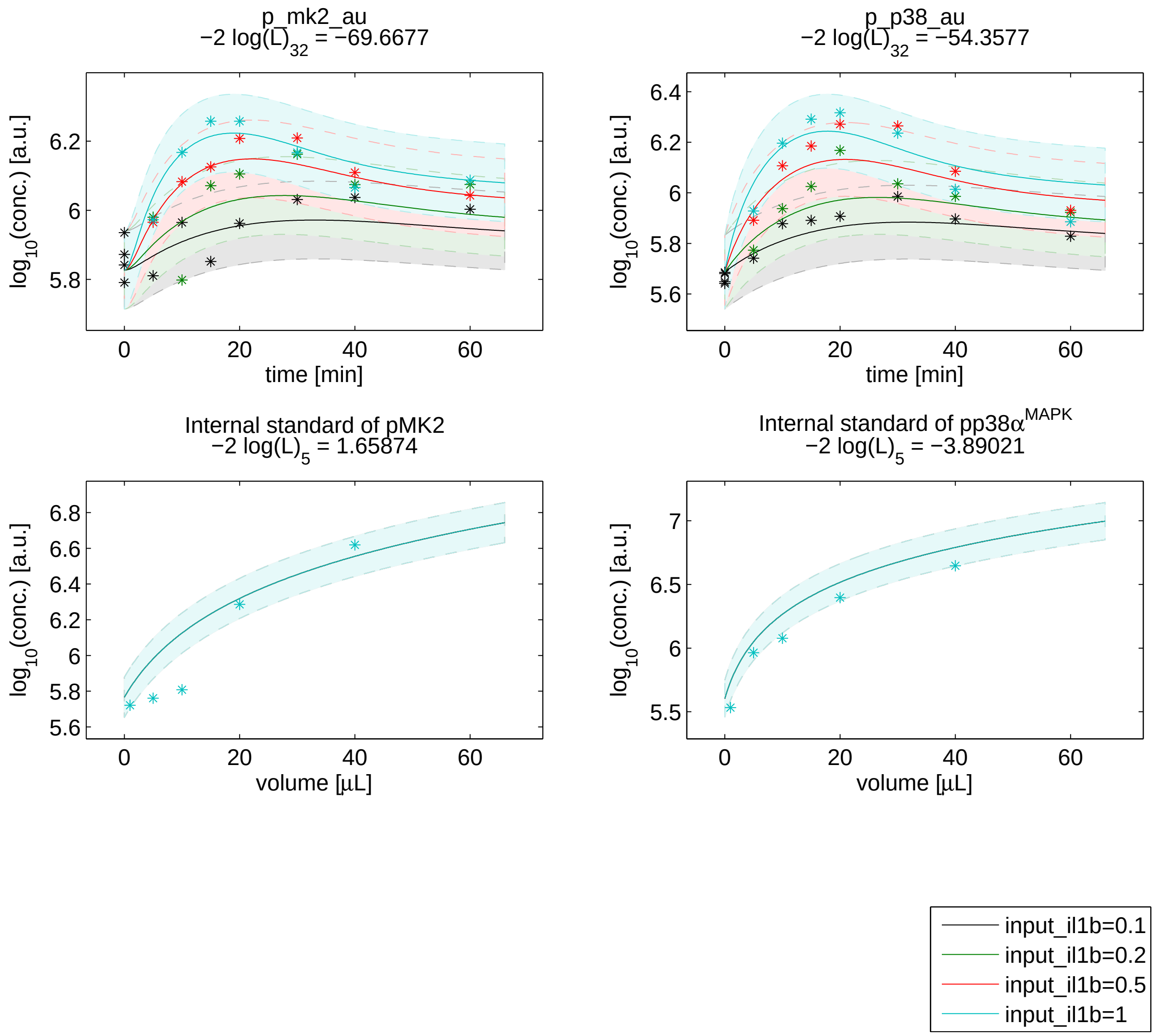

Figure 16: 100504_pagedate100512_wt_il1_0u01u02u05u1_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	341090	526025
5	919734	577067
10	1.19395e+06	643572
20	2.48881e+06	1.93437e+06
40	4.42954e+06	4.16300e+06

Table 24: Internal standard for the experiment 100504_pagedate100512_wt_il1_0u01u02u05u1_pmk2_pp38

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au(intstd)} = \text{offset\_gel\_pMK2\_100504\_100512} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_100504\_100512} \cdot \text{intstd}}{\text{V}} \quad (138)$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \text{sd\_pMK2\_au} \quad (139)$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au(intstd)} = \text{offset\_gel\_pp38\_100504\_100512} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_100504\_100512} \cdot \text{intstd}}{\text{V}} \quad (140)$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \text{sd\_pp38\_au} \quad (141)$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \rightarrow 0.1 \mid 0.2 \mid 0.5 \mid 1$$

$$\text{scale\_pMK2\_100504\_100512} \rightarrow \frac{\text{scale\_pMK2\_100504\_100512}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_100504\_100512} \rightarrow \frac{\text{scale\_pp38\_100504\_100512}}{\text{init\_p38}}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	0.1	550897	646582
5	0.2	593221	954446
5	0.5	779551	923157
5	1	848287	938554
10	0.1	754585	922032
10	0.2	866653	628859
10	0.5	1.27894e+06	1.20937e+06
10	1	1.57159e+06	1.46954e+06
15	0.1	777535	710791
15	0.2	1.06002e+06	1.17807e+06
15	0.5	1.53187e+06	1.33487e+06
15	1	1.95532e+06	1.80957e+06
20	0.1	807512	916207
20	0.2	1.47264e+06	1.27341e+06
20	0.5	1.86917e+06	1.61236e+06
20	1	2.07454e+06	1.80864e+06
30	0.1	966461	1.07429e+06
30	0.2	1.08517e+06	1.45219e+06
30	0.5	1.83886e+06	1.61689e+06
30	1	1.72210e+06	1.46825e+06
40	0.1	788372	1.08898e+06
40	0.2	968676	1.18565e+06
40	0.5	1.21770e+06	1.28502e+06
40	1	1.03184e+06	1.16326e+06
60	0.1	672987	1.00642e+06
60	0.2	837162	1.18775e+06
60	0.5	852687	1.10349e+06
60	1	767548	1.22126e+06
0	0.1	444955	695275
0	0.1	438132	618163
0	0.1	484372	861630
0	0.1	479522	745207

Table 25: Experimental data for the experiment 100504_pagedate100520_wt_il1_0u01u02u05u1_pmk2_pp38

2.2.12 Experiment: 100504_pagedate100520_wt_il1_0u01u02u05u1_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 0.1–1 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 25 and 26, yields a value of the objective function $-2\log(L) = -92.2201$ for 74 data points in this data set. The model observables and the experimental data is show in Figure 17.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \text{offset\_gel\_pMK2\_100504\_100520} + [\text{pMK2}] \cdot \text{scale\_pMK2\_100504\_100520} \quad (142)$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \text{sd\_pMK2\_au} \quad (143)$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au(t)} = \text{offset\_gel\_pp38\_100504\_100520} + [\text{pp38}] \cdot \text{scale\_pp38\_100504\_100520} \quad (144)$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \text{sd\_pp38\_au} \quad (145)$$

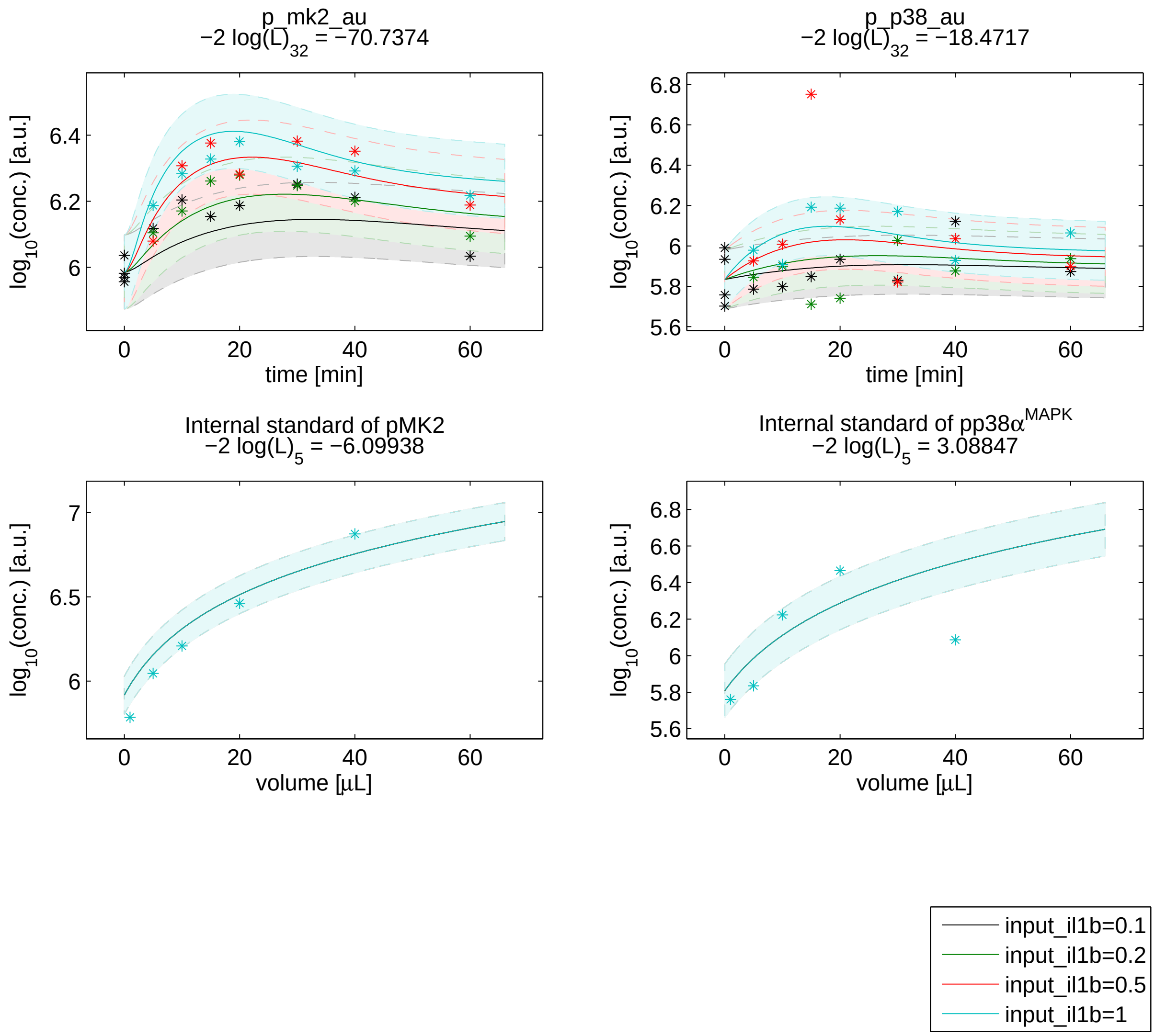

Figure 17: 100504_pagedate100520_wt_il1_0u01u02u05u1_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	341090	526025
5	919734	577067
10	1.19395e+06	643572
20	2.48881e+06	1.93437e+06
40	4.42954e+06	4.16300e+06

Table 26: Internal standard for the experiment 100504_pagedate100520_wt_il1_0u01u02u05u1_pmk2_pp38

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au(intstd)} = \quad \text{offset\_gel\_pMK2\_100504\_100520} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_100504\_100520} \cdot \text{intstd}}{\text{V}} \tag{146}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \quad \text{sd\_pMK2\_au} \tag{147}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au(intstd)} = \quad \text{offset\_gel\_pp38\_100504\_100520} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_100504\_100520} \cdot \text{intstd}}{\text{V}} \tag{148}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_au} \tag{149}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \quad \rightarrow \quad 0.1 \mid 0.2 \mid 0.5 \mid 1$$

$$\text{scale\_pMK2\_100504\_100520} \quad \rightarrow \quad \frac{\text{scale\_pMK2\_100504\_100520}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_100504\_100520} \quad \rightarrow \quad \frac{\text{scale\_pp38\_100504\_100520}}{\text{init\_p38}}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	0.1	611388	1.31108e+06
5	0.2	700501	1.27185e+06
5	0.5	843973	1.20029e+06
5	1	953226	1.53775e+06
10	0.1	627227	1.59945e+06
10	0.2	793338	1.48103e+06
10	0.5	1.01861e+06	2.03053e+06
10	1	808778	1.91912e+06
15	0.1	705661	1.42510e+06
15	0.2	514395	1.82443e+06
15	0.5	5.64022e+06	2.37820e+06
15	1	1.55542e+06	2.12796e+06
20	0.1	858252	1.53842e+06
20	0.2	550771	1.90316e+06
20	0.5	1.35245e+06	1.91573e+06
20	1	1.53784e+06	2.40599e+06
30	0.1	675127	1.78579e+06
30	0.2	1.06472e+06	1.76892e+06
30	0.5	663295	2.41105e+06
30	1	1.48249e+06	2.02300e+06
40	0.1	1.32378e+06	1.62853e+06
40	0.2	752021	1.58714e+06
40	0.5	1.08471e+06	2.24647e+06
40	1	847625	1.95800e+06
60	0.1	746054	1.07998e+06
60	0.2	864440	1.24344e+06
60	0.5	793432	1.54367e+06
60	1	1.16038e+06	1.65111e+06
0	0.1	857935	932919
0	0.1	572159	903869
0	0.1	978195	1.08669e+06
0	0.1	503616	959204

Table 27: Experimental data for the experiment 100517_page100610a_wt_il1_0u001u005u01u02_pmk2_pp38

2.2.13 Experiment: 100517_page100610a_wt_il1_0u001u005u01u02_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 0.01–0.2 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 27 and 28, yields a value of the objective function $-2\log(L) = -134.815$ for 74 data points in this data set. The model observables and the experimental data is show in Figure 18.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \text{offset\_gel\_pMK2\_100517\_100610a} + [\text{pMK2}] \cdot \text{scale\_pMK2\_100517\_100610a} \tag{150}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \text{sd\_pMK2\_au} \tag{151}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au(t)} = \text{offset\_gel\_pp38\_100517\_100610a} + [\text{pp38}] \cdot \text{scale\_pp38\_100517\_100610a} \tag{152}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \text{sd\_pp38\_au} \tag{153}$$

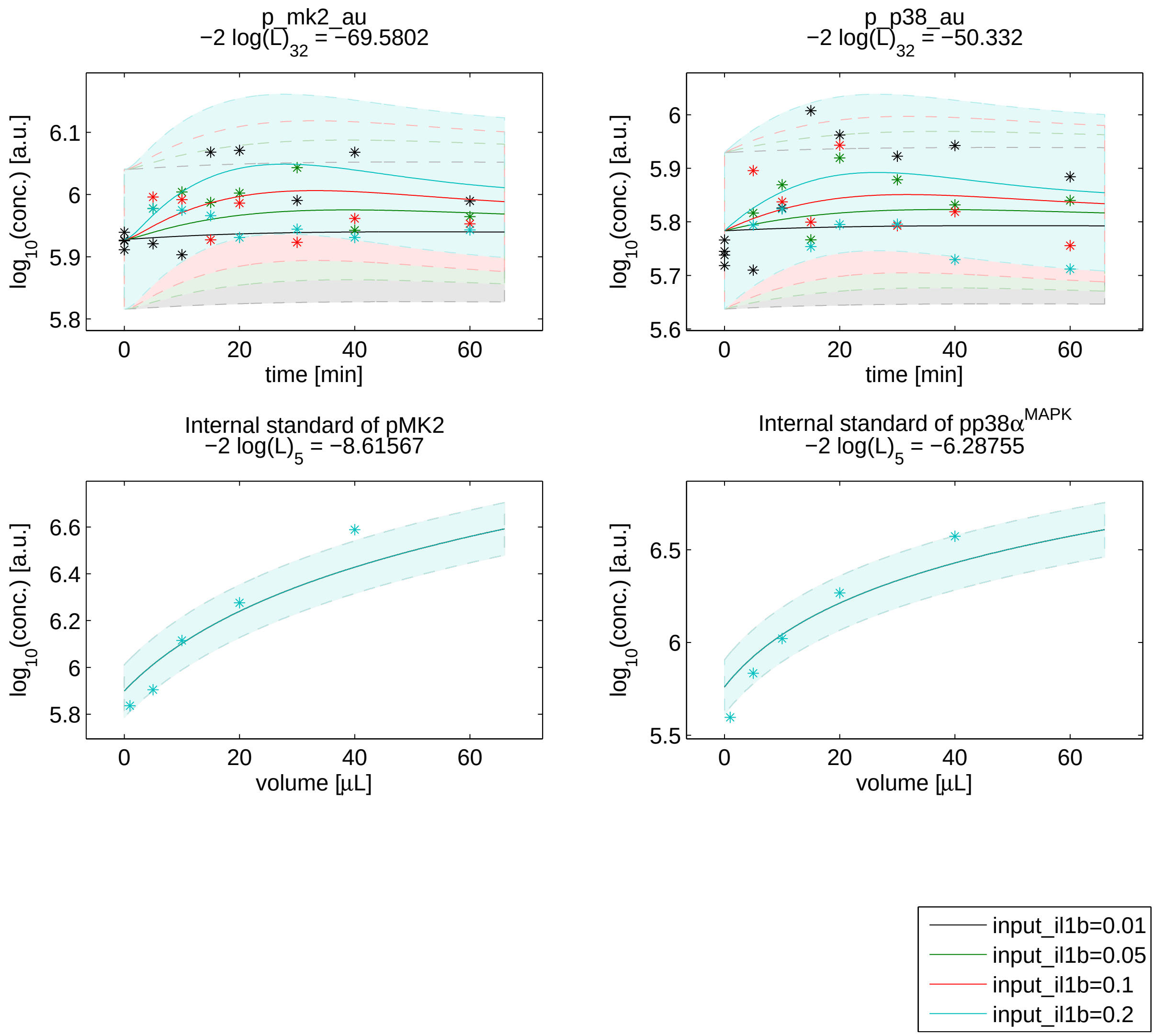

Figure 18: 100517_page100610a_wt_il1_0u001u005u01u02_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	575955	610735
5	684132	1.11098e+06
10	1.67026e+06	1.61732e+06
20	2.92129e+06	2.89679e+06
40	1.21973e+06	7.45377e+06

Table 28: Internal standard for the experiment 100517_page100610a_wt_il1_0u001u005u01u02_pmk2_pp38

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au}(\text{intstd}) = \quad \text{offset\_gel\_pMK2\_100517\_100610a} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_100517\_100610a} \cdot \text{intstd}}{\text{V}} \tag{154}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \quad \text{sd\_pMK2\_au} \tag{155}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au}(\text{intstd}) = \quad \text{offset\_gel\_pp38\_100517\_100610a} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_100517\_100610a} \cdot \text{intstd}}{\text{V}} \tag{156}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_au} \tag{157}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \quad \rightarrow \quad 0.01 \mid 0.05 \mid 0.1 \mid 0.2$$

$$\text{scale\_pMK2\_100517\_100610a} \quad \rightarrow \quad \frac{\text{scale\_pMK2\_100517\_100610a}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_100517\_100610a} \quad \rightarrow \quad \frac{\text{scale\_pp38\_100517\_100610a}}{\text{init\_p38}}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	0	512904	1.21761e+06
5	0.1	655351	1.04402e+06
5	0.1	786666	1.23575e+06
5	0.2	622180	1.19598e+06
10	0	669629	1.20979e+06
10	0.1	740234	1.21667e+06
10	0.1	687462	1.03375e+06
10	0.2	666854	1.14704e+06
15	0	1.01786e+06	1.33826e+06
15	0.1	583867	1.25687e+06
15	0.1	630434	1.04149e+06
15	0.2	567266	1.08303e+06
20	0	916585	1.43808e+06
20	0.1	830774	1.12124e+06
20	0.1	877106	1.09974e+06
20	0.2	623863	944999
30	0	836922	1.27386e+06
30	0.1	756458	1.22893e+06
30	0.1	620519	1.01399e+06
30	0.2	624886	1.05330e+06
40	0	876375	1.51971e+06
40	0.1	678762	1.27345e+06
40	0.1	658906	1.09799e+06
40	0.2	536348	931296
60	0	766241	1.12814e+06
60	0.1	691864	1.17149e+06
60	0.1	569824	1.17547e+06
60	0.2	515089	1.04646e+06
0	0	583520	950892
0	0	546991	938847
0	0	522963	940606
0	0	556109	999735

Table 29: Experimental data for the experiment 100517_page100610b_wt_il1_0u001u005u01u02_pmk2_pp38

2.2.14 Experiment: 100517_page100610b_wt_il1_0u001u005u01u02_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 0.01–0.2 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 29 and 30, yields a value of the objective function $-2\log(L) = -131.12$ for 74 data points in this data set. The model observables and the experimental data is show in Figure 19.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \quad \text{offset\_gel\_pMK2\_100517\_100610b} + [\text{pMK2}] \cdot \text{scale\_pMK2\_100517\_100610b} \tag{158}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \quad \text{sd\_pMK2\_au} \tag{159}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au(t)} = \quad \text{offset\_gel\_pp38\_100517\_100610b} + [\text{pp38}] \cdot \text{scale\_pp38\_100517\_100610b} \tag{160}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \quad \text{sd\_pp38\_au} \tag{161}$$

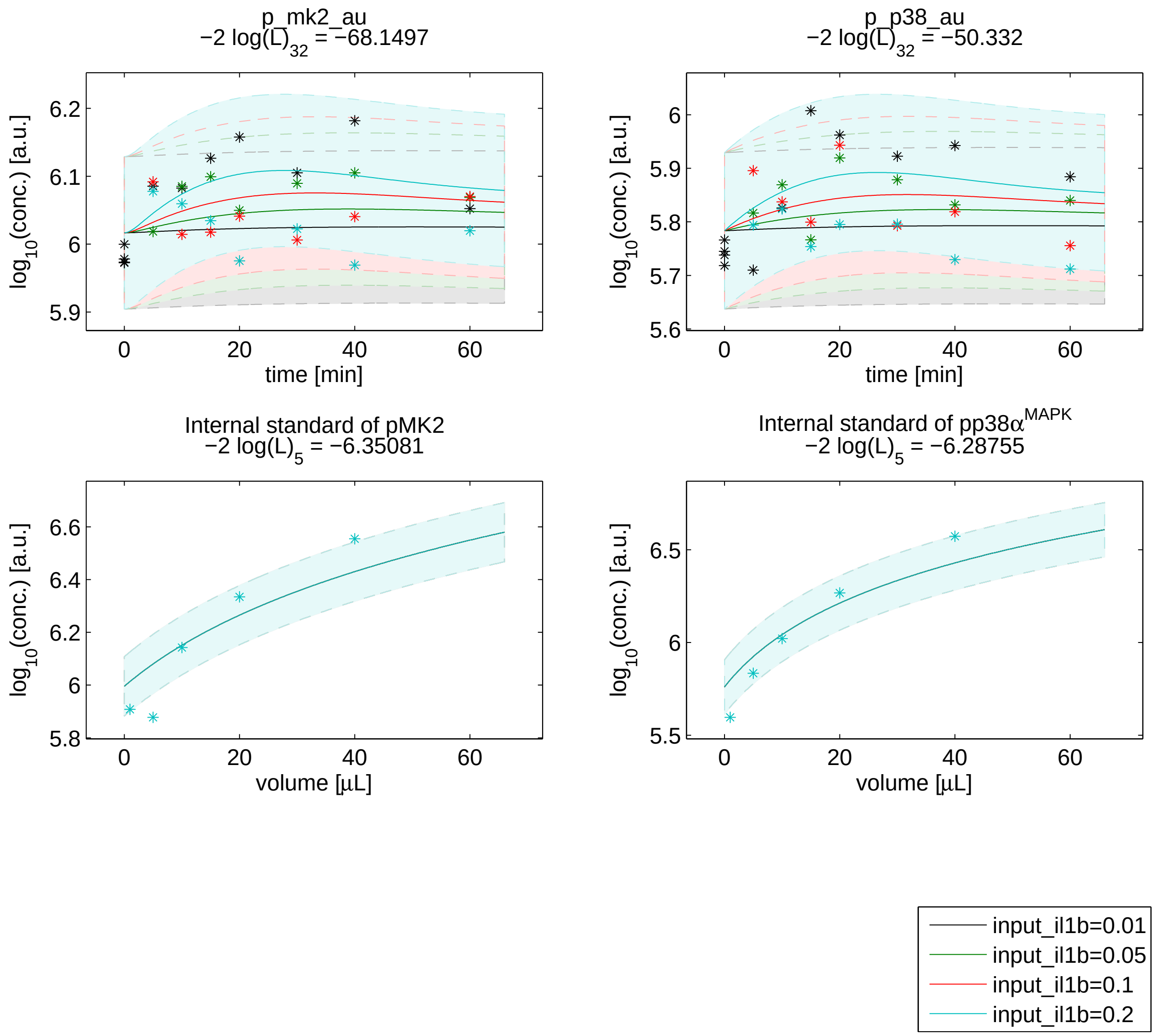

Figure 19: 100517_page100610b_wt_il1_0u001u005u01u02_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	395377	809644
5	682798	754921
10	1.04934e+06	1.38762e+06
20	1.85184e+06	2.16022e+06
40	3.73713e+06	3.58624e+06

Table 30: Internal standard for the experiment 100517_page100610b_wt_il1_0u001u005u01u02_pmk2_pp38

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au(intstd)} = \quad \text{offset\_gel\_pMK2\_100517\_100610b} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_100517\_100610b} \cdot \text{intstd}}{\text{V}} \tag{162}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \quad \text{sd\_pMK2\_au} \tag{163}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au(intstd)} = \quad \text{offset\_gel\_pp38\_100517\_100610b} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_100517\_100610b} \cdot \text{intstd}}{\text{V}} \tag{164}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_au} \tag{165}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \quad \rightarrow \quad 0.01 \mid 0.05 \mid 0.1 \mid 0.2$$

$$\text{scale\_pMK2\_100517\_100610b} \quad \rightarrow \quad \frac{\text{scale\_pMK2\_100517\_100610b}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_100517\_100610b} \quad \rightarrow \quad \frac{\text{scale\_pp38\_100517\_100610b}}{\text{init\_p38}}$$

time [min]	input_il1b [$ng \cdot ml^{-1}$]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	0.1	722748	1.23312e+06
5	0.2	853284	1.41382e+06
5	0.5	795463	1.31188e+06
5	1	729087	1.31844e+06
10	0.1	890756	1.28138e+06
10	0.2	940408	1.48264e+06
10	0.5	940873	1.64226e+06
10	1	1.12751e+06	1.95073e+06
15	0.1	910431	1.56493e+06
15	0.2	976939	1.67838e+06
15	0.5	1.15763e+06	2.00292e+06
15	1	883537	1.82138e+06
20	0.1	845467	1.37735e+06
20	0.2	898157	1.80550e+06
20	0.5	1.30277e+06	2.15814e+06
20	1	1.11108e+06	2.10824e+06
30	0.1	838474	1.38483e+06
30	0.2	821183	1.46551e+06
30	0.5	1.25536e+06	1.92678e+06
30	1	862630	1.74131e+06
40	0.1	929900	1.46569e+06
40	0.2	943543	1.69050e+06
40	0.5	833884	1.62309e+06
40	1	884284	1.68571e+06
60	0.1	742860	1.35426e+06
60	0.2	680502	1.31949e+06
60	0.5	1.06434e+06	1.80862e+06
60	1	627056	1.69537e+06
0	0.1	688344	1.07255e+06
0	0.1	848932	1.29901e+06

Table 31: Experimental data for the experiment 100628b_page100727_wt_il1_0u01u02u05u1_pmk2_pp38

2.2.15 Experiment: 100628b_page100727_wt_il1_0u01u02u05u1_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 0.1–1 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 31 and 32, yields a value of the objective function $-2\log(L) = -128.85$ for 70 data points in this data set. The model observables and the experimental data is show in Figure 20.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \text{offset\_gel\_pMK2\_100628b\_100727} + [\text{pMK2}] \cdot \text{scale\_pMK2\_100628b\_100727} \tag{166}$$

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	853993	1.06075e+06
5	1.22405e+06	1.16091e+06
10	2.35711e+06	1.94750e+06
20	4.04057e+06	3.47802e+06
40	6.68282e+06	7.35191e+06

Table 32: Internal standard for the experiment 100628b_page100727_wt_il1_0u01u02u05u1_pmk2_pp38

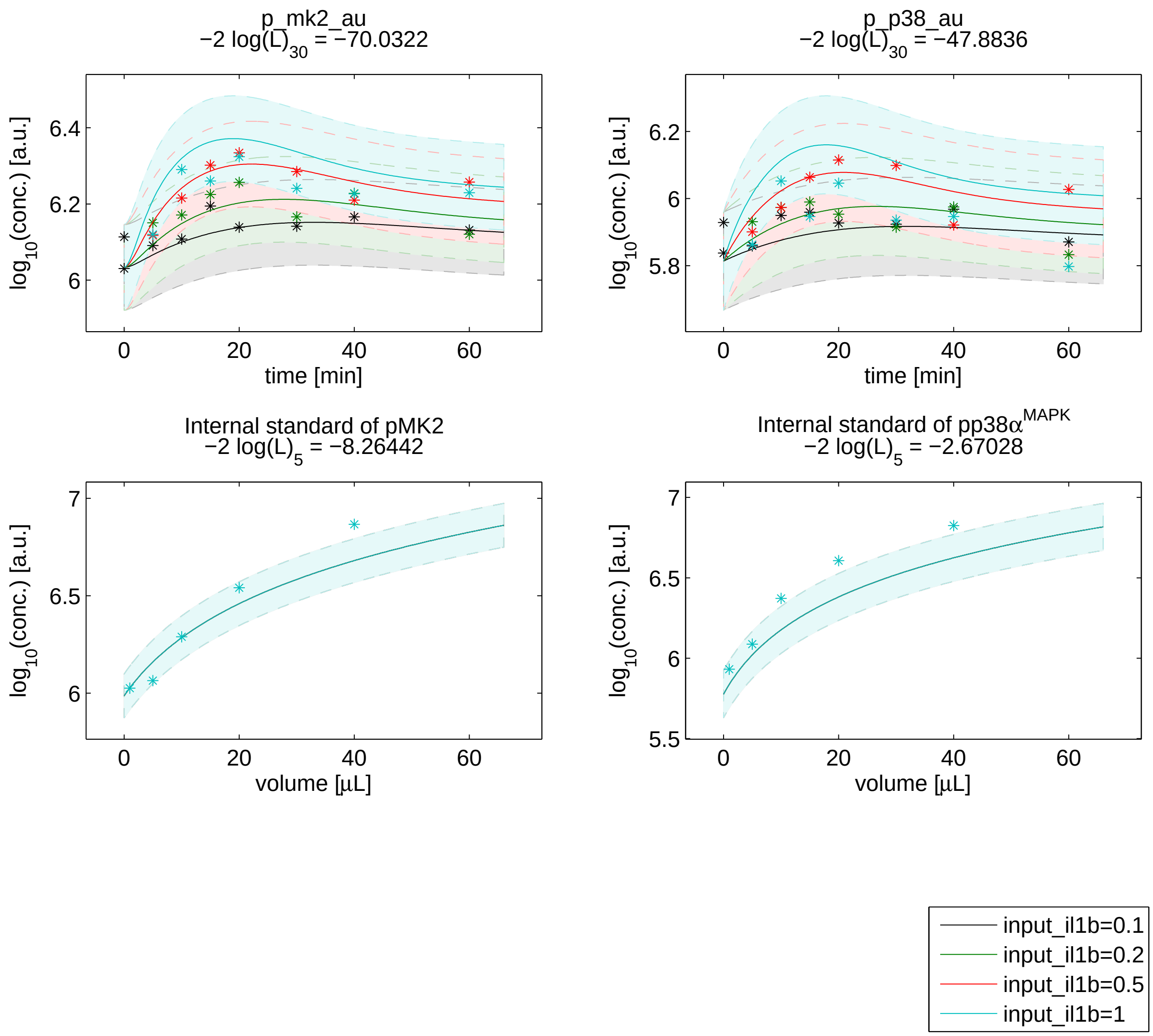

Figure 20: 100628b_page100727_wt_il1_0u01u02u05u1_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

Unit: conc. [a.u.]; With error model:

$$\sigma\{\mathrm{p\_mk2\_au}\}(\mathrm{t}) = \quad \mathrm{sd\_pMK2\_au} \tag{167}$$

- **Observable:** p_p38_au

$$\mathrm{p\_p38\_au}(\mathrm{t}) = \quad \mathrm{offset\_gel\_pp38\_100628b\_100727} + [\mathrm{pp38}] \cdot \mathrm{scale\_pp38\_100628b\_100727} \tag{168}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\mathrm{p\_p38\_au}\}(\mathrm{t}) = \quad \mathrm{sd\_pp38\_au} \tag{169}$$

- **Observable:** int_p_mk2_au

$$\mathrm{int\_p\_mk2\_au}(\mathrm{intstd}) = \quad \mathrm{offset\_gel\_pMK2\_100628b\_100727} + \frac{\mathrm{scale\_pMK2} \cdot \mathrm{scale\_pMK2\_100628b\_100727} \cdot \mathrm{intstd}}{\mathrm{V}} \tag{170}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\mathrm{int\_p\_mk2\_au}\}(\mathrm{intstd}) = \quad \mathrm{sd\_pMK2\_au} \tag{171}$$

- **Observable:** int_p_p38_au

$$\mathrm{int\_p\_p38\_au}(\mathrm{intstd}) = \quad \mathrm{offset\_gel\_pp38\_100628b\_100727} + \frac{\mathrm{scale\_pp38} \cdot \mathrm{scale\_pp38\_100628b\_100727} \cdot \mathrm{intstd}}{\mathrm{V}} \tag{172}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\mathrm{int\_p\_p38\_au}\}(\mathrm{intstd}) = \quad \mathrm{sd\_pp38\_au} \tag{173}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\mathrm{input\_il1b} \quad \rightarrow \quad 0.1 \mid 0.2 \mid 0.5 \mid 1$$

$$\mathrm{scale\_pMK2\_100628b\_100727} \quad \rightarrow \quad \frac{\mathrm{scale\_pMK2\_100628b\_100727}}{\mathrm{init\_MK2}}$$

$$\mathrm{scale\_pp38\_100628b\_100727} \quad \rightarrow \quad \frac{\mathrm{scale\_pp38\_100628b\_100727}}{\mathrm{init\_p38}}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	0.1	722952	1.03004e+06
5	0.2	615439	1.20730e+06
5	0.5	761457	1.08321e+06
5	1	610840	1.20782e+06
10	0.1	619458	1.01476e+06
10	0.2	833647	929497
10	0.5	796891	1.34044e+06
10	1	834316	1.48273e+06
15	0.1	613677	1.15900e+06
15	0.2	684809	1.01944e+06
15	0.5	659067	1.36406e+06
15	1	863195	1.65046e+06
20	0.1	687624	863952
20	0.2	680610	1.59208e+06
20	0.5	688219	1.01759e+06
20	1	1.04158e+06	1.67175e+06
30	0.1	613909	1.20728e+06
30	0.2	861346	1.21168e+06
30	0.5	795048	1.05817e+06
30	1	814250	1.96829e+06
40	0.1	811689	990572
40	0.2	630124	1.16036e+06
40	0.5	788092	1.42571e+06
40	1	933532	1.48742e+06
60	0.1	622588	1.06130e+06
60	0.2	630252	1.40708e+06
60	0.5	679701	1.36327e+06
60	1	749906	1.28721e+06
0	0.1	700990	942007
0	0.1	680600	1.07009e+06

Table 33: Experimental data for the experiment 100628b_page100728a_wt_il1_0u01u02u05u1_pmk2_pp38

2.2.16 Experiment: 100628b_page100728a_wt_il1_0u01u02u05u1_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 0.1–1 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 33 and 34, yields a value of the objective function $-2\log(L) = -132.704$ for 70 data points in this data set. The model observables and the experimental data is show in Figure 21.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \text{offset\_gel\_pMK2\_100628b\_100728a} + [\text{pMK2}] \cdot \text{scale\_pMK2\_100628b\_100728a} \tag{174}$$

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	497475	831934
5	938067	992907
10	1.65583e+06	1.63055e+06
20	3.10860e+06	3.20702e+06
40	2.92403e+06	3.60867e+06

Table 34: Internal standard for the experiment 100628b_page100728a_wt_il1_0u01u02u05u1_pmk2_pp38

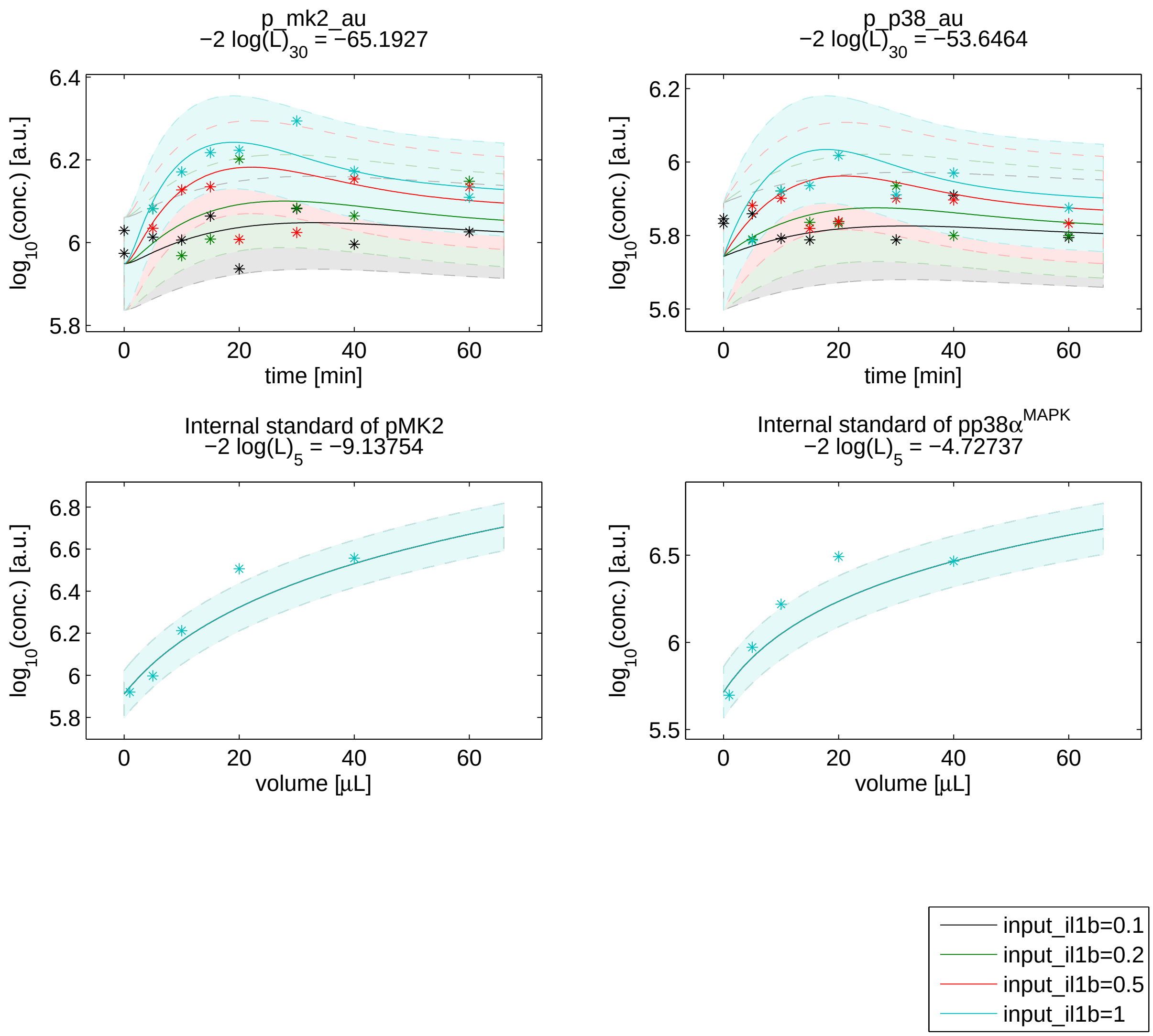

Figure 21: 100628b_page100728a_wt_il1_0u01u02u05u1_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \quad \text{sd\_pMK2\_au} \tag{175}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au}(\text{t}) = \quad \text{offset\_gel\_pp38\_100628b\_100728a} + [\text{pp38}] \cdot \text{scale\_pp38\_100628b\_100728a} \tag{176}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \quad \text{sd\_pp38\_au} \tag{177}$$

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au}(\text{intstd}) = \quad \text{offset\_gel\_pMK2\_100628b\_100728a} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_100628b\_100728a} \cdot \text{intstd}}{\text{V}} \tag{178}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \quad \text{sd\_pMK2\_au} \tag{179}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au}(\text{intstd}) = \quad \text{offset\_gel\_pp38\_100628b\_100728a} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_100628b\_100728a} \cdot \text{intstd}}{\text{V}} \tag{180}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_au} \tag{181}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \quad \rightarrow \quad 0.1 \mid 0.2 \mid 0.5 \mid 1$$

$$\text{scale\_pMK2\_100628b\_100727} \quad \rightarrow \quad \frac{\text{scale\_pMK2\_100628b\_100727}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_100628b\_100728a} \quad \rightarrow \quad \frac{\text{scale\_pp38\_100628b\_100728a}}{\text{init\_p38}}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	0.1	686212	1.07256e+06
5	0.2	724354	927487
5	0.5	647093	913891
5	1	735123	1.10162e+06
10	0.1	578242	1.02273e+06
10	0.2	585371	1.00378e+06
10	0.5	758707	1.52011e+06
10	1	944310	1.82361e+06
15	0.1	635523	950488
15	0.2	660105	1.30188e+06
15	0.5	665869	1.49120e+06
15	1	938847	1.58311e+06
20	0.1	733571	769158
20	0.2	653741	1.15237e+06
20	0.5	697333	1.62825e+06
20	1	908029	1.51383e+06
30	0.1	654582	1.04047e+06
30	0.2	532231	1.07726e+06
30	0.5	837961	1.14097e+06
30	1	878256	1.56617e+06
40	0.1	644657	827687
40	0.2	696826	1.29390e+06
40	0.5	846472	1.52030e+06
40	1	794731	1.51025e+06
60	0.1	700220	1.07511e+06
60	0.2	837888	1.35190e+06
60	0.5	679119	1.45311e+06
60	1	680833	1.34025e+06
0	0.1	752977	965299
0	0.1	619005	826662

Table 35: Experimental data for the experiment 100628b_page100728b_wt_il1_0u01u02u05u1_pmk2_pp38

2.2.17 Experiment: 100628b_page100728b_wt_il1_0u01u02u05u1_pmk2_pp38

Comments In this experiment the primary hepatocytes were treated with IL-1β doses from 0.1–1 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 35 and 36, yields a value of the objective function $-2\log(L) = -136.472$ for 70 data points in this data set. The model observables and the experimental data is show in Figure 22.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \text{offset\_gel\_pMK2\_100628b\_100728b} + [\text{pMK2}] \cdot \text{scale\_pMK2\_100628b\_100728b} \tag{182}$$

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	755987	798249
5	1.05470e+06	932393
10	1.39170e+06	1.25241e+06
20	2.34829e+06	2.75439e+06
40	3.73817e+06	5.30541e+06

Table 36: Internal standard for the experiment 100628b_page100728b_wt_il1_0u01u02u05u1_pmk2_pp38

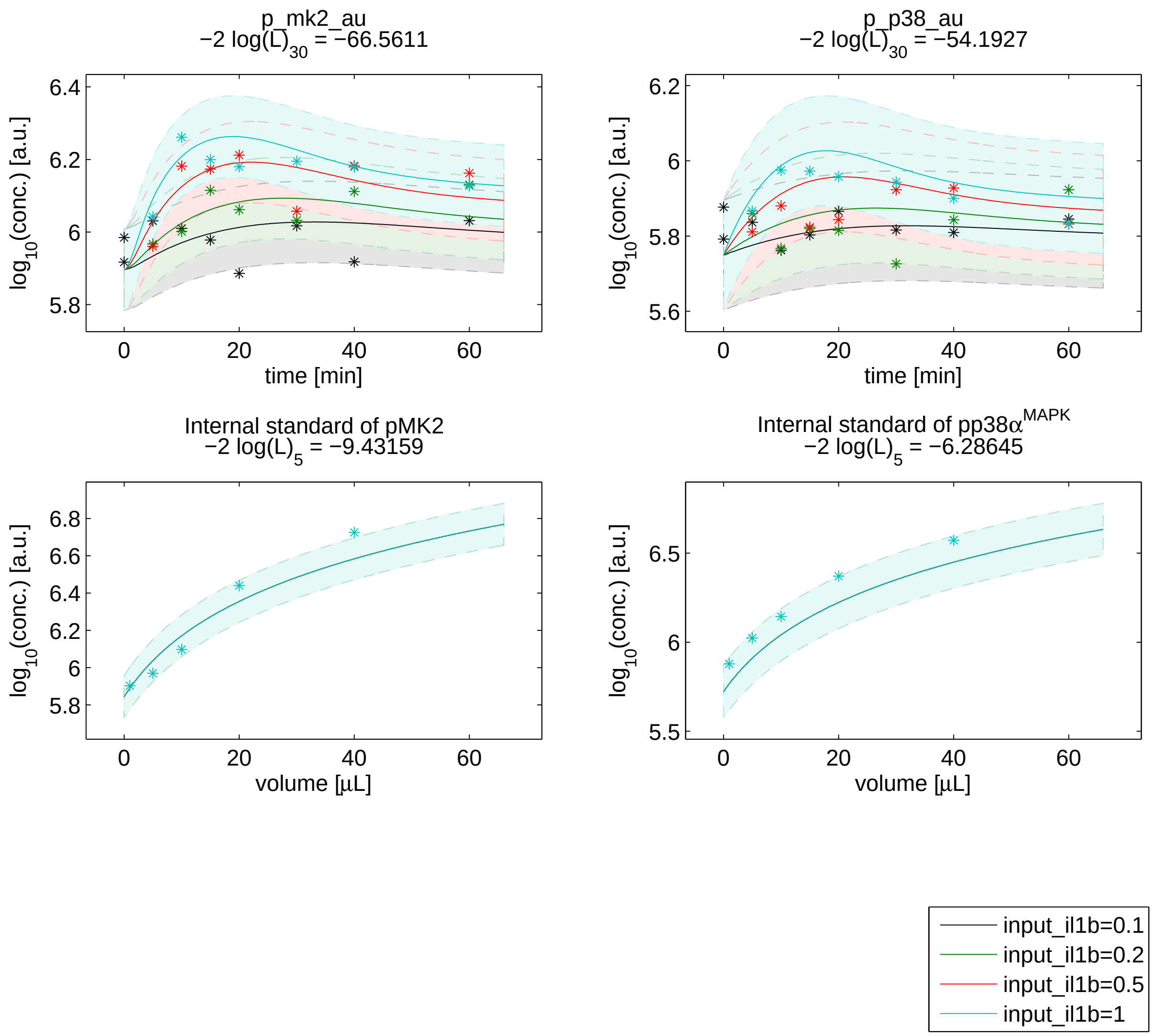

Figure 22: 100628b_page100728b_wt_il1_0u01u02u05u1_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \quad \text{sd\_pMK2\_au} \tag{183}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au}(\text{t}) = \quad \text{offset\_gel\_pp38\_100628b\_100728b} + [\text{pp38}] \cdot \text{scale\_pp38\_100628b\_100728b} \tag{184}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \quad \text{sd\_pp38\_au} \tag{185}$$

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au}(\text{intstd}) = \quad \text{offset\_gel\_pMK2\_100628b\_100728b} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_100628b\_100728b} \cdot \text{intstd}}{\text{V}} \tag{186}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \quad \text{sd\_pMK2\_au} \tag{187}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au}(\text{intstd}) = \quad \text{offset\_gel\_pp38\_100628b\_100728b} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_100628b\_100728b} \cdot \text{intstd}}{\text{V}} \tag{188}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_au} \tag{189}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \quad \rightarrow \quad 0.1 \mid 0.2 \mid 0.5 \mid 1$$

$$\text{scale\_pMK2\_100628b\_100728b} \quad \rightarrow \quad \frac{\text{scale\_pMK2\_100628b\_100728b}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_100628b\_100728b} \quad \rightarrow \quad \frac{\text{scale\_pp38\_100628b\_100728b}}{\text{init\_p38}}$$

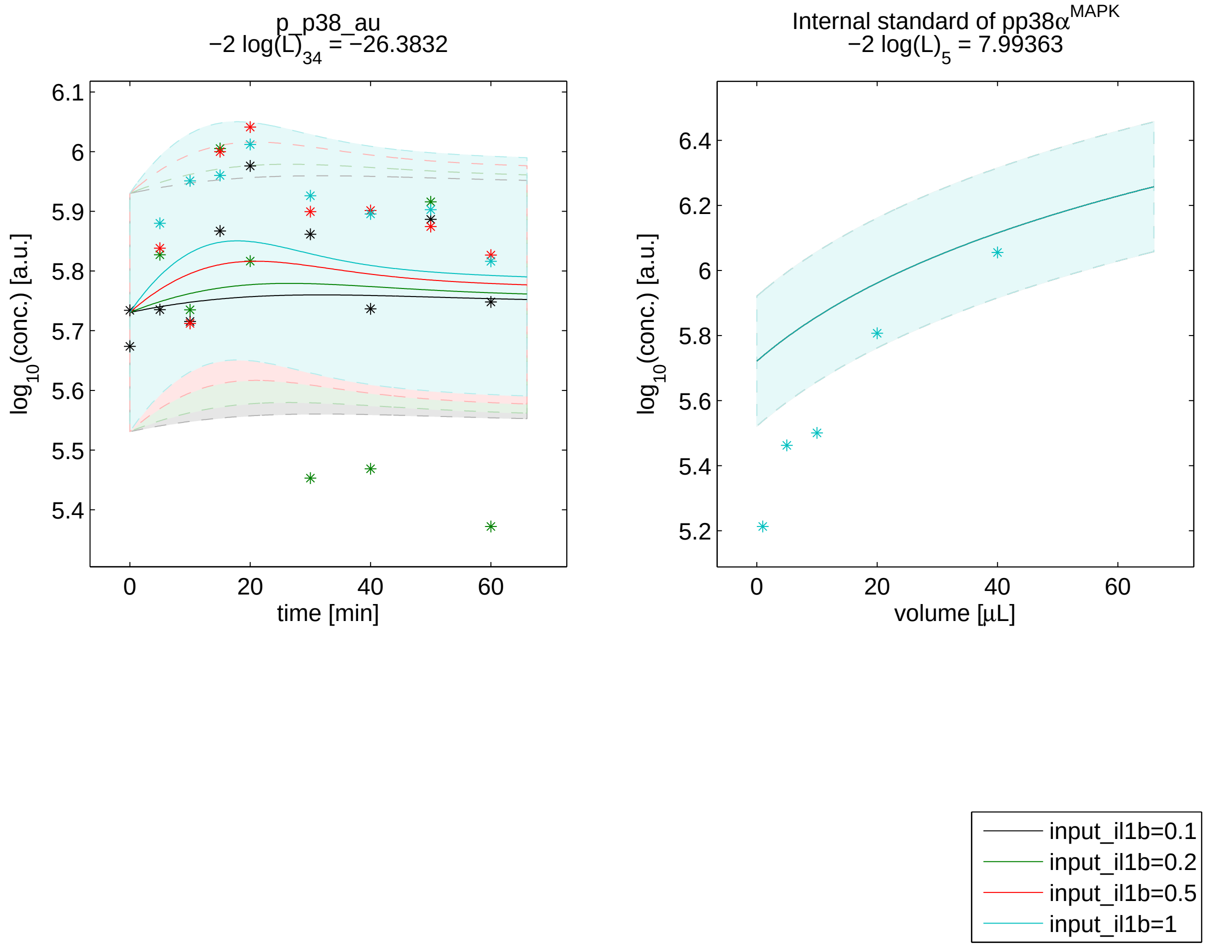

Figure 23: 100708_page100715_mk2ko_il1_0u01u02u05u1_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.18 Experiment: 100708_page100715_mk2ko_il1_0u01u02u05u1_pp38

Comments In this experiment the primary hepatocytes from MK2 knockout mice were treated with IL-1β doses from 0.1–1 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 37 and 38, yields a value of the objective function $-2\log(L) = -18.3896$ for 39 data points in this data set. The model observables and the experimental data is show in Figure 23.

Observables The following observables are added in this data set:

- **Observable:** p_p38_au

$$\text{p\_p38\_au(t)} = \quad \text{offset\_gel\_pp38\_100708\_100715} + [\text{pp38}] \cdot \text{scale\_pp38\_100708\_100715} \tag{190}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \quad \text{sd\_pp38\_mk2ko\_au} \tag{191}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]
0	0.1	471660
0	0.1	542351
5	0.1	543452
5	0.2	672041
5	0.5	689239
5	1	758785
10	0.1	519485
10	0.2	543243
10	0.5	515491
10	1	893561
15	0.1	736482
15	0.2	1.01229e+06
15	0.5	999797
15	1	912484
20	0.1	946794
20	0.2	655664
20	0.5	1.09972e+06
20	1	1.02823e+06
30	0.1	726980
30	0.2	283747
30	0.5	793640
30	1	843829
40	0.1	545233
40	0.2	294180
40	0.5	796746
40	1	786521
50	0.1	770414
50	0.2	824163
50	0.5	748981
50	1	799512
60	0.1	559958
60	0.2	235539
60	0.5	671028
60	1	655039

Table 37: Experimental data for the experiment 100708_page100715_mk2ko_il1_0u01u02u05u1_pp38

intstd [μL]	int_p_p38_au conc. [a.u.]
1	163348
5	290048
10	316838
20	641530
40	1.13665e+06

Table 38: Internal standard for the experiment 100708_page100715_mk2ko_il1_0u01u02u05u1_pp38

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au}(\text{intstd}) = \quad \text{offset\_gel\_pp38\_100708\_100715} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_100708\_100715} \cdot \text{intstd}}{\text{V}} \tag{192}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_mk2ko\_au} \tag{193}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

init_pMK2	→	0	0	0	0
input_il1b	→	0.1	0.2	0.5	1
mk2_ko	→	1	1	1	1

$$\text{scale\_pp38\_100708\_100715} \quad \rightarrow \quad \frac{\text{scale\_pp38\_100708\_100715}}{\text{init\_p38}}$$

time [min]	input_il1b [$ng \cdot ml^{-1}$]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	0.1	97135	1915
5	0.2	82234	1970
5	0.5	146671	539
5	1	161571	1283
10	0.1	83978	1778
10	0.2	52779	352
10	0.5	48381	917
10	1	46537	589
15	0.1	141415	1272
15	0.2	342034	904
15	0.5	526824	1906
15	1	427968	599
20	0.1	260521	1456
20	0.2	312900	695
20	0.5	480261	1242
20	1	570023	668
30	0.1	97293	1639
30	0.2	171201	1111
30	0.5	400935	1269
30	1	267549	1354
40	0.1	110081	1403
40	0.2	162383	976
40	0.5	297922	1430
40	1	234021	1646
60	0.1	145303	449
60	0.2	256956	1354
60	0.5	186469	699
60	1	247898	560
0	0.1	52436.8	1244

Table 39: Experimental data for the experiment 110317a_page110406a_mk2ko_il1_0u01u02u05u1_pmk2_pp38

2.2.19 Experiment: 110317a_page110406a_mk2ko_il1_0u01u02u05u1_pmk2_pp38

Comments In this experiment the primary hepatocytes from MK2 knockout mice were treated with IL-1β doses from 0.1–1 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 39 and 40, yields a value of the objective function $-2\log(L) = 30.5296$ for 68 data points in this data set. The model observables and the experimental data is show in Figure 24.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \text{offset\_gel\_pMK2\_110317a\_110406a} + [\text{pMK2}] \cdot \text{scale\_pMK2\_110317a\_110406a} \tag{194}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \text{sd\_pMK2\_mk2ko\_au} \tag{195}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au(t)} = \text{offset\_gel\_pp38\_110317a\_110406a} + [\text{pp38}] \cdot \text{scale\_pp38\_110317a\_110406a} \tag{196}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \text{sd\_pp38\_mk2ko\_au} \tag{197}$$

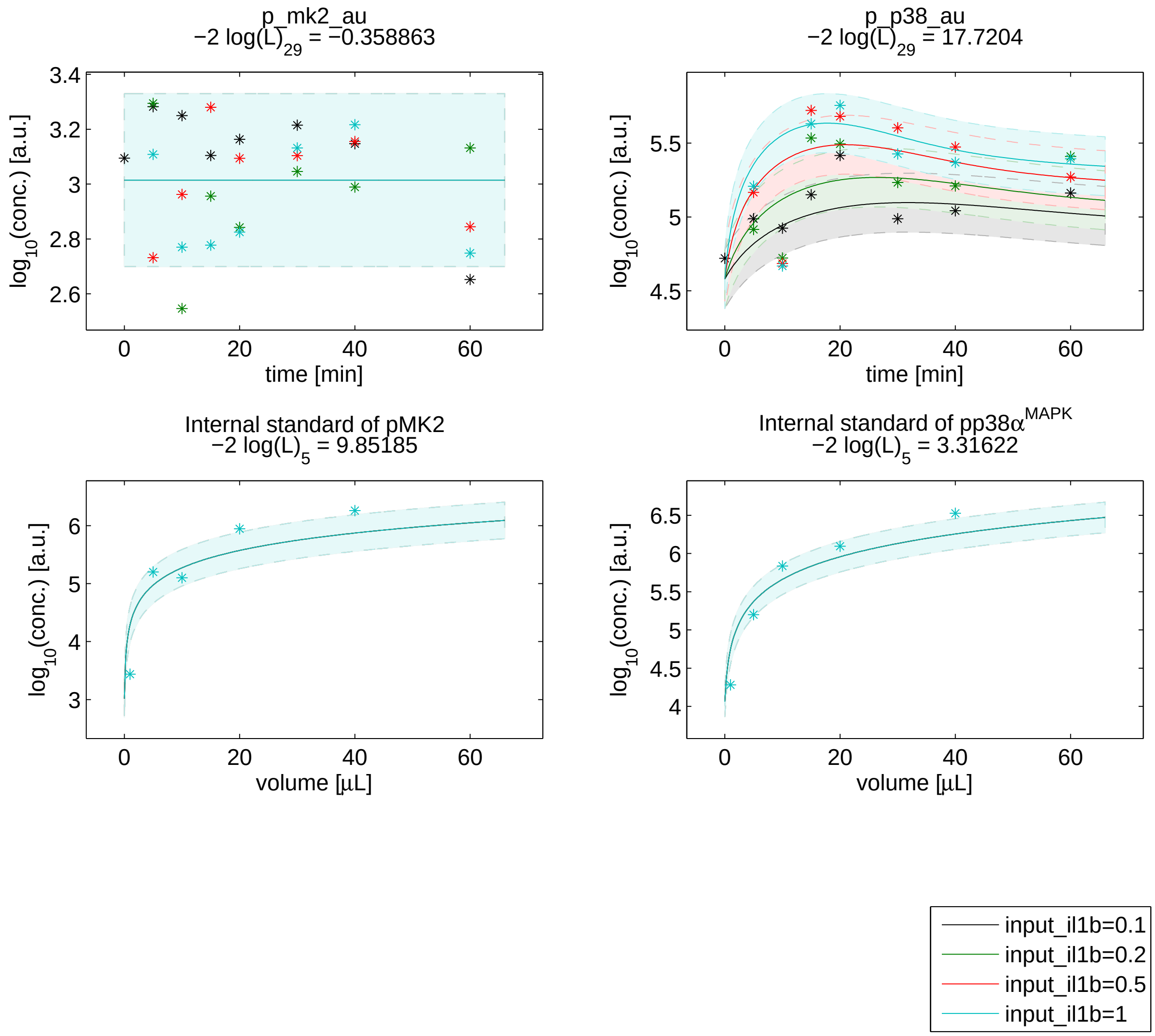

Figure 24: 110317a_page110406a_mk2ko_il1_0u01u02u05u1_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	19189	2749
5	158482	158846
10	686623	125961
20	1.24233e+06	881268
40	3.35953e+06	1.82000e+06

Table 40: Internal standard for the experiment 110317a_page110406a_mk2ko_il1_0u01u02u05u1_pmk2_pp38

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au(intstd)} = \text{offset\_gel\_pMK2\_110317a\_110406a} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_110317a\_110406a} \cdot \text{intstd}}{\text{V}} \tag{198}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \text{sd\_pMK2\_mk2ko\_au} \tag{199}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au(intstd)} = \text{offset\_gel\_pp38\_110317a\_110406a} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_110317a\_110406a} \cdot \text{intstd}}{\text{V}} \tag{200}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \text{sd\_pp38\_mk2ko\_au} \tag{201}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

init_pMK2	→	0	0	0	0
input_il1b	→	0.1	0.2	0.5	1
mk2_ko	→	1	1	1	1

$$\text{scale\_pMK2\_110317a\_110406a} \rightarrow \frac{\text{scale\_pMK2\_110317a\_110406a}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_110317a\_110406a} \rightarrow \frac{\text{scale\_pp38\_110317a\_110406a}}{\text{init\_p38}}$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	0.1	197334	1862
5	0.2	187852	1933
5	0.5	192547	1048
5	1	313470	1829
10	0.1	256709	1576
10	0.2	471102	644
10	0.5	620356	1175
10	1	986698	1661
15	0.1	530063	1260
15	0.2	590219	841
15	0.5	893335	760
15	1	1.12626e+06	740
20	0.1	390573	1404
20	0.2	672365	1028
20	0.5	1.19592e+06	773
20	1	1.31411e+06	1682
30	0.1	254872	1455
30	0.2	568442	1125
30	0.5	508149	935
30	1	673881	1653
40	0.1	178479	1791
40	0.2	485888	1370
40	0.5	560572	1376
40	1	494034	900
60	0.1	373746	2271
60	0.2	516312	1393
60	0.5	430163	556
60	1	358029	1619
0	0.1	74994	1864
0	0.1	107340	828
0	0.1	78317	1798
0	0.1	98164	1339

Table 41: Experimental data for the experiment 110317b_page110405a_mk2ko_il1_0u01u02u05u1_pmk2_pp38

2.2.20 Experiment: 110317b_page110405a_mk2ko_il1_0u01u02u05u1_pmk2_pp38

Comments In this experiment the primary hepatocytes from MK2 knockout mice were treated with IL-1β doses from 0.1–1 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 41 and 42, yields a value of the objective function $-2\log(L) = -36.4771$ for 74 data points in this data set. The model observables and the experimental data is show in Figure 25.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \text{offset\_gel\_pMK2\_110317b\_110405a} + [\text{pMK2}] \cdot \text{scale\_pMK2\_110317b\_110405a} \tag{202}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \text{sd\_pMK2\_mk2ko\_au} \tag{203}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au(t)} = \text{offset\_gel\_pp38\_110317b\_110405a} + [\text{pp38}] \cdot \text{scale\_pp38\_110317b\_110405a} \tag{204}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \text{sd\_pp38\_mk2ko\_au} \tag{205}$$

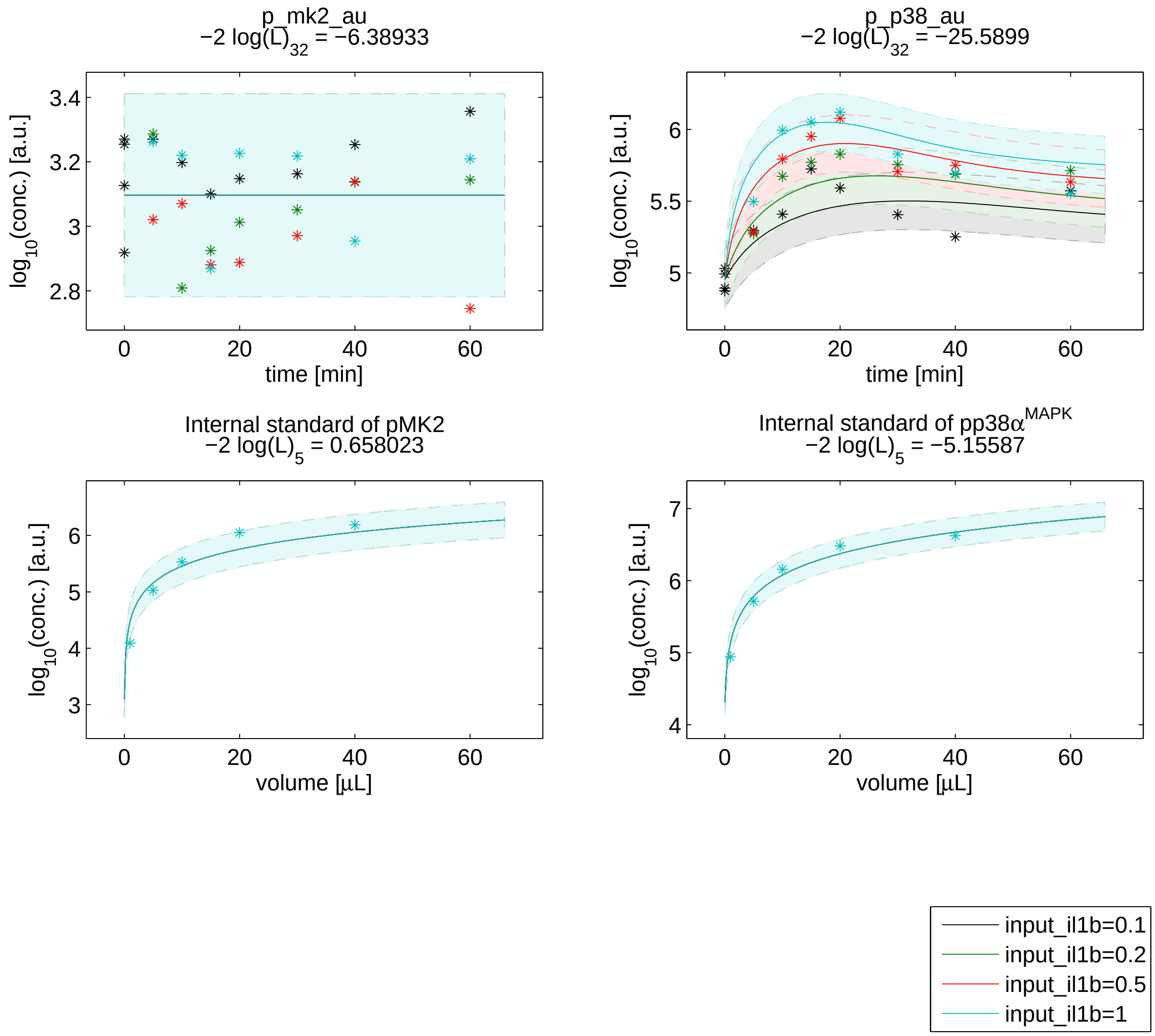

Figure 25: 110317b_page110405a_mk2ko_il1_0u01u02u05u1_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	87314	12350
5	516245	106423
10	1.43372e+06	339135
20	3.02486e+06	1.12443e+06
40	4.19630e+06	1.54314e+06

Table 42: Internal standard for the experiment 110317b_page110405a_mk2ko_il1_0u01u02u05u1_pmk2_pp38

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au}(\text{intstd}) = \quad \text{offset\_gel\_pMK2\_110317b\_110405a} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_110317b\_110405a} \cdot \text{intstd}}{\text{V}} \tag{206}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \quad \text{sd\_pMK2\_mk2ko\_au} \tag{207}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au}(\text{intstd}) = \quad \text{offset\_gel\_pp38\_110317b\_110405a} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_110317b\_110405a} \cdot \text{intstd}}{\text{V}} \tag{208}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_mk2ko\_au} \tag{209}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\begin{array}{lcr|r|r|l} \text{init\_pMK2} & \rightarrow & 0 & 0 & 0 & 0 \\ \text{input\_il1b} & \rightarrow & 0.1 & 0.2 & 0.5 & 1 \\ \text{mk2\_ko} & \rightarrow & 1 & 1 & 1 & 1 \end{array}$$

$$\begin{array}{lcl} \text{scale\_pMK2\_110317b\_110405a} & \rightarrow & \frac{\text{scale\_pMK2\_110317b\_110405a}}{\text{init\_MK2}} \\ \text{scale\_pp38\_110317b\_110405a} & \rightarrow & \frac{\text{scale\_pp38\_110317b\_110405a}}{\text{init\_p38}} \end{array}$$

time [min]	input_il1b $[ng \cdot ml^{-1}]$	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
5	0.1	148327	1832
5	0.2	187653	74
5	0.5	226551	389
5	1	231847	832
10	0.1	188980	1934
10	0.2	395707	512
10	0.5	613017	110
10	1	723956	1367
15	0.1	398911	331
15	0.2	624777	1042
15	0.5	875329	942
15	1	986283	346
20	0.1	332037	912
20	0.2	511633	921
20	0.5	905815	1440
20	1	830682	373
30	0.1	190136	1244
30	0.2	440311	1777
30	0.5	524312	456
30	1	547606	53
40	0.1	254455	1289
40	0.2	409144	1246
40	0.5	441799	1576
40	1	381959	565
60	0.1	229065	1261
60	0.2	415263	1086
60	0.5	338963	515
60	1	427740	1472
0	0.1	112547	544
0	0.1	86139	1381
0	0.1	84687	1149
0	0.1	88053	666

Table 43: Experimental data for the experiment 110317b_page110405b_mk2ko_il1_0u01u02u05u1_pmk2_pp38

2.2.21 Experiment: 110317b_page110405b_mk2ko_il1_0u01u02u05u1_pmk2_pp38

Comments In this experiment the primary hepatocytes from MK2 knockout mice were treated with IL-1β doses from 0.1–1 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 43 and 44, yields a value of the objective function $-2\log(L) = 24.7832$ for 74 data points in this data set. The model observables and the experimental data is show in Figure 26.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \text{offset\_gel\_pMK2\_110317b\_110405b} + [\text{pMK2}] \cdot \text{scale\_pMK2\_110317b\_110405b} \quad (210)$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \text{sd\_pMK2\_mk2ko\_au} \quad (211)$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au(t)} = \text{offset\_gel\_pp38\_110317b\_110405b} + [\text{pp38}] \cdot \text{scale\_pp38\_110317b\_110405b} \quad (212)$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \text{sd\_pp38\_mk2ko\_au} \quad (213)$$

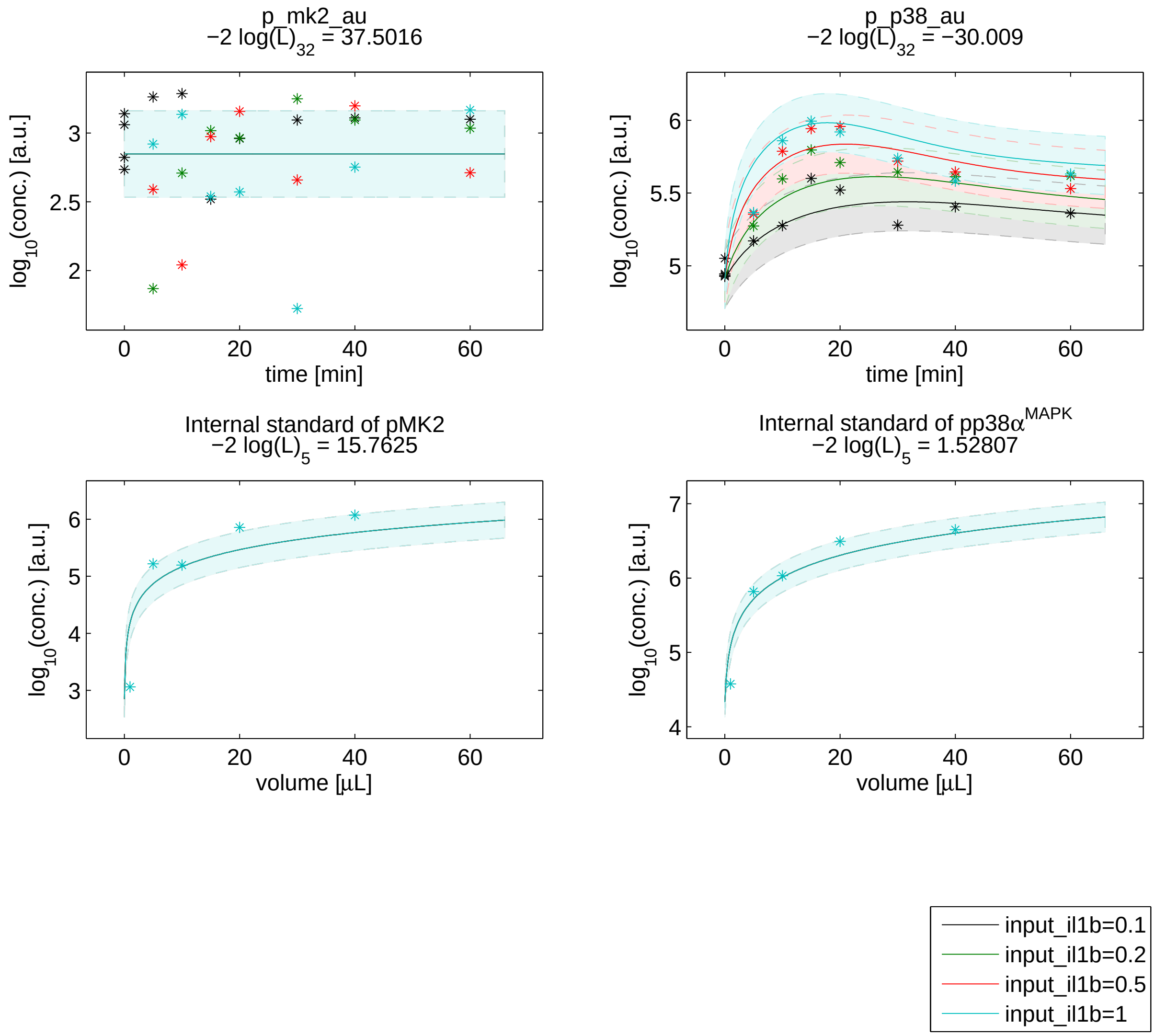

Figure 26: 110317b_page110405b_mk2ko_il1_0u01u02u05u1_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	37792	1152
5	658621	165154
10	1.07282e+06	157547
20	3.12227e+06	720680
40	4.47625e+06	1.18408e+06

Table 44: Internal standard for the experiment 110317b_page110405b_mk2ko_il1_0u01u02u05u1_pmk2_pp38

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au}(\text{intstd}) = \quad \text{offset\_gel\_pMK2\_110317b\_110405b} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_110317b\_110405b} \cdot \text{intstd}}{\text{V}} \tag{214}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \quad \text{sd\_pMK2\_mk2ko\_au} \tag{215}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au}(\text{intstd}) = \quad \text{offset\_gel\_pp38\_110317b\_110405b} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_110317b\_110405b} \cdot \text{intstd}}{\text{V}} \tag{216}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_mk2ko\_au} \tag{217}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

init_pMK2	→	0	0	0	0
input_il1b	→	0.1	0.2	0.5	1
mk2_ko	→	1	1	1	1

$$\text{scale\_pMK2\_110317b\_110405b} \quad \rightarrow \quad \frac{\text{scale\_pMK2\_110317b\_110405b}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_110317b\_110405b} \quad \rightarrow \quad \frac{\text{scale\_pp38\_110317b\_110405b}}{\text{init\_p38}}$$

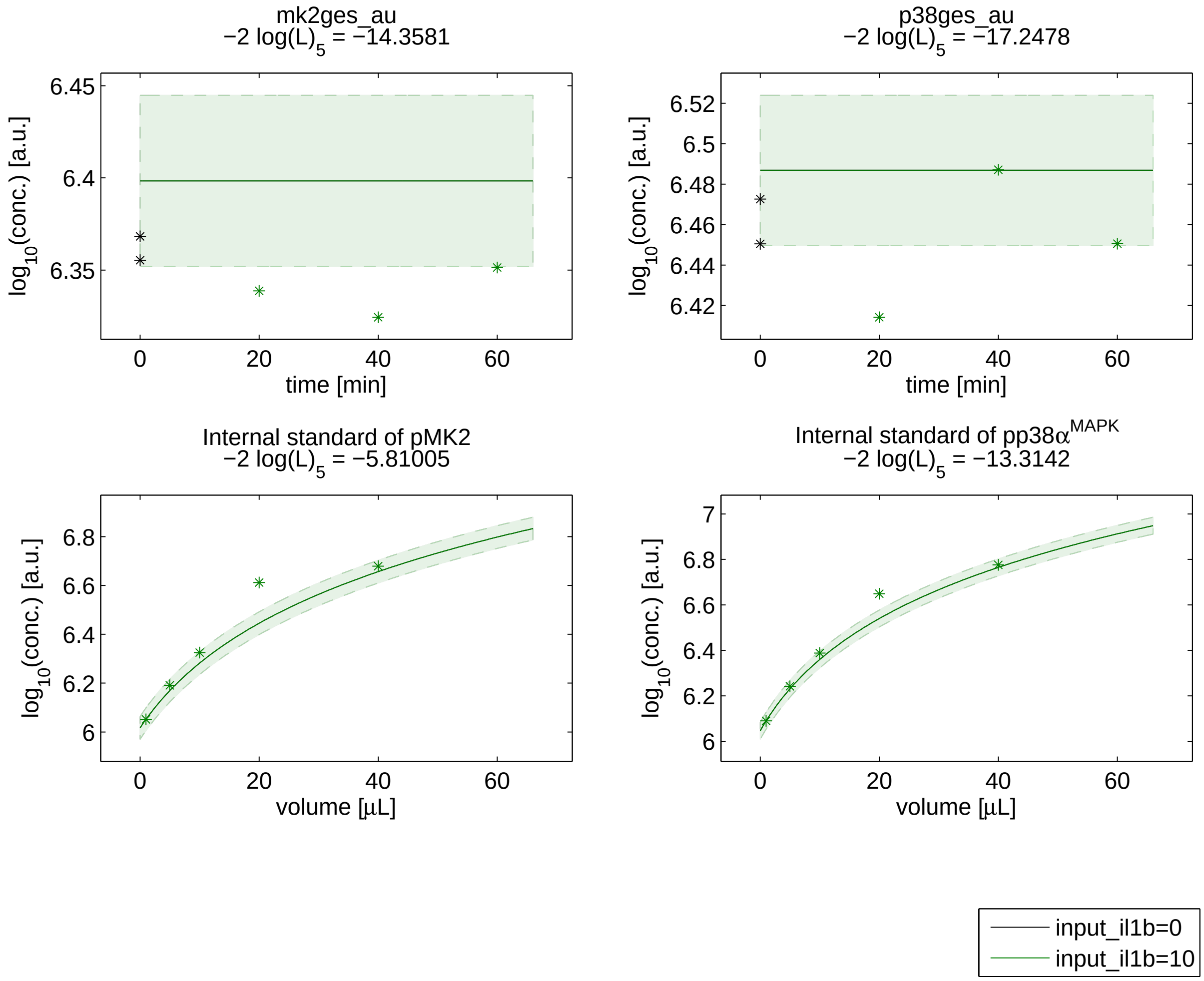

Figure 27: total_mk2_p38_100421_page111026a_wt_il1_10_mk2_p38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.22 Experiment: total_mk2_p38_100421_page111026a_wt_il1_10_mk2_p38

Comments In this experiment total amount of p38 and MK2 was measured. The primary hepatocytes were treated with IL-1β doses from 0–10 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 45 and 46, yields a value of the objective function $-2\log(L) = -50.7301$ for 20 data points in this data set. The model observables and the experimental data is show in Figure 27.

Observables The following observables are added in this data set:

- **Observable:** mk2ges_au

$$\text{mk2ges\_au(t)} = \quad \text{offset\_MK2ges\_100421\_111026a} + \text{scale\_MK2ges\_100421\_111026a} \cdot ([\text{MK2}] + [\text{pMK2}]) \quad (218)$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{mk2ges\_au}\}(\text{t}) = \quad \text{sd\_MK2ges\_au} \quad (219)$$

time [min]	input_il1b $[\text{ng} \cdot \text{ml}^{-1}]$	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
0	0	2.82171e+06	2.26655e+06
0	0	2.96895e+06	2.33498e+06
20	10	2.59523e+06	2.18127e+06
40	10	3.06990e+06	2.11051e+06
60	10	2.82180e+06	2.24559e+06

Table 45: Experimental data for the experiment total_mk2_p38_100421_page111026a_wt_il1_10_mk2_p38

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	1.22937e+06	1.12596e+06
5	1.74551e+06	1.55161e+06
10	2.44295e+06	2.11495e+06
20	4.45987e+06	4.09525e+06
40	5.96806e+06	4.78014e+06

Table 46: Internal standard for the experiment total_mk2_p38_100421_page111026a_wt_il1_10_mk2_p38

- **Observable:** p38ges_au

$$\text{p38ges\_au}(t) = \text{offset\_p38ges\_100421\_111026a} + \text{scale\_p38ges\_100421\_111026a} \cdot ([\text{p38}] + [\text{pp38}]) \tag{220}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p38ges\_au}\}(t) = \text{sd\_p38ges\_au} \tag{221}$$

- **Observable:** int_mk2ges_au

$$\text{int\_mk2ges\_au}(\text{intstd}) = \text{offset\_MK2ges\_100421\_111026a} + \frac{\text{scale\_MK2\_total} \cdot \text{scale\_MK2ges\_100421\_111026a} \cdot \text{intstd}}{\text{V}} \tag{222}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_mk2ges\_au}\}(\text{intstd}) = \text{sd\_MK2ges\_au} \tag{223}$$

- **Observable:** int_p38ges_au

$$\text{int\_p38ges\_au}(\text{intstd}) = \text{offset\_p38ges\_100421\_111026a} + \frac{\text{scale\_p38\_total} \cdot \text{scale\_p38ges\_100421\_111026a} \cdot \text{intstd}}{\text{V}} \tag{224}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p38ges\_au}\}(\text{intstd}) = \text{sd\_p38ges\_au} \tag{225}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \rightarrow 0 \mid 10$$

$$\text{scale\_MK2ges\_100421\_111026a} \rightarrow \frac{\text{scale\_MK2ges\_100421\_111026a}}{\text{init\_MK2}}$$

$$\text{scale\_p38ges\_100421\_111026a} \rightarrow \frac{\text{scale\_p38ges\_100421\_111026a}}{\text{init\_p38}}$$

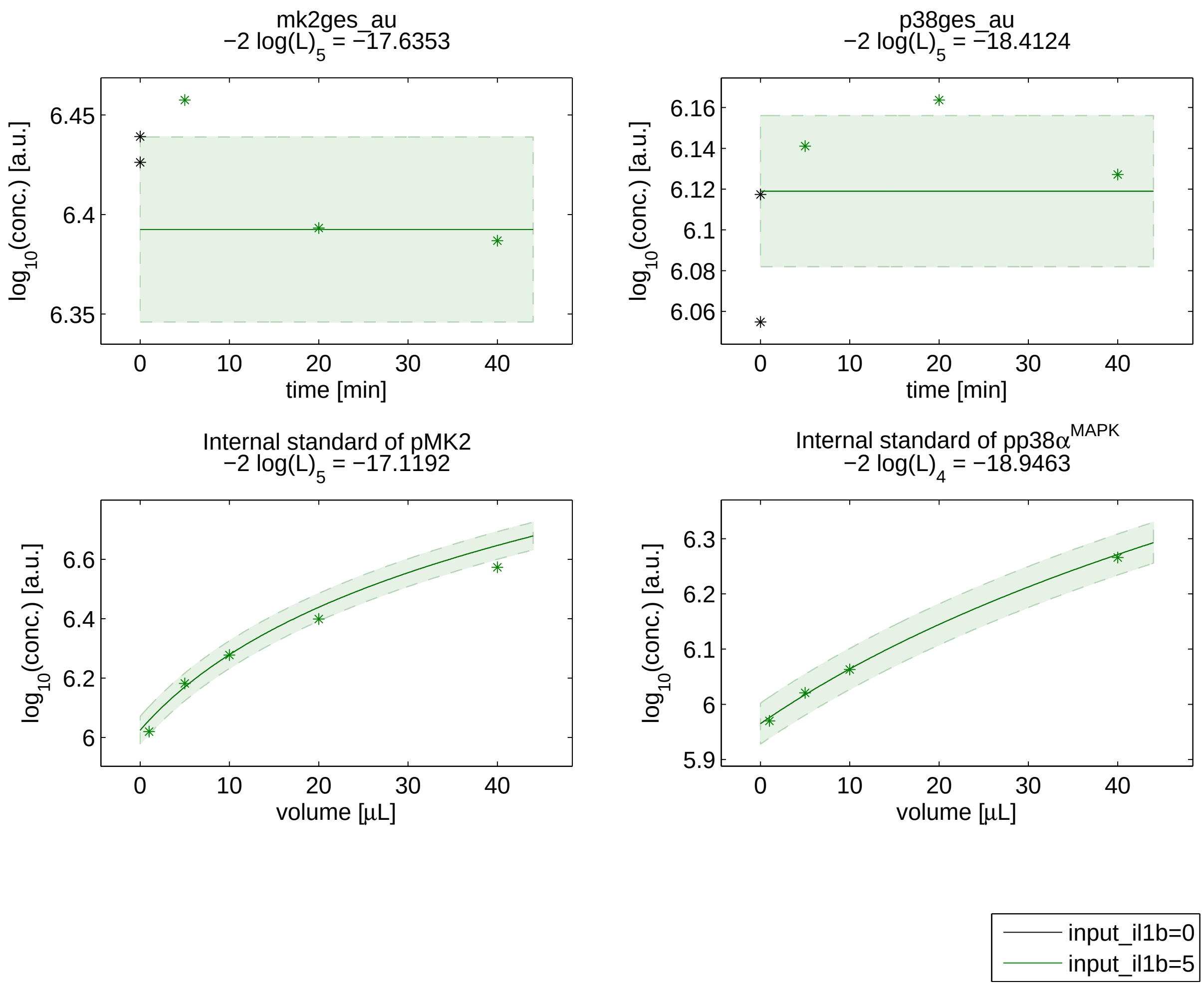

Figure 28: total_mk2_p38_100504_page111027a_wt_il1_5_mk2_p38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.23 Experiment: total_mk2_p38_100504_page111027a_wt_il1_5_mk2_p38

Comments In this experiment total amount of p38 and MK2 was measured. The primary hepatocytes were treated with IL-1β doses from 0–5 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 47 and 48, yields a value of the objective function $-2\log(L) = -72.1133$ for 19 data points in this data set. The model observables and the experimental data is show in Figure 28.

Observables The following observables are added in this data set:

- **Observable:** mk2ges_au

$$\text{mk2ges\_au(t)} = \quad \text{offset\_MK2ges\_100504\_111027a} + \text{scale\_MK2ges\_100504\_111027a} \cdot ([\text{MK2}] + [\text{pMK2}]) \quad (226)$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{mk2ges\_au}\}(\text{t}) = \quad \text{sd\_MK2ges\_au} \quad (227)$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
0	0	1.13458e+06	2.74896e+06
0	0	1.31037e+06	2.66821e+06
5	5	1.38379e+06	2.86749e+06
20	5	1.45768e+06	2.47299e+06
40	5	1.34023e+06	2.43708e+06

Table 47: Experimental data for the experiment total_mk2_p38_100504_page111027a_wt_il1_5_mk2_p38

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	933036	1.04596e+06
5	1.04899e+06	1.52063e+06
10	1.15622e+06	1.89575e+06
20		2.50508e+06
40	1.84423e+06	3.74103e+06

Table 48: Internal standard for the experiment total_mk2_p38_100504_page111027a_wt_il1_5_mk2_p38

- **Observable:** p38ges_au

$$\text{p38ges\_au}(t) = \text{offset\_p38ges\_100504\_111027a} + \text{scale\_p38ges\_100504\_111027a} \cdot ([\text{p38}] + [\text{pp38}]) \tag{228}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p38ges\_au}\}(t) = \text{sd\_p38ges\_au} \tag{229}$$

- **Observable:** int_mk2ges_au

$$\text{int\_mk2ges\_au}(\text{intstd}) = \text{offset\_MK2ges\_100504\_111027a} + \frac{\text{scale\_MK2\_total} \cdot \text{scale\_MK2ges\_100504\_111027a} \cdot \text{intstd}}{\text{V}} \tag{230}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_mk2ges\_au}\}(\text{intstd}) = \text{sd\_MK2ges\_au} \tag{231}$$

- **Observable:** int_p38ges_au

$$\text{int\_p38ges\_au}(\text{intstd}) = \text{offset\_p38ges\_100504\_111027a} + \frac{\text{scale\_p38\_total} \cdot \text{scale\_p38ges\_100504\_111027a} \cdot \text{intstd}}{\text{V}} \tag{232}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p38ges\_au}\}(\text{intstd}) = \text{sd\_p38ges\_au} \tag{233}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \rightarrow 0 \mid 5$$

$$\text{scale\_MK2ges\_100504\_111027a} \rightarrow \frac{\text{scale\_MK2ges\_100504\_111027a}}{\text{init\_MK2}}$$

$$\text{scale\_p38ges\_100504\_111027a} \rightarrow \frac{\text{scale\_p38ges\_100504\_111027a}}{\text{init\_p38}}$$

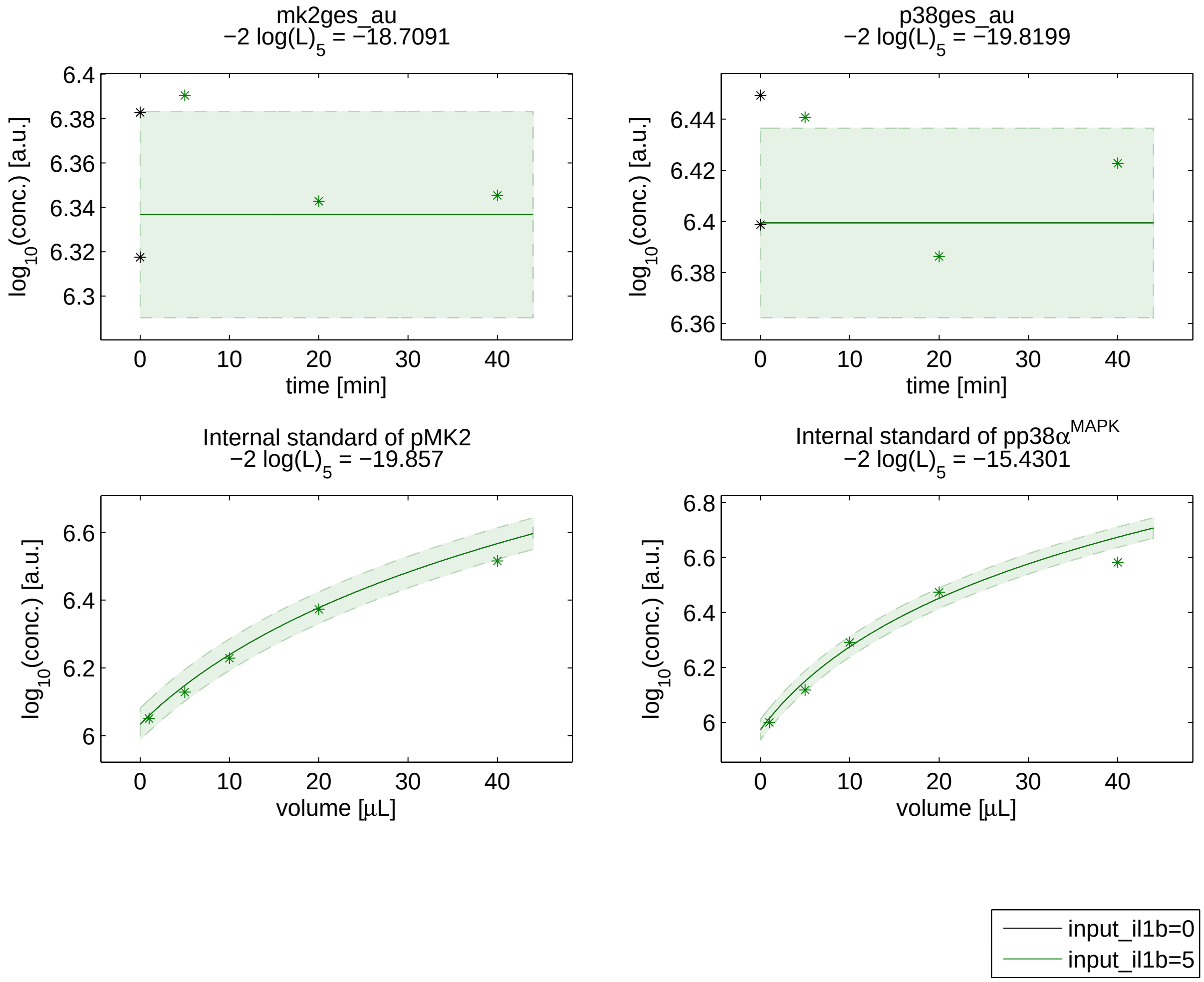

Figure 29: total_mk2_p38_100504_page111027b_wt_il1_5_mk2_p38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.24 Experiment: total_mk2_p38_100504_page111027b_wt_il1_5_mk2_p38

Comments In this experiment total amount of p38 and MK2 was measured. The primary hepatocytes were treated with IL-1β doses from 0–5 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 49 and 50, yields a value of the objective function $-2\log(L) = -73.8161$ for 20 data points in this data set. The model observables and the experimental data is show in Figure 29.

Observables The following observables are added in this data set:

- **Observable:** mk2ges_au

$$\text{mk2ges\_au(t)} = \text{offset\_MK2ges\_100504\_111027b} + \text{scale\_MK2ges\_100504\_111027b} \cdot ([\text{MK2}] + [\text{pMK2}]) \quad (234)$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{mk2ges\_au}\}(\text{t}) = \text{sd\_MK2ges\_au} \quad (235)$$

time [min]	input_il1b [ng · ml^{-1}]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
0	0	2.50455e+06	2.41411e+06
0	0	2.81358e+06	2.07751e+06
5	5	2.75888e+06	2.45709e+06
20	5	2.43368e+06	2.20163e+06
40	5	2.64688e+06	2.21497e+06

Table 49: Experimental data for the experiment total_mk2_p38_100504_page111027b_wt_il1_5_mk2_p38

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	999898	1.12246e+06
5	1.31228e+06	1.34348e+06
10	1.95430e+06	1.69211e+06
20	2.97289e+06	2.35929e+06
40	3.81699e+06	3.27855e+06

Table 50: Internal standard for the experiment total_mk2_p38_100504_page111027b_wt_il1_5_mk2_p38

- **Observable:** p38ges_au

$$\text{p38ges\_au}(t) = \text{offset\_p38ges\_100504\_111027b} + \text{scale\_p38ges\_100504\_111027b} \cdot ([\text{p38}] + [\text{pp38}]) \tag{236}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p38ges\_au}\}(t) = \text{sd\_p38ges\_au} \tag{237}$$

- **Observable:** int_mk2ges_au

$$\text{int\_mk2ges\_au}(\text{intstd}) = \text{offset\_MK2ges\_100504\_111027b} + \frac{\text{scale\_MK2\_total} \cdot \text{scale\_MK2ges\_100504\_111027b} \cdot \text{intstd}}{\text{V}} \tag{238}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_mk2ges\_au}\}(\text{intstd}) = \text{sd\_MK2ges\_au} \tag{239}$$

- **Observable:** int_p38ges_au

$$\text{int\_p38ges\_au}(\text{intstd}) = \text{offset\_p38ges\_100504\_111027b} + \frac{\text{scale\_p38\_total} \cdot \text{scale\_p38ges\_100504\_111027b} \cdot \text{intstd}}{\text{V}} \tag{240}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p38ges\_au}\}(\text{intstd}) = \text{sd\_p38ges\_au} \tag{241}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \rightarrow 0 \mid 5$$

$$\text{scale\_MK2ges\_100504\_111027b} \rightarrow \frac{\text{scale\_MK2ges\_100504\_111027b}}{\text{init\_MK2}}$$

$$\text{scale\_p38ges\_100504\_111027b} \rightarrow \frac{\text{scale\_p38ges\_100504\_111027b}}{\text{init\_p38}}$$

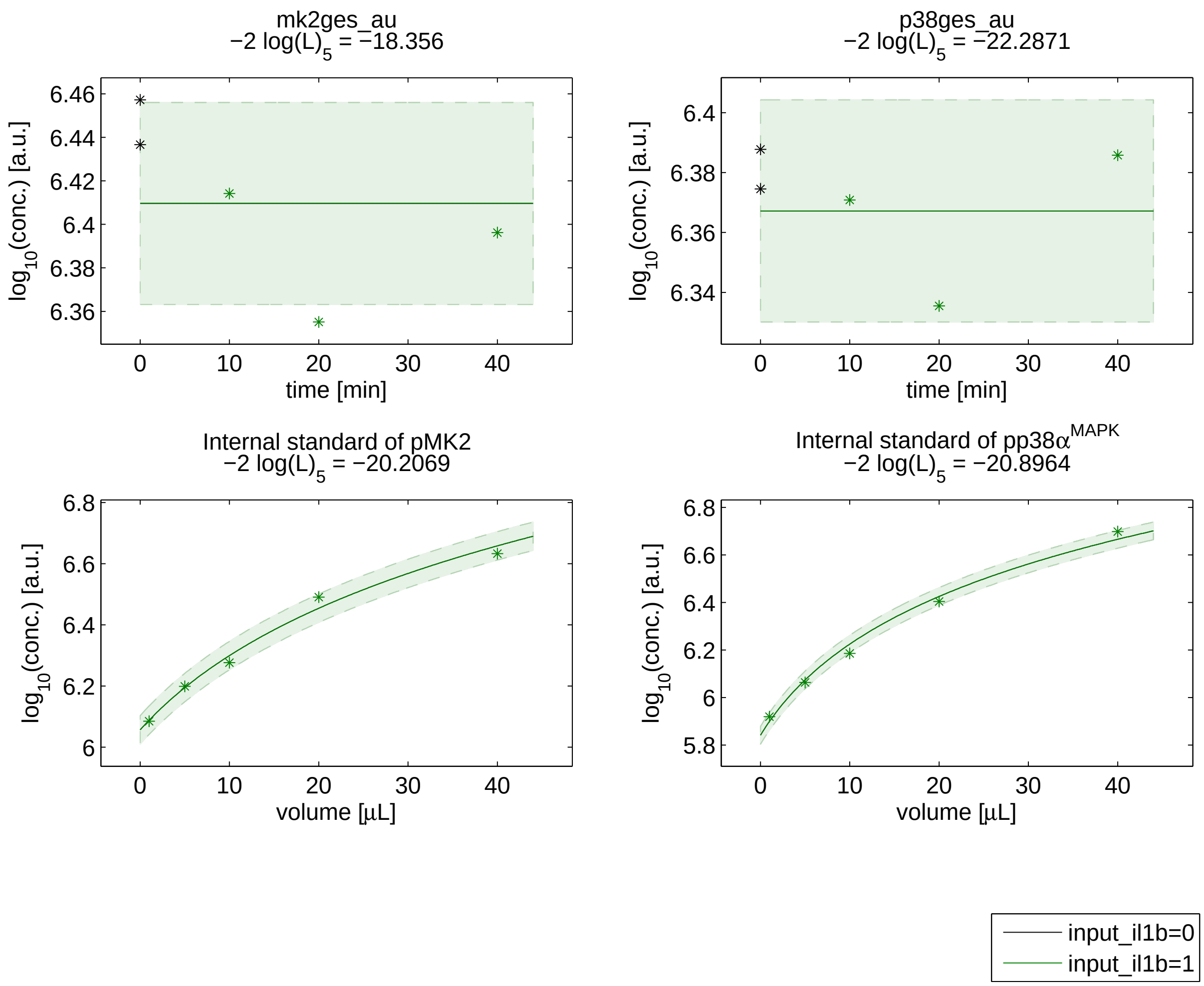

Figure 30: total_mk2_p38_100628b_page111027b_wt_il1_1_mk2_p38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.25 Experiment: total_mk2_p38_100628b_page111027b_wt_il1_1_mk2_p38

Comments In this experiment total amount of p38 and MK2 was measured. The primary hepatocytes were treated with IL-1β doses from 0–1 ng/ml and the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 51 and 52, yields a value of the objective function $-2\log(L) = -81.7463$ for 20 data points in this data set. The model observables and the experimental data is show in Figure 30.

Observables The following observables are added in this data set:

- **Observable:** mk2ges_au

$$\text{mk2ges\_au}(t) = \quad \text{offset\_MK2ges\_100628b\_111027b} + \text{scale\_MK2ges\_100628b\_111027b} \cdot ([\text{MK2}] + [\text{pMK2}]) \quad (242)$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{mk2ges\_au}\}(t) = \quad \text{sd\_MK2ges\_au} \quad (243)$$

time [min]	input_il1b [$ng \cdot ml^{-1}$]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
0	0	2.36876e+06	2.86563e+06
0	0	2.44209e+06	2.73325e+06
10	1	2.34872e+06	2.59539e+06
20	1	2.16521e+06	2.26539e+06
40	1	2.43101e+06	2.49016e+06

Table 51: Experimental data for the experiment total_mk2_p38_100628b_page111027b_wt_il1_1_mk2_p38

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	830642	1.21564e+06
5	1.15726e+06	1.58153e+06
10	1.53408e+06	1.89023e+06
20	2.53425e+06	3.09650e+06
40	4.99150e+06	4.29449e+06

Table 52: Internal standard for the experiment total_mk2_p38_100628b_page111027b_wt_il1_1_mk2_p38

- **Observable:** p38ges_au

$$\text{p38ges\_au}(t) = \text{offset\_p38ges\_100628b\_111027b} + \text{scale\_p38ges\_100628b\_111027b} \cdot ([\text{p38}] + [\text{pp38}]) \tag{244}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p38ges\_au}\}(t) = \text{sd\_p38ges\_au} \tag{245}$$

- **Observable:** int_mk2ges_au

$$\text{int\_mk2ges\_au}(\text{intstd}) = \text{offset\_MK2ges\_100628b\_111027b} + \frac{\text{scale\_MK2\_total} \cdot \text{scale\_MK2ges\_100628b\_111027b} \cdot \text{intstd}}{\text{V}} \tag{246}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_mk2ges\_au}\}(\text{intstd}) = \text{sd\_MK2ges\_au} \tag{247}$$

- **Observable:** int_p38ges_au

$$\text{int\_p38ges\_au}(\text{intstd}) = \text{offset\_p38ges\_100628b\_111027b} + \frac{\text{scale\_p38\_total} \cdot \text{scale\_p38ges\_100628b\_111027b} \cdot \text{intstd}}{\text{V}} \tag{248}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p38ges\_au}\}(\text{intstd}) = \text{sd\_p38ges\_au} \tag{249}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\text{input\_il1b} \rightarrow 0 \mid 1$$

$$\text{scale\_MK2ges\_100628b\_111027b} \rightarrow \frac{\text{scale\_MK2ges\_100628b\_111027b}}{\text{init\_MK2}}$$

$$\text{scale\_p38ges\_100628b\_111027b} \rightarrow \frac{\text{scale\_p38ges\_100628b\_111027b}}{\text{init\_p38}}$$

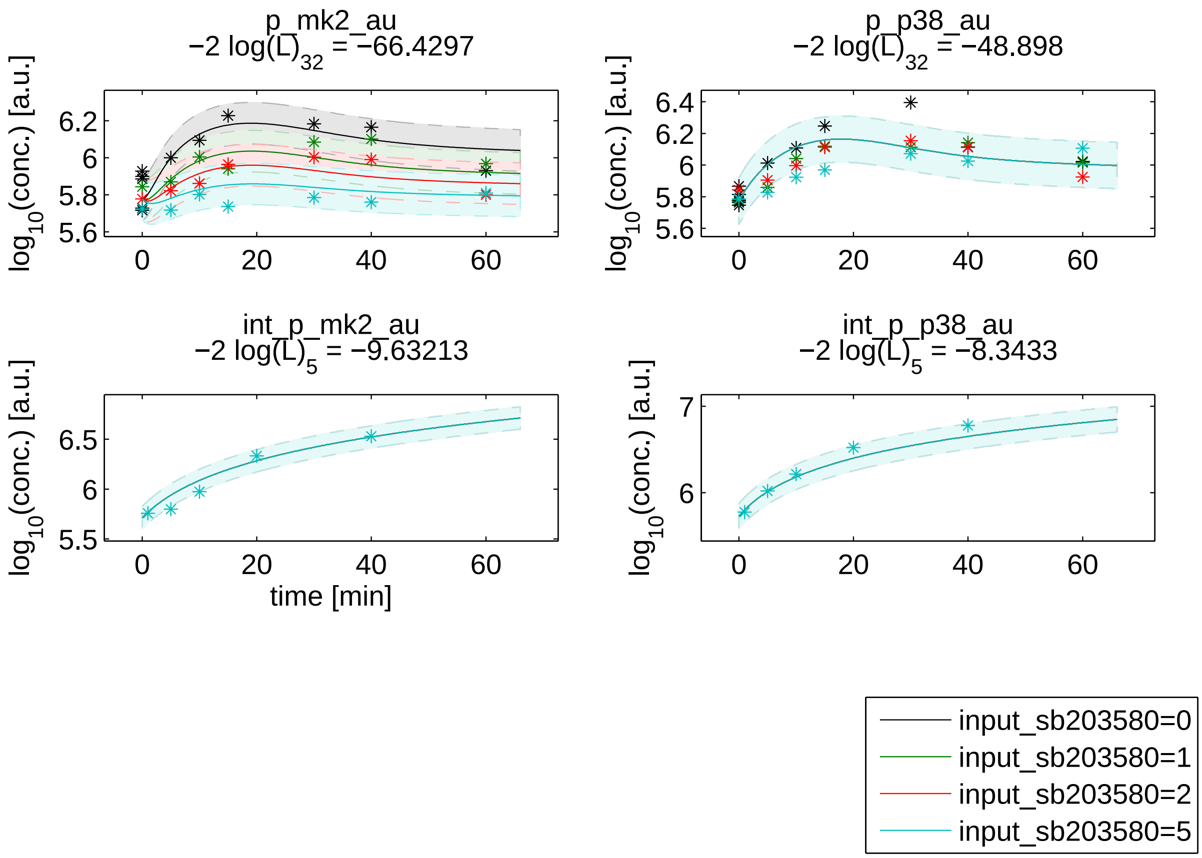

Figure 31: 101029_page101103_wt_sb203580_0u1u2u5_IL1_0u1_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.26 Experiment: 101029_page101103_wt_sb203580_0u1u2u5_IL1_0u1_pmk2_pp38

Comments In this experiment the MK2 phosphorylation inhibitor SB203580 was applied. For this the primary hepatocytes were treated with 1 ng/ml IL-1β and SB203580 doses from 0–5 μM. Additionally the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 53 and 54, yields a value of the objective function $-2\log(L) = -133.303$ for 74 data points in this data set. The model observables and the experimental data is show in Figure 31.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au(t)} = \quad \text{offset\_gel\_pMK2\_101029\_101103} + [\text{pMK2}] \cdot \text{scale\_pMK2\_101029\_101103} \tag{250}$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \quad \text{sd\_pMK2\_au} \tag{251}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au(t)} = \quad \text{offset\_gel\_pp38\_101029\_101103} + [\text{pp38}] \cdot \text{scale\_pp38\_101029\_101103} \tag{252}$$

time [min]	input_il1b [ng · ml^{-1}]	input_sb203580 [μM]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
0	1	0	735284	848361
0	1	1	603951	697907
0	1	2	696307	599446
0	1	5	611001	529219
5	1	0	1.02896e+06	999565
5	1	1	722458	740718
5	1	2	803861	664841
5	1	5	671255	521877
10	1	0	1.28109e+06	1.24114e+06
10	1	1	1.09860e+06	1.00994e+06
10	1	2	993429	727516
10	1	5	837672	634761
15	1	0	1.76656e+06	1.68886e+06
15	1	1	1.31511e+06	871951
15	1	2	1.29623e+06	919964
15	1	5	931075	544657
30	1	0	2.48634e+06	1.52388e+06
30	1	1	1.29507e+06	1.21566e+06
30	1	2	1.42330e+06	1.00706e+06
30	1	5	1.17927e+06	609843
40	1	0	1.29936e+06	1.46279e+06
40	1	1	1.38636e+06	1.26362e+06
40	1	2	1.29148e+06	977088
40	1	5	1.05906e+06	577322
60	1	0	1.05453e+06	851922
60	1	1	1.03397e+06	929609
60	1	2	840976	630960
60	1	5	1.27959e+06	645061
0	1	0	652016	792501
0	1	0	580202	520617
0	1	0	593352	768107
0	1	0	557860	534190

Table 53: Experimental data for the experiment 101029_page101103_wt_sb203580_0u1u2u5_IL1_0u1_pmk2_pp38

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	595912	571008
5	1.04455e+06	630084
10	1.63935e+06	942521
20	3.32822e+06	2.15618e+06
40	5.99954e+06	3.38350e+06

Table 54: Internal standard for the experiment 101029_page101103_wt_sb203580_0u1u2u5_IL1_0u1_pmk2_pp38

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \quad \text{sd\_pp38\_au} \tag{253}$$

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au}(\text{intstd}) = \quad \text{offset\_gel\_pMK2\_101029\_101103} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_101029\_101103} \cdot \text{intstd}}{\text{V}} \tag{254}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \quad \text{sd\_pMK2\_au} \tag{255}$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au}(\text{intstd}) = \quad \text{offset\_gel\_pp38\_101029\_101103} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_101029\_101103} \cdot \text{intstd}}{\text{V}} \tag{256}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \quad \text{sd\_pp38\_au} \tag{257}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\begin{array}{lcc|c|c|c} \text{input\_il1b} & \rightarrow & 1 & 1 & 1 & 1 \\ \text{input\_sb203580} & \rightarrow & 0 & 1 & 2 & 5 \end{array}$$

$$\text{scale\_pMK2\_101029\_101103} \quad \rightarrow \quad \frac{\text{scale\_pMK2\_101029\_101103}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_101029\_101103} \quad \rightarrow \quad \frac{\text{scale\_pp38\_101029\_101103}}{\text{init\_p38}}$$

time [min]	input_il1b [ng · ml^{-1}]	input_sb203580 [μM]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
0	1	0	103658	586856
0	1	1	77856	733768
0	1	2	74155	698585
0	1	5	72443	811885
5	1	0	312633	923500
5	1	1	172327	922656
5	1	2	157775	700111
5	1	5	128307	742669
10	1	0	667776	1.47309e+06
10	1	1	256140	739410
10	1	2	247303	780899
10	1	5	231791	815149
15	1	0	549225	1.42542e+06
15	1	1	319101	826135
15	1	2	308990	986727
15	1	5	308797	759980
30	1	0	959532	1.48212e+06
30	1	1	633826	1.40186e+06
30	1	2	440344	767252
30	1	5	428702	952018
40	1	0	758419	1.44705e+06
40	1	1	368355	1.25521e+06
40	1	2	438241	953201
40	1	5	391364	827865
60	1	0	74562	1.10879e+06
60	1	1	277138	949016
60	1	2	235699	845418
60	1	5	388385	862444
0	1	0	102305	793036
0	1	0	7909	781798
0	1	0	92686	816210
0	1	0	67749	660193

Table 55: Experimental data for the experiment 101029_page101104_wt_sb203580_0u1u2u5_IL1_0u1_pmk2_pp38

2.2.27 Experiment: 101029_page101104_wt_sb203580_0u1u2u5_IL1_0u1_pmk2_pp38

Comments In this experiment the MK2 phosphorylation inhibitor SB203580 was applied. For this the primary hepatocytes were treated with 1 ng/ml IL-1β and SB203580 doses from 0–5 μM. Additionally the internal standard was measured.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 55 and 56, yields a value of the objective function $-2\log(L) = -22.2383$ for 74 data points in this data set. The model observables and the experimental data is show in Figure 32.

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au}(t) = \text{offset\_gel\_pMK2\_101029\_101104} + [\text{pMK2}] \cdot \text{scale\_pMK2\_101029\_101104} \quad (258)$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(t) = \text{sd\_pMK2\_au} \quad (259)$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au}(t) = \text{offset\_gel\_pp38\_101029\_101104} + [\text{pp38}] \cdot \text{scale\_pp38\_101029\_101104} \quad (260)$$

  Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(t) = \text{sd\_pp38\_au} \quad (261)$$

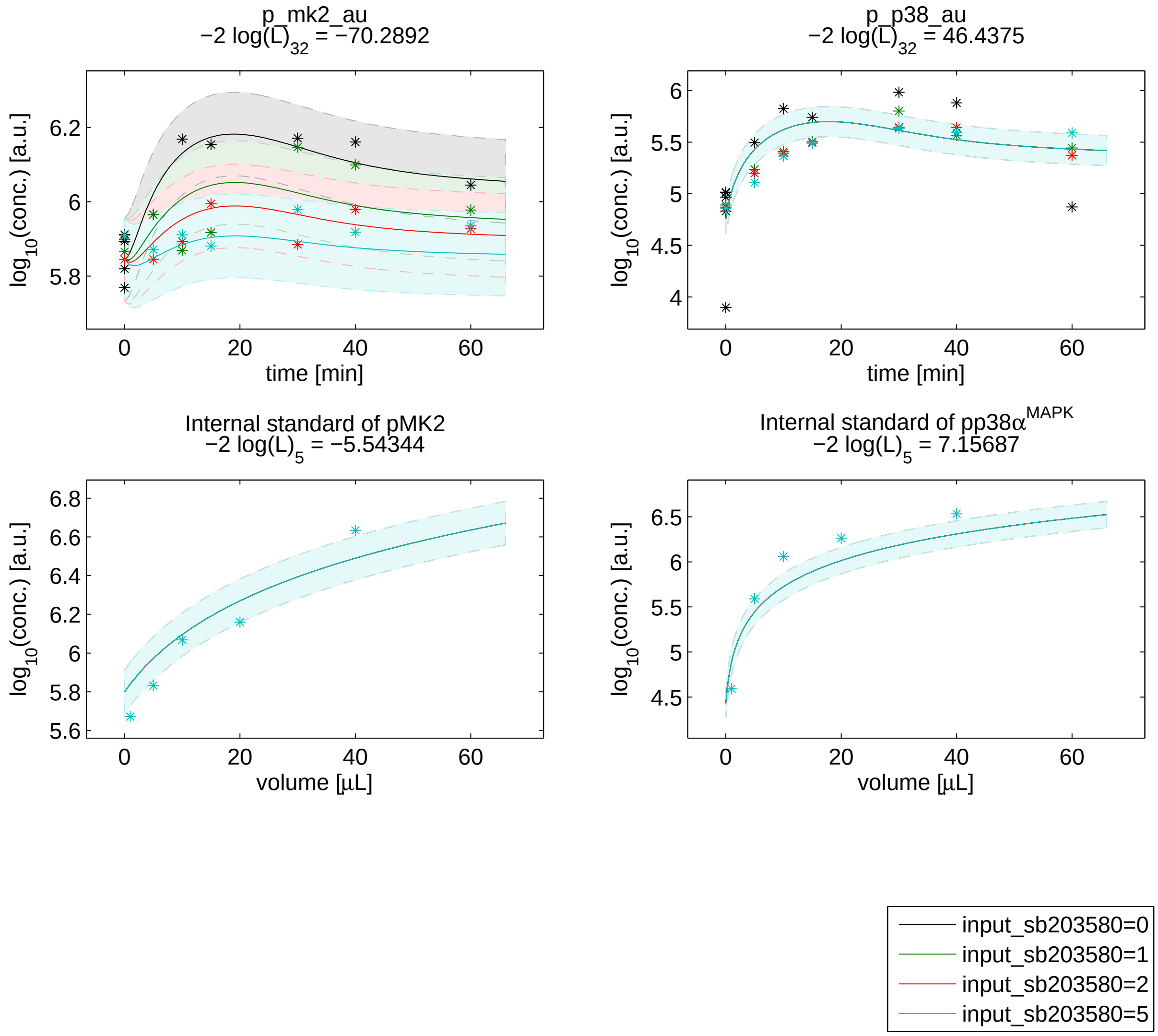

Figure 32: 101029_page101104_wt_sb203580_0u1u2u5_IL1_0u1_pmk2_pp38 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

intstd [μL]	int_p_p38_au conc. [a.u.]	int_p_mk2_au conc. [a.u.]
1	39099	469560
5	389222	678027
10	1.14619e+06	1.16915e+06
20	1.83635e+06	1.44178e+06
40	3.41852e+06	4.30400e+06

Table 56: Internal standard for the experiment 101029_page101104_wt_sb203580_0u1u2u5_IL1_0u1_pmk2_pp38

- **Observable:** int_p_mk2_au

$$\text{int\_p\_mk2\_au(intstd)} = \text{offset\_gel\_pMK2\_101029\_101104} + \frac{\text{scale\_pMK2} \cdot \text{scale\_pMK2\_101029\_101104} \cdot \text{intstd}}{\text{V}} \quad (262)$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_mk2\_au}\}(\text{intstd}) = \text{sd\_pMK2\_au} \quad (263)$$

- **Observable:** int_p_p38_au

$$\text{int\_p\_p38\_au(intstd)} = \text{offset\_gel\_pp38\_101029\_101104} + \frac{\text{scale\_pp38} \cdot \text{scale\_pp38\_101029\_101104} \cdot \text{intstd}}{\text{V}} \quad (264)$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{int\_p\_p38\_au}\}(\text{intstd}) = \text{sd\_pp38\_au} \quad (265)$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

input_il1b	→	1	1	1	1
input_sb203580	→	0	1	2	5

$$\text{scale\_pMK2\_101029\_101104} \rightarrow \frac{\text{scale\_pMK2\_101029\_101104}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_101029\_101104} \rightarrow \frac{\text{scale\_pp38\_101029\_101104}}{\text{init\_p38}}$$

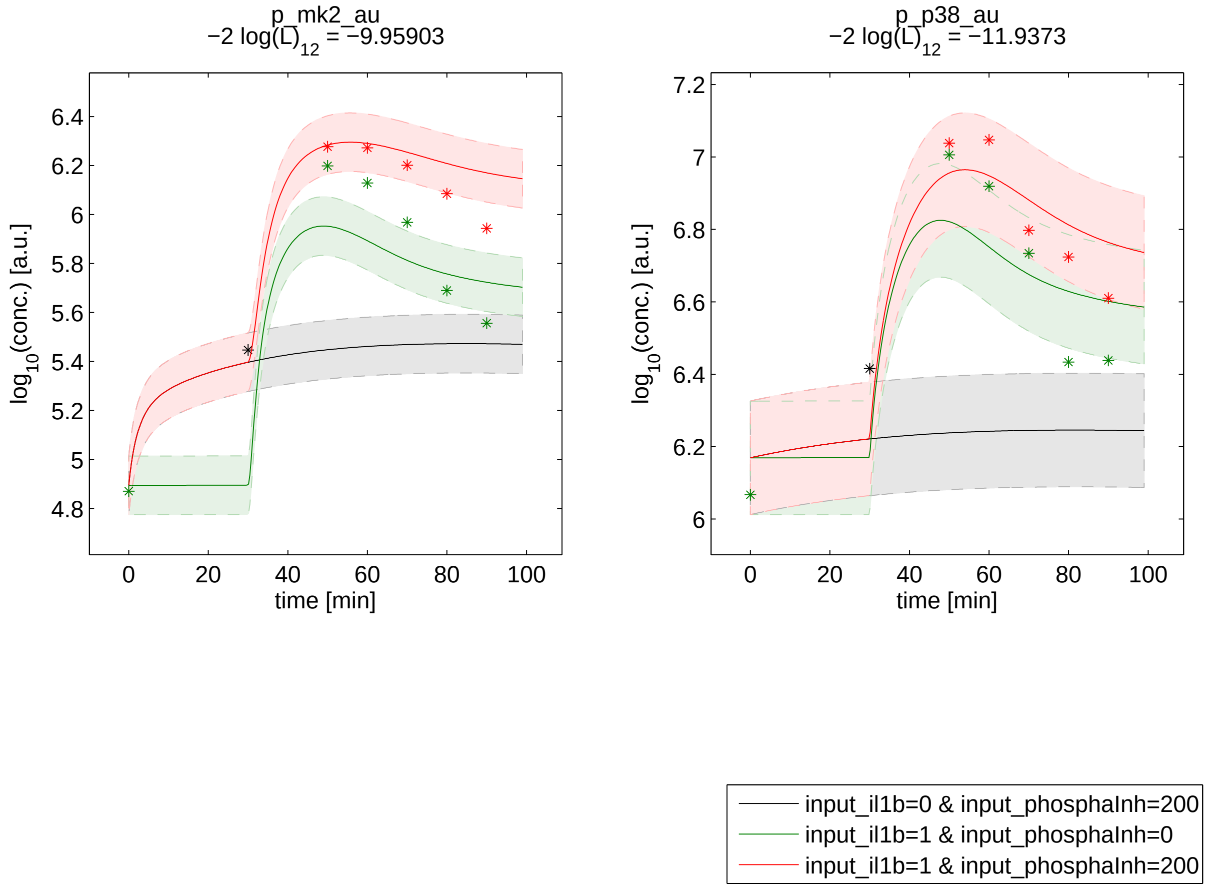

Figure 33: phosphatase_inhibitor_121024_pagewb121029 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.28 Experiment: phosphatase_inhibitor_121024_pagewb121029

Comments In this experiment the cells were treated with phosphatase inhibitors. After 30 minutes 1 ng/ml IL-1β was added. This is modeled by an inverse tangent which turns from zero to one at 30 minutes.

Modelfit and plots The agreement of the model observables and the experimental data, given in Table 57, yields a value of the objective function $-2\log(L) = -21.8964$ for 24 data points in this data set. The model observables and the experimental data is show in Figure 33.

Input variables The following inputs variables are modified in this data set:

- **Input variable 1:** IL1b

$$[\mathrm{IL1b}](\mathrm{t}) = \quad \mathrm{input\_il1b} \cdot \left(\frac{\arctan(1000.0 \cdot \mathrm{t} - 30000.0)}{\pi} + \frac{1}{2} \right) \tag{266}$$

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\mathrm{p\_mk2\_au}(\mathrm{t}) = \quad \mathrm{offset\_gel\_pMK2\_121024\_wb121029} + [\mathrm{pMK2}] \cdot \mathrm{scale\_pMK2\_121024\_wb121029} \tag{267}$$

time [min]	input_il1b [$ng \cdot ml^{-1}$]	input_phosphaInh [μM]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
0	1	0	1.16717e+06	74139
30	0	200	2.60536e+06	279697
50	1	0	1.01351e+07	1.57927e+06
50	1	200	1.09184e+07	1.89352e+06
60	1	0	8.30094e+06	1.34497e+06
60	1	200	1.11480e+07	1.87178e+06
70	1	0	5.42071e+06	928693
70	1	200	6.27355e+06	1.58877e+06
80	1	0	2.71386e+06	489766
80	1	200	5.29587e+06	1.21616e+06
90	1	0	2.74134e+06	359892
90	1	200	4.07690e+06	877404

Table 57: Experimental data for the experiment phosphatase_inhibitor_121024_pagewb121029

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(t) = \text{sd\_pMK2\_phosphaInh\_au} \tag{268}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au}(t) = \text{offset\_gel\_pp38\_121024\_wb121029} + [\text{pp38}] \cdot \text{scale\_pp38\_121024\_wb121029} \tag{269}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(t) = \text{sd\_pp38\_phosphaInh\_au} \tag{270}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\begin{array}{lcr|c|r} \text{input\_il1b} & \rightarrow & 0 & 1 & 1 \\ \text{input\_phosphaInh} & \rightarrow & 200 & 0 & 200 \end{array}$$

$$\text{scale\_pMK2\_121024\_wb121029} \rightarrow \frac{\text{scale\_pMK2\_121024\_wb121029}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_121024\_wb121029} \rightarrow \frac{\text{scale\_pp38\_121024\_wb121029}}{\text{init\_p38}}$$

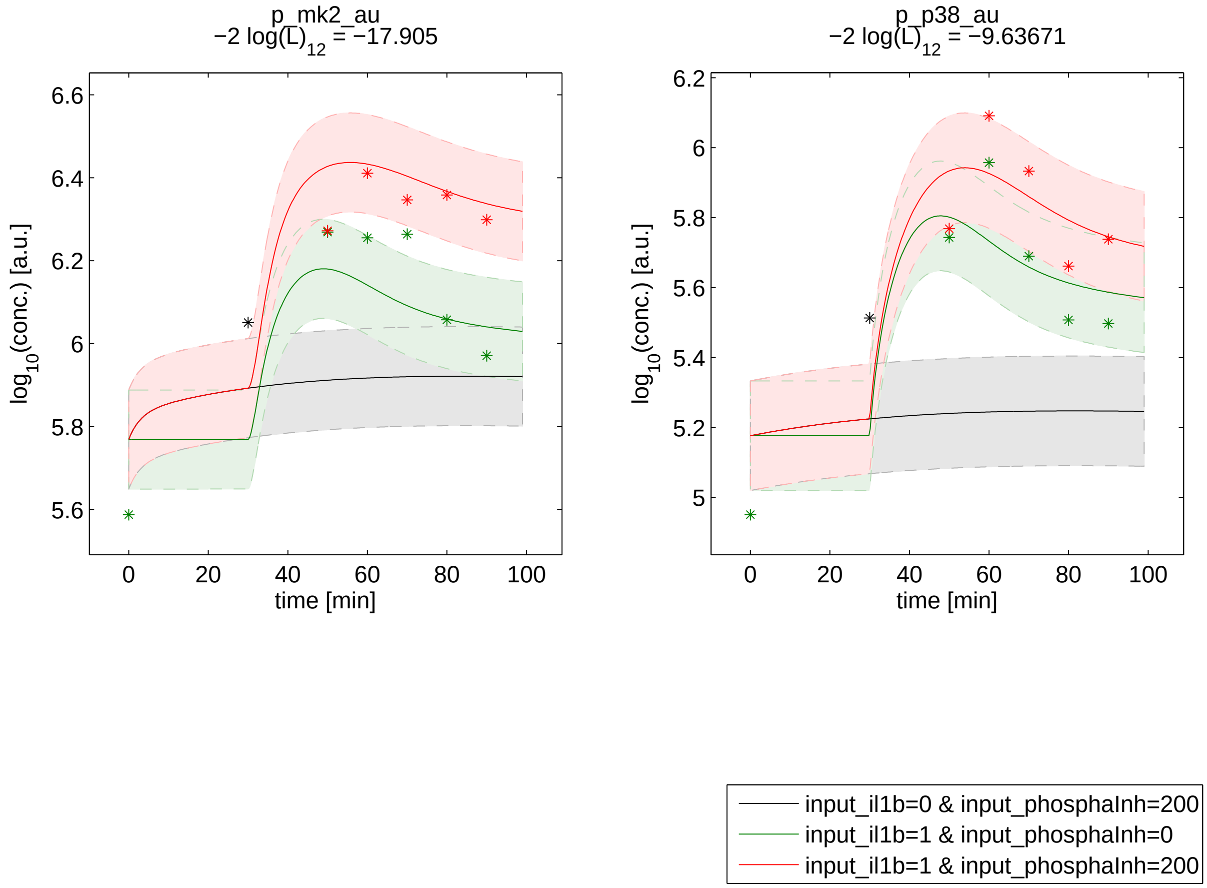

Figure 34: phosphatase_inhibitor_121031A_pagewb121105 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.29 Experiment: phosphatase_inhibitor_121031A_pagewb121105

Comments In this experiment the cells were treated with phosphatase inhibitors. After 30 minutes 1 ng/ml IL-1β was added. This is modeled by an inverse tangent which turns from zero to one at 30 minutes.

Modelfit and plots The agreement of the model observables and the experimental data, given in Table 58, yields a value of the objective function $-2\log(L) = -27.5417$ for 24 data points in this data set. The model observables and the experimental data is show in Figure 34.

Input variables The following inputs variables are modified in this data set:

- **Input variable 1:** IL1b

$$[\text{IL1b}](\text{t}) = \quad \text{input\_il1b} \cdot \left(\frac{\arctan(1000.0 \cdot \text{t} - 30000.0)}{\pi} + \frac{1}{2} \right) \tag{271}$$

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\text{p\_mk2\_au}(\text{t}) = \quad \text{offset\_gel\_pMK2\_121031A\_wb121105} + [\text{pMK2}] \cdot \text{scale\_pMK2\_121031A\_wb121105} \tag{272}$$

time [min]	input_il1b [$ng \cdot ml^{-1}$]	input_phosphaInh [μM]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
0	1	0	89268	386742
30	0	200	325608	1.12428e+06
50	1	0	553657	1.85810e+06
50	1	200	586548	1.87078e+06
60	1	0	906081	1.80025e+06
60	1	200	1.23349e+06	2.57584e+06
70	1	0	489339	1.83536e+06
70	1	200	857009	2.22222e+06
80	1	0	321624	1.14132e+06
80	1	200	458335	2.28364e+06
90	1	0	314085	934820
90	1	200	547105	1.99048e+06

Table 58: Experimental data for the experiment phosphatase_inhibitor_121031A_pagewb121105

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(t) = \text{sd\_pMK2\_phosphaInh\_au} \tag{273}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au}(t) = \text{offset\_gel\_pp38\_121031A\_wb121105} + [\text{pp38}] \cdot \text{scale\_pp38\_121031A\_wb121105} \tag{274}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(t) = \text{sd\_pp38\_phosphaInh\_au} \tag{275}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\begin{array}{lcr|r|r} \text{input\_il1b} & \rightarrow & 0 & 1 & 1 \\ \text{input\_phosphaInh} & \rightarrow & 200 & 0 & 200 \end{array}$$

$$\text{scale\_pMK2\_121031A\_wb121105} \rightarrow \frac{\text{scale\_pMK2\_121031A\_wb121105}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_121031A\_wb121105} \rightarrow \frac{\text{scale\_pp38\_121031A\_wb121105}}{\text{init\_p38}}$$

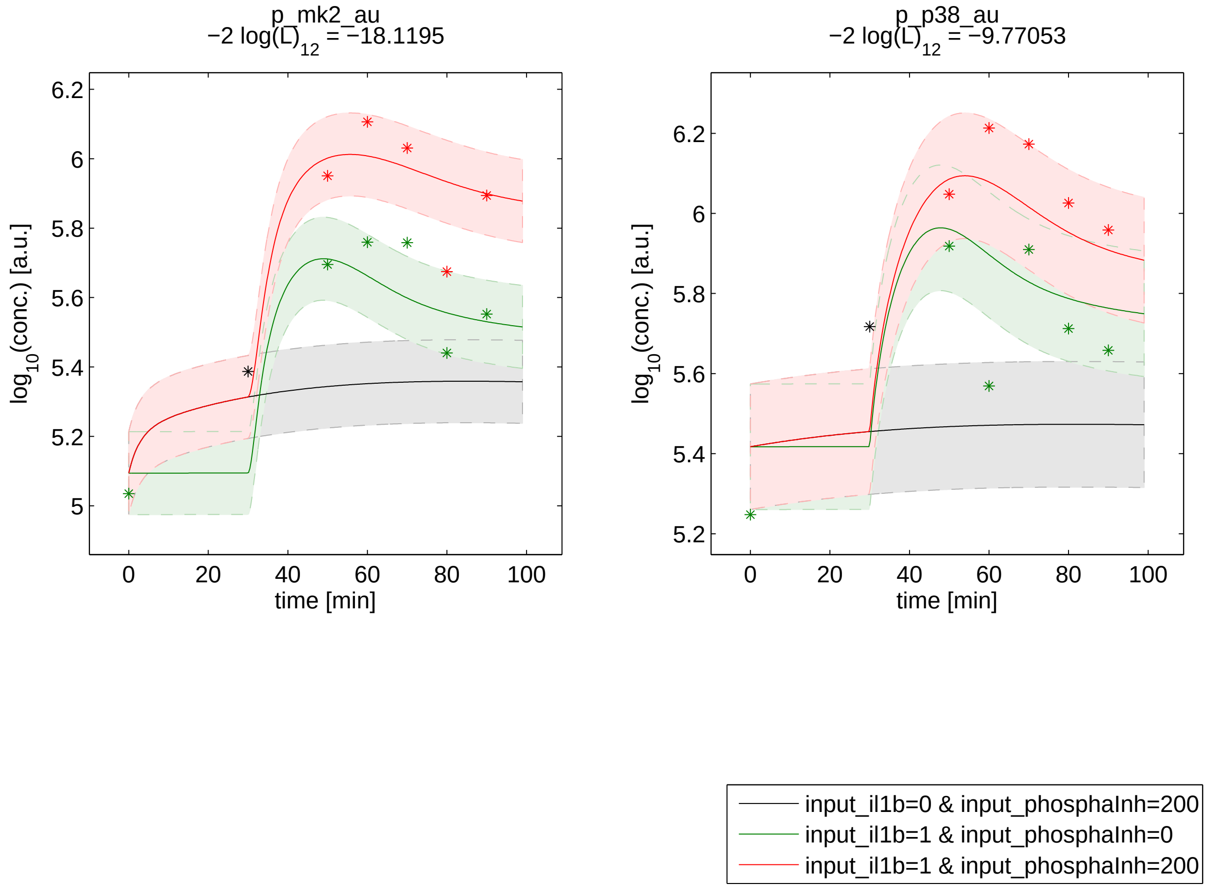

Figure 35: phosphatase_inhibitor_121031B_pagewb121105 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.30 Experiment: phosphatase_inhibitor_121031B_pagewb121105

Comments In this experiment the cells were treated with phosphatase inhibitors. After 30 minutes 1 ng/ml IL-1β was added. This is modeled by an inverse tangent which turns from zero to one at 30 minutes.

Modelfit and plots The agreement of the model observables and the experimental data, given in Table 59, yields a value of the objective function $-2\log(L) = -27.89$ for 24 data points in this data set. The model observables and the experimental data is show in Figure 35.

Input variables The following inputs variables are modified in this data set:

- **Input variable 1:** IL1b

$$[\mathrm{IL1b}](\mathrm{t}) = \quad \mathrm{input\_il1b} \cdot \left(\frac{\arctan(1000.0 \cdot \mathrm{t} - 30000.0)}{\pi} + \frac{1}{2} \right) \tag{276}$$

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\mathrm{p\_mk2\_au}(\mathrm{t}) = \quad \mathrm{offset\_gel\_pMK2\_121031B\_wb121105} + [\mathrm{pMK2}] \cdot \mathrm{scale\_pMK2\_121031B\_wb121105} \tag{277}$$

time [min]	input_il1b [$ng \cdot ml^{-1}$]	input_phosphaInh [μM]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
0	1	0	177029	108376
30	0	200	521556	243801
50	1	0	828271	495849
50	1	200	1.11618e+06	892591
60	1	0	370678	574631
60	1	200	1.63418e+06	1.27762e+06
70	1	0	812240	572737
70	1	200	1.48880e+06	1.07299e+06
80	1	0	515901	275781
80	1	200	1.06130e+06	472729
90	1	0	454857	356962
90	1	200	909068	783494

Table 59: Experimental data for the experiment phosphatase_inhibitor_121031B_pagewb121105

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \quad \text{sd\_pMK2\_phosphaInh\_au} \tag{278}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au}(\text{t}) = \quad \text{offset\_gel\_pp38\_121031B\_wb121105} + [\text{pp38}] \cdot \text{scale\_pp38\_121031B\_wb121105} \tag{279}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \quad \text{sd\_pp38\_phosphaInh\_au} \tag{280}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\begin{array}{lcr|c|r} \text{input\_il1b} & \rightarrow & 0 & 1 & 1 \\ \text{input\_phosphaInh} & \rightarrow & 200 & 0 & 200 \end{array}$$

$$\text{scale\_pMK2\_121031B\_wb121105} \rightarrow \frac{\text{scale\_pMK2\_121031B\_wb121105}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_121031B\_wb121105} \rightarrow \frac{\text{scale\_pp38\_121031B\_wb121105}}{\text{init\_p38}}$$

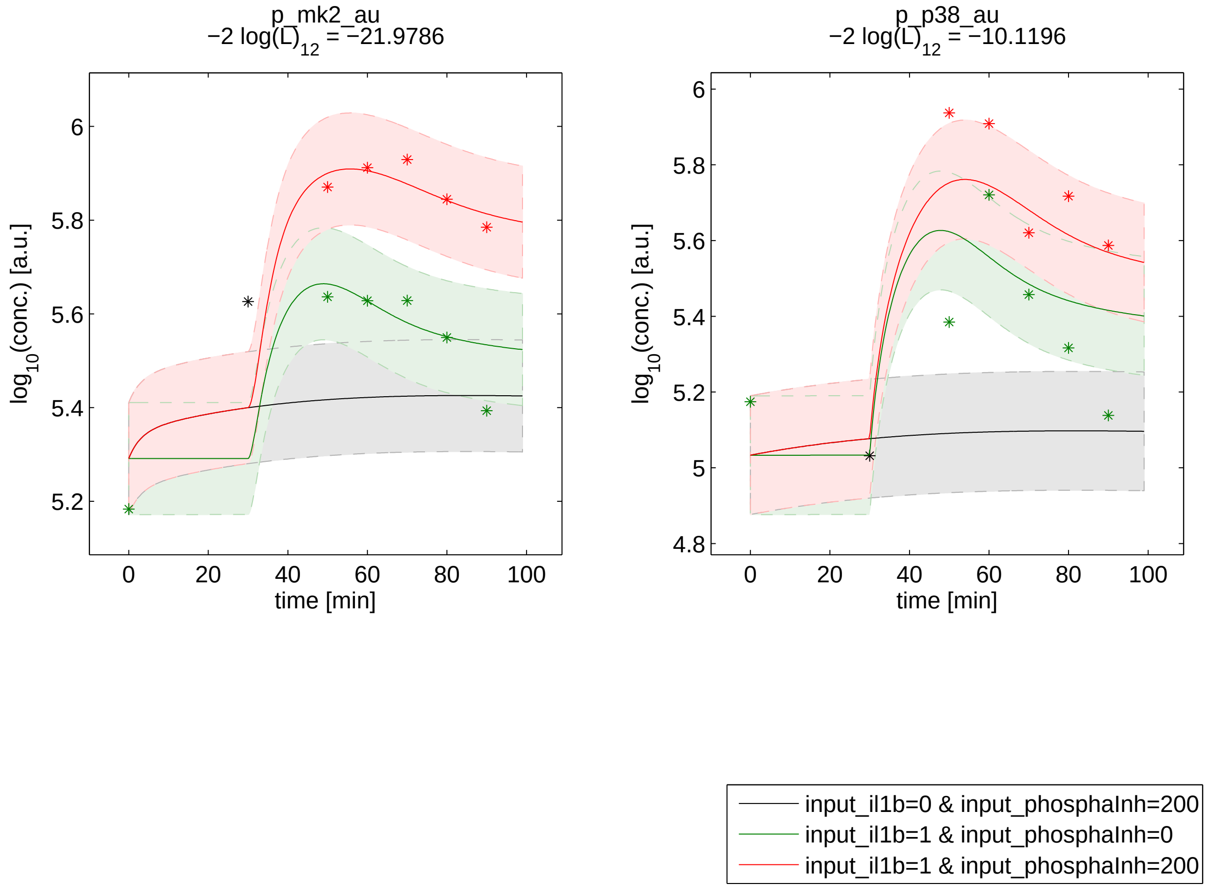

Figure 36: phosphatase_inhibitor_121114A_pagewb121119 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.31 Experiment: phosphatase_inhibitor_121114A_pagewb121119

Comments In this experiment the cells were treated with phosphatase inhibitors. After 30 minutes 1 ng/ml IL-1β was added. This is modeled by an inverse tangent which turns from zero to one at 30 minutes.

Model fit and plots The agreement of the model observables and the experimental data, given in Table 60, yields a value of the objective function $-2\log(L) = -32.0982$ for 24 data points in this data set. The model observables and the experimental data is show in Figure 36.

Input variables The following inputs variables are modified in this data set:

- **Input variable 1:** IL1b

$$[\mathrm{IL1b}](\mathrm{t}) = \quad \mathrm{input\_il1b} \cdot \left(\frac{\arctan(1000.0 \cdot \mathrm{t} - 30000.0)}{\pi} + \frac{1}{2} \right) \tag{281}$$

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\mathrm{p\_mk2\_au}(\mathrm{t}) = \quad \mathrm{offset\_gel\_pMK2\_121114A\_wb121119} + [\mathrm{pMK2}] \cdot \mathrm{scale\_pMK2\_121114A\_wb121119} \tag{282}$$

time [min]	input_il1b [ng · ml^{-1}]	input_phosphaInh [μM]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
0	1	0	149371	152581
30	0	200	107611	423049
50	1	0	242583	432968
50	1	200	864848	742429
60	1	0	525795	424501
60	1	200	810508	816665
70	1	0	286639	424908
70	1	200	417462	849717
80	1	0	207168	354398
80	1	200	521571	699460
90	1	0	137469	247320
90	1	200	386281	609517

Table 60: Experimental data for the experiment phosphatase_inhibitor_121114A_pagewb121119

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(\text{t}) = \quad \text{sd\_pMK2\_phosphaInh\_au} \tag{283}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au}(\text{t}) = \quad \text{offset\_gel\_pp38\_121114A\_wb121119} + [\text{pp38}] \cdot \text{scale\_pp38\_121114A\_wb121119} \tag{284}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(\text{t}) = \quad \text{sd\_pp38\_phosphaInh\_au} \tag{285}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

input_il1b	→	0	1	1
input_phosphaInh	→	200	0	200

$$\text{scale\_pMK2\_121114A\_wb121119} \rightarrow \frac{\text{scale\_pMK2\_121114A\_wb121119}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_121114A\_wb121119} \rightarrow \frac{\text{scale\_pp38\_121114A\_wb121119}}{\text{init\_p38}}$$

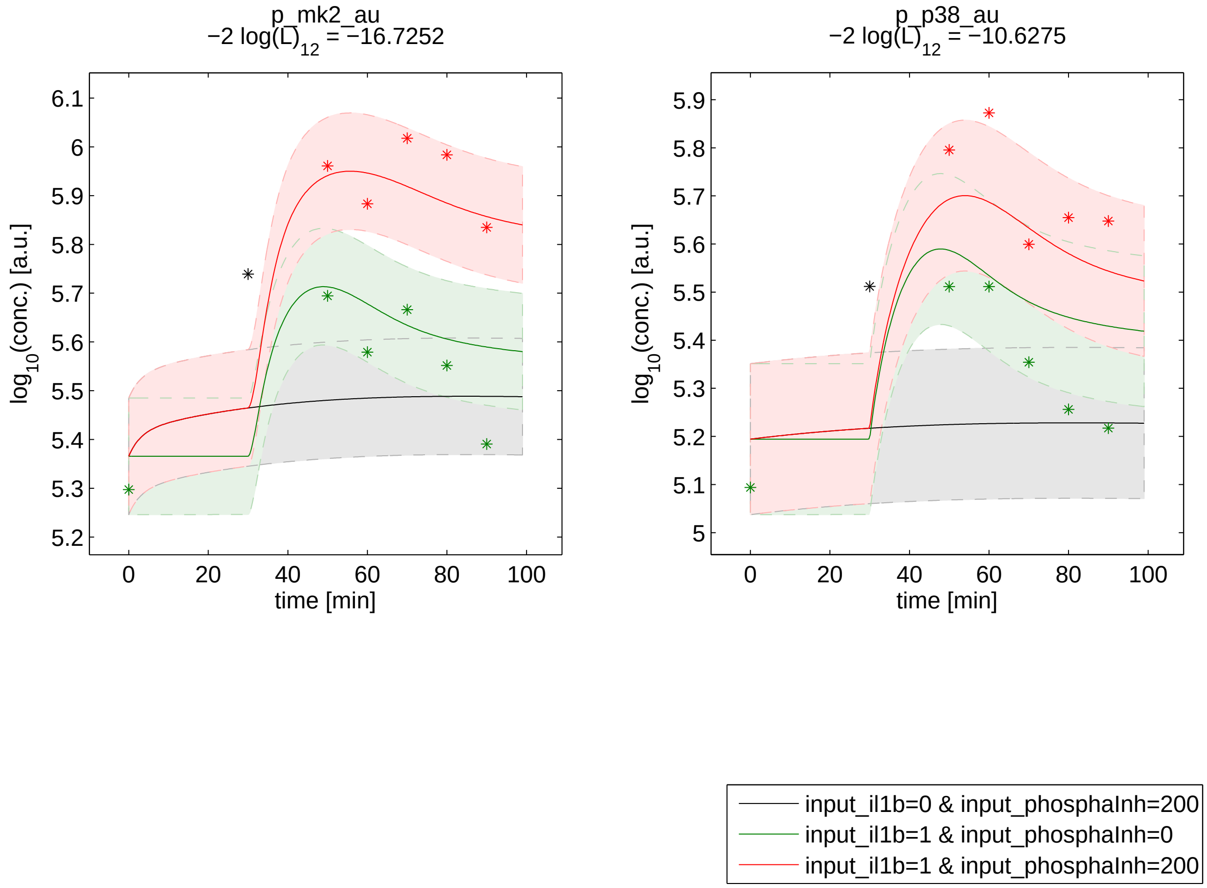

Figure 37: phosphatase_inhibitor_121114B_pagewb121119 observables and experimental data for the experiment. The observables are displayed as solid lines. The error model that describes the measurement noise is indicated by shades.

2.2.32 Experiment: phosphatase_inhibitor_121114B_pagewb121119

Comments In this experiment the cells were treated with phosphatase inhibitors. After 30 minutes 1 ng/ml IL-1β was added. This is modeled by an inverse tangent which turns from zero to one at 30 minutes.

Modelfit and plots The agreement of the model observables and the experimental data, given in Table 61, yields a value of the objective function $-2\log(L) = -27.3527$ for 24 data points in this data set. The model observables and the experimental data is show in Figure 37.

Input variables The following inputs variables are modified in this data set:

- **Input variable 1:** IL1b

$$[\mathrm{IL1b}](\mathrm{t}) = \quad \mathrm{input\_il1b} \cdot \left(\frac{\arctan(1000.0 \cdot \mathrm{t} - 30000.0)}{\pi} + \frac{1}{2} \right) \tag{286}$$

Observables The following observables are added in this data set:

- **Observable:** p_mk2_au

$$\mathrm{p\_mk2\_au}(\mathrm{t}) = \quad \mathrm{offset\_gel\_pMK2\_121114B\_wb121119} + [\mathrm{pMK2}] \cdot \mathrm{scale\_pMK2\_121114B\_wb121119} \tag{287}$$

time [min]	input_il1b $[ng \cdot ml^{-1}]$	input_phosphaInh [μM]	p_p38_au conc. [a.u.]	p_mk2_au conc. [a.u.]
0	1	0	124097	198255
30	0	200	325015	548473
50	1	0	324828	494813
50	1	200	624428	913986
60	1	0	324602	379371
60	1	200	745521	764129
70	1	0	226158	463513
70	1	200	397655	1.04176e+06
80	1	0	180346	356365
80	1	200	451579	963283
90	1	0	165000	245840
90	1	200	444486	683812

Table 61: Experimental data for the experiment phosphatase_inhibitor_121114B_pagewb121119

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_mk2\_au}\}(t) = \text{sd\_pMK2\_phosphaInh\_au} \tag{288}$$

- **Observable:** p_p38_au

$$\text{p\_p38\_au}(t) = \text{offset\_gel\_pp38\_121114B\_wb121119} + [\text{pp38}] \cdot \text{scale\_pp38\_121114B\_wb121119} \tag{289}$$

Unit: conc. [a.u.]; With error model:

$$\sigma\{\text{p\_p38\_au}\}(t) = \text{sd\_pp38\_phosphaInh\_au} \tag{290}$$

Conditions To evaluate the ODE system of Equation 23 – 27 for the conditions in this experiment, the following parameter transformations are applied:

$$\begin{array}{lcr|r|r} \text{input\_il1b} & \rightarrow & 0 & 1 & 1 \\ \text{input\_phosphaInh} & \rightarrow & 200 & 0 & 200 \end{array}$$

$$\text{scale\_pMK2\_121114B\_wb121119} \rightarrow \frac{\text{scale\_pMK2\_121114B\_wb121119}}{\text{init\_MK2}}$$

$$\text{scale\_pp38\_121114B\_wb121119} \rightarrow \frac{\text{scale\_pp38\_121114B\_wb121119}}{\text{init\_p38}}$$

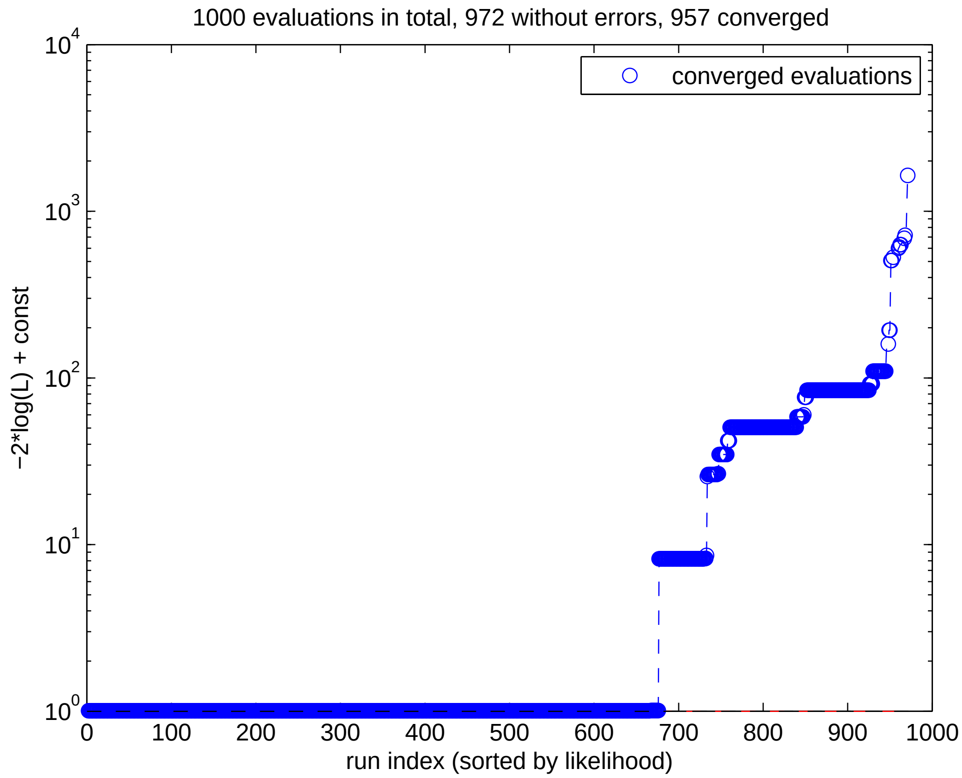

Figure 38: Sorted values of the objective function obtained by 1000 parameter estimation runs initialized with parameter sets choosen by a latin hypercube sampling. The different levels correspond to different local optima. More than 65 % of all fits reached the lowest local optimum. This is a strong indication that we found the global optimum.

2.3 Estimated model parameters

In total 169 parameters are estimated from the experimental data. In order to reveal possible local optima we performed in total 1000 parameter estimation runs with different random sampled starting parameters. More than 650 runs directed to the same optimum, which is a strong hint that we found the global optimum (Figure 38). Local minima were found by our approach, however, at likelihood values that are significantly worse than the global optimum and can be neglected for the further investigation. The best optimum yields a value of the objective function $-2\log(L) = -2113.29$ for a total of 1676 data points. The model parameter were estimated by maximum likelihood estimation applying the MATLAB lsqnonlin algorithm. In Table 62–65 the estimated parameter values are given. Parameters highlighted in red color indicate parameter values close to their bounds. The parameter name prefix init_ indicates the initial value of a dynamic variable. The parameter name prefix offset_ indicates a offset of the experimental data. The parameter name prefix scale_ indicates a scaling factor of the experimental data. The parameter name prefix sd_ indicates the magnitude of the measurement noise for a specific measurement.

	name	θ_{min}	$\hat{\theta}$	θ_{max}	log	non-log $\hat{\theta}$	fitted
1	V	-5	-0.0355	+3	1	$+9.21 \cdot 10^{-01}$	1
2	conc_MK2_total_calibrator	-5	-0.5154	+8	1	$+3.05 \cdot 10^{-01}$	1
3	conc_p38_total_calibrator	-5	+0.1990	+8	1	$+1.58 \cdot 10^{+00}$	1
4	dePhospho_inh	-5	-2.1641	+3	1	$+6.85 \cdot 10^{-03}$	1
5	il1b_sat	-5	-0.2806	+3	1	$+5.24 \cdot 10^{-01}$	1
6	init_MK2	-5	+0.6582	+3	1	$+4.55 \cdot 10^{+00}$	1
7	init_p38	-5	-0.4462	+3	1	$+3.58 \cdot 10^{-01}$	1
8	intstd_in_MK2_total_calibrator	-5	+0.0773	+8	1	$+1.19 \cdot 10^{+00}$	1
9	intstd_in_p38_total_calibrator	-5	+1.8997	+8	1	$+7.94 \cdot 10^{+01}$	1
10	intstd_in_pMK2_calibrator	-5	+0.4249	+8	1	$+2.66 \cdot 10^{+00}$	1
11	intstd_in_pp38_calibrator	-5	+1.7431	+8	1	$+5.53 \cdot 10^{+01}$	1
12	mk2_act_p38	-5	+1.0070	+3	1	$+1.02 \cdot 10^{+01}$	1
13	mk2_dea	-5	-0.1461	+3	1	$+7.14 \cdot 10^{-01}$	1
14	mk2_inh_sb	-5	+0.0113	+3	1	$+1.03 \cdot 10^{+00}$	1
15	mkp_prod_pp38	-5	-2.0752	+3	1	$+8.41 \cdot 10^{-03}$	1
16	offset_BSA_MK2_total	-5	+7.5103	+1e+01	1	$+3.24 \cdot 10^{+07}$	1
17	offset_BSA_p38_total	-5	+7.5837	+1e+01	1	$+3.83 \cdot 10^{+07}$	1
18	offset_MK2ges_100421_111026a	-5	+6.0172	+9	1	$+1.04 \cdot 10^{+06}$	1
19	offset_MK2ges_100504_111027a	-5	+6.0242	+9	1	$+1.06 \cdot 10^{+06}$	1
20	offset_MK2ges_100504_111027b	-5	+6.0337	+9	1	$+1.08 \cdot 10^{+06}$	1
21	offset_MK2ges_100628b_111027b	-5	+6.0567	+9	1	$+1.14 \cdot 10^{+06}$	1
22	offset_cal_intstd_MK2_total	-5	+5.7909	+8	1	$+6.18 \cdot 10^{+05}$	1
23	offset_cal_intstd_p38_total	-5	+5.4939	+8	1	$+3.12 \cdot 10^{+05}$	1
24	offset_cal_intstd_pMK2	-5	+5.6331	+8	1	$+4.30 \cdot 10^{+05}$	1
25	offset_cal_intstd_pp38	-5	+5.7534	+8	1	$+5.67 \cdot 10^{+05}$	1
26	offset_gel_pMK2_090102	-5	+4.2896	+9	1	$+1.95 \cdot 10^{+04}$	1
27	offset_gel_pMK2_090615d_090922a	-5	+4.4093	+9	1	$+2.57 \cdot 10^{+04}$	1
28	offset_gel_pMK2_090615d_090922b	-5	+4.4304	+9	1	$+2.69 \cdot 10^{+04}$	1
29	offset_gel_pMK2_090615d_090922d	-5	+4.4950	+9	1	$+3.13 \cdot 10^{+04}$	1
30	offset_gel_pMK2_090615d_100416	-5	-5.0000	+9	1	$+1.00 \cdot 10^{-05}$	1
31	offset_gel_pMK2_090615d_110419	-5	-5.0000	+9	1	$+1.00 \cdot 10^{-05}$	1
32	offset_gel_pMK2_100241_100428	-5	+5.8299	+9	1	$+6.76 \cdot 10^{+05}$	1
33	offset_gel_pMK2_100241_100430	-5	-5.0000	+9	1	$+1.00 \cdot 10^{-05}$	1
34	offset_gel_pMK2_100241_100505	-5	+5.8473	+9	1	$+7.03 \cdot 10^{+05}$	1
35	offset_gel_pMK2_100504_100512	-5	+5.7662	+9	1	$+5.84 \cdot 10^{+05}$	1
36	offset_gel_pMK2_100504_100520	-5	+5.9173	+9	1	$+8.27 \cdot 10^{+05}$	1
37	offset_gel_pMK2_100504_100527	-5	+5.8801	+9	1	$+7.59 \cdot 10^{+05}$	1
38	offset_gel_pMK2_100517_100610a	-5	+5.8992	+9	1	$+7.93 \cdot 10^{+05}$	1
39	offset_gel_pMK2_100517_100610b	-5	+5.9955	+9	1	$+9.90 \cdot 10^{+05}$	1
40	offset_gel_pMK2_100628b_100727	-5	+5.9865	+9	1	$+9.69 \cdot 10^{+05}$	1
41	offset_gel_pMK2_100628b_100728a	-5	+5.9107	+9	1	$+8.14 \cdot 10^{+05}$	1
42	offset_gel_pMK2_100628b_100728b	-5	+5.8436	+9	1	$+6.98 \cdot 10^{+05}$	1
43	offset_gel_pMK2_101029_101103	-5	+5.7141	+9	1	$+5.18 \cdot 10^{+05}$	1
44	offset_gel_pMK2_101029_101104	-5	+5.7991	+9	1	$+6.30 \cdot 10^{+05}$	1
45	offset_gel_pMK2_110317a_110406a	-5	+3.0145	+9	1	$+1.03 \cdot 10^{+03}$	1
46	offset_gel_pMK2_110317b_110405a	-5	+3.0962	+9	1	$+1.25 \cdot 10^{+03}$	1
47	offset_gel_pMK2_110317b_110405b	-5	+2.8479	+9	1	$+7.05 \cdot 10^{+02}$	1
48	offset_gel_pMK2_121024_wb121029	-5	+3.8283	+9	1	$+6.73 \cdot 10^{+03}$	1
49	offset_gel_pMK2_121031A_wb121105	-5	+5.7038	+9	1	$+5.06 \cdot 10^{+05}$	1

Table 62: Estimated parameter values
$\hat{\theta}$ indicates the estimated value of the parameters. θ_{min} and θ_{max} indicate the upper and lower bounds for the parameters. The log-column indicates if the value of a parameter was log-transformed. If log = 1 the non-log-column indicates the non-logarithmic value of the estimate. The fitted-column indicates if the parameter value was estimated (1), was temporarily fixed (0) or if its value was fixed to a constant value (2).

	name	θ_{min}	$\hat{\theta}$	θ_{max}	log	non-log $\hat{\theta}$	fitted
50	offset_gel_pMK2_121031B_wb121105	-5	+4.9546	+9	1	$+9.01 \cdot 10^{+04}$	1
51	offset_gel_pMK2_121114A_wb121119	-5	+5.2362	+9	1	$+1.72 \cdot 10^{+05}$	1
52	offset_gel_pMK2_121114B_wb121119	-5	+5.3162	+9	1	$+2.07 \cdot 10^{+05}$	1
53	offset_gel_pp38_090615d_090922a	-5	-5.0000	+9	1	$+1.00 \cdot 10^{-05}$	1
54	offset_gel_pp38_090615d_090922b	-5	-5.0000	+9	1	$+1.00 \cdot 10^{-05}$	1
55	offset_gel_pp38_090615d_090922d	-5	-4.9914	+9	1	$+1.02 \cdot 10^{-05}$	1
56	offset_gel_pp38_090615d_100416	-5	+5.1495	+9	1	$+1.41 \cdot 10^{+05}$	1
57	offset_gel_pp38_090615d_110419	-5	-5.0000	+9	1	$+1.00 \cdot 10^{-05}$	1
58	offset_gel_pp38_100241_100428	-5	+5.7216	+9	1	$+5.27 \cdot 10^{+05}$	1
59	offset_gel_pp38_100241_100430	-5	+5.7253	+9	1	$+5.31 \cdot 10^{+05}$	1
60	offset_gel_pp38_100241_100505	-5	+5.6845	+9	1	$+4.84 \cdot 10^{+05}$	1
61	offset_gel_pp38_100504_100512	-5	+5.6026	+9	1	$+4.00 \cdot 10^{+05}$	1
62	offset_gel_pp38_100504_100520	-5	+5.8084	+9	1	$+6.43 \cdot 10^{+05}$	1
63	offset_gel_pp38_100504_100527	-5	+5.7863	+9	1	$+6.11 \cdot 10^{+05}$	1
64	offset_gel_pp38_100517_100610a	-5	+5.7604	+9	1	$+5.76 \cdot 10^{+05}$	1
65	offset_gel_pp38_100517_100610b	-5	+5.7604	+9	1	$+5.76 \cdot 10^{+05}$	1
66	offset_gel_pp38_100628b_100727	-5	+5.7763	+9	1	$+5.97 \cdot 10^{+05}$	1
67	offset_gel_pp38_100628b_100728a	-5	+5.7139	+9	1	$+5.17 \cdot 10^{+05}$	1
68	offset_gel_pp38_100628b_100728b	-5	+5.7219	+9	1	$+5.27 \cdot 10^{+05}$	1
69	offset_gel_pp38_100708_100715	-5	+5.7211	+9	1	$+5.26 \cdot 10^{+05}$	1
70	offset_gel_pp38_101029_101103	-5	+5.7268	+9	1	$+5.33 \cdot 10^{+05}$	1
71	offset_gel_pp38_101029_101104	-5	+4.4295	+9	1	$+2.69 \cdot 10^{+04}$	1
72	offset_gel_pp38_110317a_110406a	-5	+4.0614	+9	1	$+1.15 \cdot 10^{+04}$	1
73	offset_gel_pp38_110317b_110405a	-5	+4.3062	+9	1	$+2.02 \cdot 10^{+04}$	1
74	offset_gel_pp38_110317b_110405b	-5	+4.3315	+9	1	$+2.15 \cdot 10^{+04}$	1
75	offset_gel_pp38_121024_wb121029	-5	+6.0517	+9	1	$+1.13 \cdot 10^{+06}$	1
76	offset_gel_pp38_121031A_wb121105	-5	+5.0689	+9	1	$+1.17 \cdot 10^{+05}$	1
77	offset_gel_pp38_121031B_wb121105	-5	+5.3367	+9	1	$+2.17 \cdot 10^{+05}$	1
78	offset_gel_pp38_121114A_wb121119	-5	+4.9382	+9	1	$+8.67 \cdot 10^{+04}$	1
79	offset_gel_pp38_121114B_wb121119	-5	+5.1487	+9	1	$+1.41 \cdot 10^{+05}$	1
80	offset_p38ges_100421_111026a	-5	+6.0465	+9	1	$+1.11 \cdot 10^{+06}$	1
81	offset_p38ges_100504_111027a	-5	+5.9650	+9	1	$+9.23 \cdot 10^{+05}$	1
82	offset_p38ges_100504_111027b	-5	+5.9732	+9	1	$+9.40 \cdot 10^{+05}$	1
83	offset_p38ges_100628b_111027b	-5	+5.8417	+9	1	$+6.95 \cdot 10^{+05}$	1
84	p38_act_basal	-5	-3.8209	+3	1	$+1.51 \cdot 10^{-04}$	1
85	p38_act_il1b	-5	-2.0419	+3	1	$+9.08 \cdot 10^{-03}$	1
86	p38_dea_const	-5	-5.0000	+3	1	$+1.00 \cdot 10^{-05}$	1
87	p38_dea_mkp	-5	+1.4912	+3	1	$+3.10 \cdot 10^{+01}$	1
88	scale_BSA_MK2_total	-5	+8.2940	+1e+01	1	$+1.97 \cdot 10^{+08}$	1
89	scale_BSA_p38_total	-5	+8.2408	+1e+01	1	$+1.74 \cdot 10^{+08}$	1
90	scale_MK2ges_100421_111026a	-5	+6.1569	+9	1	$+1.44 \cdot 10^{+06}$	1
91	scale_MK2ges_100504_111027a	-5	+6.1416	+9	1	$+1.39 \cdot 10^{+06}$	1
92	scale_MK2ges_100504_111027b	-5	+6.0297	+9	1	$+1.07 \cdot 10^{+06}$	1
93	scale_MK2ges_100628b_111027b	-5	+6.1468	+9	1	$+1.40 \cdot 10^{+06}$	1
94	scale_cal_intstd_MK2_total	-5	+4.8905	+8	1	$+7.77 \cdot 10^{+04}$	1
95	scale_cal_intstd_p38_total	-5	+4.8289	+8	1	$+6.74 \cdot 10^{+04}$	1
96	scale_cal_intstd_pMK2	-5	+5.0035	+8	1	$+1.01 \cdot 10^{+05}$	1
97	scale_cal_intstd_pp38	-5	+4.5826	+8	1	$+3.82 \cdot 10^{+04}$	1
98	scale_p38ges_100421_111026a	-5	+6.2895	+9	1	$+1.95 \cdot 10^{+06}$	1
99	scale_p38ges_100504_111027a	-5	+5.5923	+9	1	$+3.91 \cdot 10^{+05}$	1

Table 63: Estimated parameter values
$\hat{\theta}$ indicates the estimated value of the parameters. θ_{min} and θ_{max} indicate the upper and lower bounds for the parameters. The log-column indicates if the value of a parameter was log-transformed. If log = 1 the non-log-column indicates the non-logarithmic value of the estimate. The fitted-column indicates if the parameter value was estimated (1), was temporarily fixed (0) or if its value was fixed to a constant value (2).

	name	θ_{min}	$\hat{\theta}$	θ_{max}	log	non-log $\hat{\theta}$	fitted
100	scale_p38ges_100504_111027b	-5	+6.1938	+9	1	$+1.56 \cdot 10^{+06}$	1
101	scale_p38ges_100628b_111027b	-5	+6.2118	+9	1	$+1.63 \cdot 10^{+06}$	1
102	scale_pMK2_090102	-5	+5.9869	+9	1	$+9.70 \cdot 10^{+05}$	1
103	scale_pMK2_090615d_090922a	-5	+5.8836	+9	1	$+7.65 \cdot 10^{+05}$	1
104	scale_pMK2_090615d_090922b	-5	+5.9805	+9	1	$+9.56 \cdot 10^{+05}$	1
105	scale_pMK2_090615d_090922d	-5	+5.7743	+9	1	$+5.95 \cdot 10^{+05}$	1
106	scale_pMK2_090615d_100416	-5	+6.6219	+9	1	$+4.19 \cdot 10^{+06}$	1
107	scale_pMK2_090615d_110419	-5	+6.0065	+9	1	$+1.02 \cdot 10^{+06}$	1
108	scale_pMK2_100241_100428	-5	+6.3780	+9	1	$+2.39 \cdot 10^{+06}$	1
109	scale_pMK2_100241_100430	-5	+5.8056	+9	1	$+6.39 \cdot 10^{+05}$	1
110	scale_pMK2_100241_100505	-5	+6.5593	+9	1	$+3.62 \cdot 10^{+06}$	1
111	scale_pMK2_100504_100512	-5	+6.6680	+9	1	$+4.66 \cdot 10^{+06}$	1
112	scale_pMK2_100504_100520	-5	+6.8758	+9	1	$+7.51 \cdot 10^{+06}$	1
113	scale_pMK2_100504_100527	-5	+6.8767	+9	1	$+7.53 \cdot 10^{+06}$	1
114	scale_pMK2_100517_100610a	-5	+6.4660	+9	1	$+2.92 \cdot 10^{+06}$	1
115	scale_pMK2_100517_100610b	-5	+6.4214	+9	1	$+2.64 \cdot 10^{+06}$	1
116	scale_pMK2_100628b_100727	-5	+6.7724	+9	1	$+5.92 \cdot 10^{+06}$	1
117	scale_pMK2_100628b_100728a	-5	+6.6019	+9	1	$+4.00 \cdot 10^{+06}$	1
118	scale_pMK2_100628b_100728b	-5	+6.6866	+9	1	$+4.86 \cdot 10^{+06}$	1
119	scale_pMK2_101029_101103	-5	+6.6395	+9	1	$+4.36 \cdot 10^{+06}$	1
120	scale_pMK2_101029_101104	-5	+6.5813	+9	1	$+3.81 \cdot 10^{+06}$	1
121	scale_pMK2_110317a_110406a	-5	+6.0628	+9	1	$+1.16 \cdot 10^{+06}$	1
122	scale_pMK2_110317b_110405a	-5	+6.2476	+9	1	$+1.77 \cdot 10^{+06}$	1
123	scale_pMK2_110317b_110405b	-5	+5.9571	+9	1	$+9.06 \cdot 10^{+05}$	1
124	scale_pMK2_121024_wb121029	-5	+6.5813	+9	1	$+3.81 \cdot 10^{+06}$	1
125	scale_pMK2_121031A_wb121105	-5	+6.6357	+9	1	$+4.32 \cdot 10^{+06}$	1
126	scale_pMK2_121031B_wb121105	-5	+6.2600	+9	1	$+1.82 \cdot 10^{+06}$	1
127	scale_pMK2_121114A_wb121119	-5	+6.0932	+9	1	$+1.24 \cdot 10^{+06}$	1
128	scale_pMK2_121114B_wb121119	-5	+6.1227	+9	1	$+1.33 \cdot 10^{+06}$	1
129	scale_pp38_090615d_090922a	-5	+6.9452	+9	1	$+8.82 \cdot 10^{+06}$	1
130	scale_pp38_090615d_090922b	-5	+6.7429	+9	1	$+5.53 \cdot 10^{+06}$	1
131	scale_pp38_090615d_090922d	-5	+6.7266	+9	1	$+5.33 \cdot 10^{+06}$	1
132	scale_pp38_090615d_100416	-5	+7.8390	+9	1	$+6.90 \cdot 10^{+07}$	1
133	scale_pp38_090615d_110419	-5	+6.9813	+9	1	$+9.58 \cdot 10^{+06}$	1
134	scale_pp38_100241_100428	-5	+7.3757	+9	1	$+2.37 \cdot 10^{+07}$	1
135	scale_pp38_100241_100430	-5	+7.0507	+9	1	$+1.12 \cdot 10^{+07}$	1
136	scale_pp38_100241_100505	-5	+7.2076	+9	1	$+1.61 \cdot 10^{+07}$	1
137	scale_pp38_100504_100512	-5	+7.3637	+9	1	$+2.31 \cdot 10^{+07}$	1
138	scale_pp38_100504_100520	-5	+7.0163	+9	1	$+1.04 \cdot 10^{+07}$	1
139	scale_pp38_100504_100527	-5	+6.9793	+9	1	$+9.53 \cdot 10^{+06}$	1
140	scale_pp38_100517_100610a	-5	+6.9269	+9	1	$+8.45 \cdot 10^{+06}$	1
141	scale_pp38_100517_100610b	-5	+6.9269	+9	1	$+8.45 \cdot 10^{+06}$	1
142	scale_pp38_100628b_100727	-5	+7.1609	+9	1	$+1.45 \cdot 10^{+07}$	1
143	scale_pp38_100628b_100728a	-5	+6.9837	+9	1	$+9.63 \cdot 10^{+06}$	1
144	scale_pp38_100628b_100728b	-5	+6.9623	+9	1	$+9.17 \cdot 10^{+06}$	1
145	scale_pp38_100708_100715	-5	+6.4940	+9	1	$+3.12 \cdot 10^{+06}$	1
146	scale_pp38_101029_101103	-5	+7.1991	+9	1	$+1.58 \cdot 10^{+07}$	1
147	scale_pp38_101029_101104	-5	+6.9070	+9	1	$+8.07 \cdot 10^{+06}$	1
148	scale_pp38_110317a_110406a	-5	+6.8557	+9	1	$+7.17 \cdot 10^{+06}$	1
149	scale_pp38_110317b_110405a	-5	+7.2734	+9	1	$+1.88 \cdot 10^{+07}$	1

Table 64: Estimated parameter values
$\hat{\theta}$ indicates the estimated value of the parameters. θ_{min} and θ_{max} indicate the upper and lower bounds for the parameters. The log-column indicates if the value of a parameter was log-transformed. If log = 1 the non-log-column indicates the non-logarithmic value of the estimate. The fitted-column indicates if the parameter value was estimated (1), was temporarily fixed (0) or if its value was fixed to a constant value (2).

	name	θ_{min}	$\hat{\theta}$	θ_{max}	log	non-log $\hat{\theta}$	fitted
150	scale_pp38_110317b_110405b	-5	+7.2052	+9	1	$+1.60 \cdot 10^{+07}$	1
151	scale_pp38_121024_wb121029	-5	+7.9772	+9	1	$+9.49 \cdot 10^{+07}$	1
152	scale_pp38_121031A_wb121105	-5	+6.9491	+9	1	$+8.89 \cdot 10^{+06}$	1
153	scale_pp38_121031B_wb121105	-5	+7.0796	+9	1	$+1.20 \cdot 10^{+07}$	1
154	scale_pp38_121114A_wb121119	-5	+6.7596	+9	1	$+5.75 \cdot 10^{+06}$	1
155	scale_pp38_121114B_wb121119	-5	+6.6267	+9	1	$+4.23 \cdot 10^{+06}$	1
156	sd_BSA_MK2_total	-5	-1.4565	+9	1	$+3.50 \cdot 10^{-02}$	1
157	sd_BSA_p38_total	-5	-1.9507	+8	1	$+1.12 \cdot 10^{-02}$	1
158	sd_MK2ges_au	-5	-1.3331	+3	1	$+4.64 \cdot 10^{-02}$	1
159	sd_cal_intstd_MK2_total	-5	-1.0420	+8	1	$+9.08 \cdot 10^{-02}$	1
160	sd_cal_intstd_p38_total	-5	-1.4556	+8	1	$+3.50 \cdot 10^{-02}$	1
161	sd_cal_intstd_pMK2	-5	-1.4382	+8	1	$+3.65 \cdot 10^{-02}$	1
162	sd_cal_intstd_pp38	-5	-1.8602	+8	1	$+1.38 \cdot 10^{-02}$	1
163	sd_p38ges_au	-5	-1.4311	+3	1	$+3.71 \cdot 10^{-02}$	1
164	sd_pMK2_au	-5	-0.9498	+3	1	$+1.12 \cdot 10^{-01}$	1
165	sd_pMK2_mk2ko_au	-5	-0.5016	+3	1	$+3.15 \cdot 10^{-01}$	1
166	sd_pMK2_phosphaInh_au	-5	-0.9227	+3	1	$+1.19 \cdot 10^{-01}$	1
167	sd_pp38_au	-5	-0.8357	+3	1	$+1.46 \cdot 10^{-01}$	1
168	sd_pp38_mk2ko_au	-5	-0.6998	+3	1	$+2.00 \cdot 10^{-01}$	1
169	sd_pp38_phosphaInh_au	-5	-0.8048	+3	1	$+1.57 \cdot 10^{-01}$	1

Table 65: Estimated parameter values
$\hat{\theta}$ indicates the estimated value of the parameters. θ_{min} and θ_{max} indicate the upper and lower bounds for the parameters. The log-column indicates if the value of a parameter was log-transformed. If log = 1 the non-log-column indicates the non-logarithmic value of the estimate. The fitted-column indicates if the parameter value was estimated (1), was temporarily fixed (0) or if its value was fixed to a constant value (2).

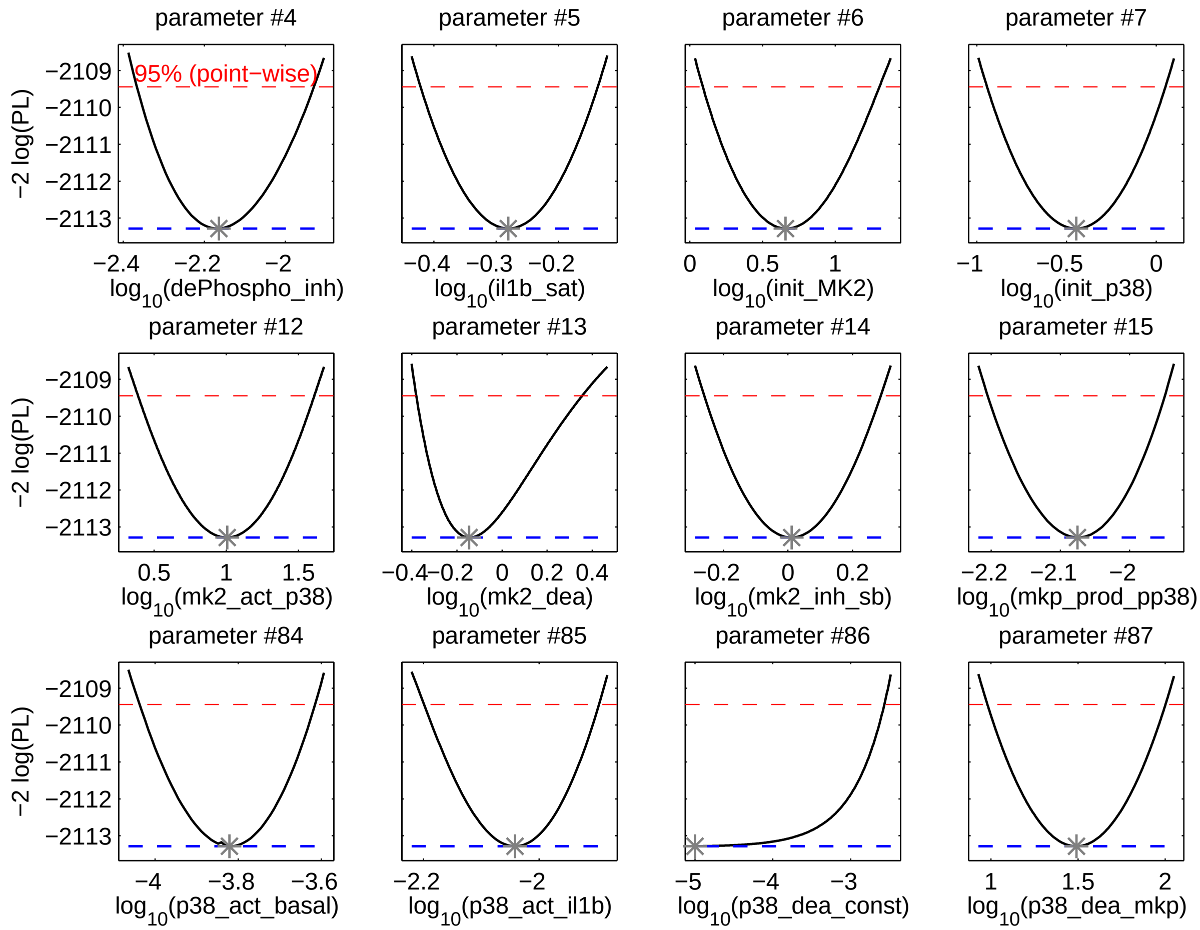

Figure 39: Overview of the profile likelihood of the model parameters
The solide lines indicate the profile likelihood. The broken lines indicate the threshold to assess confidence intervals. The asterisk indicate the optimal parameter values.

2.4 Profile likelihood of model parameters

In order to evaluate the identifiability of the model parameters and to assess confidence intervals the profile likelihood [2] was calculated. The mean calculation time of the profile likelihood per parameter was 00:02:26.04 ± 00:02:11.02. An overview for the dynamic model parameters is displayed in Figure 39.

	name	$\hat{\theta}$	σ^-	σ^+
1	V	-0.036	-0.523	+0.452
2	conc_MK2ges_kalibrator	-0.515	-0.617	-0.417
3	conc_p38ges_kalibrator	+0.199	+0.169	+0.229
4	dePhospho_inh	-2.164	-2.366	-1.929
5	il1b_sat	-0.281	-0.422	-0.137
6	init_MK2	+0.658	+0.089	+1.304
7	init_p38	-0.446	-0.942	+0.051
8	intstd_pro_MK2gesKalibrator	+0.077	-0.414	+0.348
9	intstd_pro_p38gesKalibrator	+1.900	+1.776	+1.972
10	intstd_pro_pMK2Kalibrator	+0.425	+0.315	+0.543
11	intstd_pro_pp38Kalibrator	+1.743	+1.667	+1.833
12	mk2_act_p38	+1.007	+0.388	+1.611
13	mk2_dea	-0.146	-0.380	+0.356
14	mk2_inh_sb	+0.011	-0.260	+0.288
15	mkp_prod_pp38	-2.075	-2.205	-1.949
16	offset_BSA_MK2ges	+7.510	+7.375	+7.624
17	offset_BSA_p38ges	+7.584	+7.549	+7.617
18	offset_MK2ges_100421_111026a	+6.017	+5.931	+6.097
19	offset_MK2ges_100504_111027a	+6.024	+5.936	+6.107
20	offset_MK2ges_100504_111027b	+6.034	+5.952	+6.111
21	offset_MK2ges_100628b_111027b	+6.057	+5.973	+6.135
22	offset_gel_pMK2_090102	+4.290	+3.437	+4.641
23	offset_gel_pMK2_090615d_090922a	+4.409	+3.952	+4.709
24	offset_gel_pMK2_090615d_090922b	+4.430	+3.915	+4.742
25	offset_gel_pMK2_090615d_090922d	+4.495	+4.160	+4.748
26	offset_gel_pMK2_090615d_100416	-5.000	-Inf	+4.024
27	offset_gel_pMK2_090615d_110419	-5.000	-Inf	+2.985
28	offset_gel_pMK2_100241_100428	+5.830	+5.732	+5.921
29	offset_gel_pMK2_100241_100430	-5.000	-Inf	+3.093

Table 66: Confidence intervals for the estimated parameter values derived by the profile likelihood
$\hat{\theta}$ indicates the estimated optimal parameter value. σ^- and σ^+ indicate 95% point-wise confidence intervals.

2.5 Confidence intervals for the model parameters

In Table 66 – 71, 95% confidence intervals for the estimated parameter values derived by the profile likelihood [2] are given.

	name	$\hat{\theta}$	σ^-	σ^+
30	offset_gel_pMK2_100241_100505	+5.847	+5.744	+5.942
31	offset_gel_pMK2_100504_100512	+5.766	+5.667	+5.854
32	offset_gel_pMK2_100504_100520	+5.917	+5.812	+6.009
33	offset_gel_pMK2_100504_100527	+5.880	+5.769	+5.976
34	offset_gel_pMK2_100517_100610a	+5.899	+5.840	+5.952
35	offset_gel_pMK2_100517_100610b	+5.995	+5.941	+6.045
36	offset_gel_pMK2_100628b_100727	+5.986	+5.887	+6.072
37	offset_gel_pMK2_100628b_100728a	+5.911	+5.817	+5.992
38	offset_gel_pMK2_100628b_100728b	+5.844	+5.740	+5.933
39	offset_gel_pMK2_101029_101103	+5.714	+5.633	+5.786
40	offset_gel_pMK2_101029_101104	+5.799	+5.725	+5.865
41	offset_gel_pMK2_110317a_110406a	+3.015	+2.904	+3.125
42	offset_gel_pMK2_110317b_110405a	+3.096	+2.991	+3.201
43	offset_gel_pMK2_110317b_110405b	+2.848	+2.743	+2.953
44	offset_gel_pMK2_121024_wb121029	+3.828	-Inf	+4.834
45	offset_gel_pMK2_121031A_wb121105	+5.704	+5.413	+5.923
46	offset_gel_pMK2_121031B_wb121105	+4.955	+4.554	+5.224
47	offset_gel_pMK2_121114A_wb121119	+5.236	+4.991	+5.428
48	offset_gel_pMK2_121114B_wb121119	+5.316	+5.091	+5.497
49	offset_gel_pp38_090615d_090922a	-5.000	-Inf	+3.948
50	offset_gel_pp38_090615d_090922b	-5.000	-Inf	+3.553
51	offset_gel_pp38_090615d_090922d	-4.991	-Inf	+4.231
52	offset_gel_pp38_090615d_100416	+5.149	-Inf	+5.525
53	offset_gel_pp38_090615d_110419	-5.000	-Inf	+4.056
54	offset_gel_pp38_100241_100428	+5.722	+5.561	+5.864
55	offset_gel_pp38_100241_100430	+5.725	+5.594	+5.844
56	offset_gel_pp38_100241_100505	+5.685	+5.542	+5.813
57	offset_gel_pp38_100504_100512	+5.603	+5.441	+5.733
58	offset_gel_pp38_100504_100520	+5.808	+5.702	+5.900
59	offset_gel_pp38_100504_100527	+5.786	+5.690	+5.869

Table 67: Confidence intervals for the estimated parameter values derived by the profile likelihood $\hat{\theta}$ indicates the estimated optimal parameter value. σ^- and σ^+ indicate 95% point-wise confidence intervals.

	name	$\hat{\theta}$	σ^-	σ^+
60	offset_gel_pp38_100517_100610a	+5.760	+5.692	+5.822
61	offset_gel_pp38_100517_100610b	+5.760	+5.692	+5.822
62	offset_gel_pp38_100628b_100727	+5.776	+5.661	+5.873
63	offset_gel_pp38_100628b_100728a	+5.714	+5.605	+5.805
64	offset_gel_pp38_100628b_100728b	+5.722	+5.618	+5.810
65	offset_gel_pp38_100708_100715	+5.721	+5.594	+5.818
66	offset_gel_pp38_101029_101103	+5.727	+5.619	+5.825
67	offset_gel_pp38_101029_101104	+4.429	+4.061	+4.634
68	offset_gel_pp38_110317a_110406a	+4.061	-Inf	+4.633
69	offset_gel_pp38_110317b_110405a	+4.306	-Inf	+4.856
70	offset_gel_pp38_110317b_110405b	+4.331	-Inf	+4.821
71	offset_gel_pp38_121024_wb121029	+6.052	+5.643	+6.327
72	offset_gel_pp38_121031A_wb121105	+5.069	+4.665	+5.346
73	offset_gel_pp38_121031B_wb121105	+5.337	+5.005	+5.588
74	offset_gel_pp38_121114A_wb121119	+4.938	+4.602	+5.190
75	offset_gel_pp38_121114B_wb121119	+5.149	+4.890	+5.364
76	offset_kal_intstd_MK2ges	+5.791	+5.616	+5.937
77	offset_kal_intstd_p38ges	+5.494	+5.401	+5.591
78	offset_kal_intstd_pMK2	+5.633	+5.534	+5.718
79	offset_kal_intstd_pp38	+5.753	+5.724	+5.777
80	offset_p38ges_100421_111026a	+6.047	+5.975	+6.114
81	offset_p38ges_100504_111027a	+5.965	+5.910	+6.017
82	offset_p38ges_100504_111027b	+5.973	+5.901	+6.042
83	offset_p38ges_100628b_111027b	+5.842	+5.766	+5.913
84	p38_act_basal	-3.821	-4.037	-3.615
85	p38_act_il1b	-2.042	-2.199	-1.896
86	p38_dea_const	-5.000	-Inf	-2.567
87	p38_dea_mkp	+1.491	+0.980	+2.002
88	scale_BSA_MK2ges	+8.294	+8.243	+8.342
89	scale_BSA_p38ges	+8.241	+8.224	+8.257

Table 68: Confidence intervals for the estimated parameter values derived by the profile likelihood $\hat{\theta}$ indicates the estimated optimal parameter value. σ^- and σ^+ indicate 95% point-wise confidence intervals.

	name	$\hat{\theta}$	σ^-	σ^+
90	scale_MK2ges_100421_111026a	+6.157	+6.071	+6.230
91	scale_MK2ges_100504_111027a	+6.142	+6.042	+6.223
92	scale_MK2ges_100504_111027b	+6.030	+5.914	+6.122
93	scale_MK2ges_100628b_111027b	+6.147	+6.050	+6.228
94	scale_kal_intstd_MK2ges	+4.891	+4.666	+5.056
95	scale_kal_intstd_p38ges	+4.829	+4.768	+4.894
96	scale_kal_intstd_pMK2	+5.004	+4.939	+5.061
97	scale_kal_intstd_pp38	+4.583	+4.546	+4.618
98	scale_p38ges_100421_111026a	+6.289	+6.229	+6.344
99	scale_p38ges_100504_111027a	+5.592	+5.426	+5.717
100	scale_p38ges_100504_111027b	+6.194	+6.128	+6.252
101	scale_p38ges_100628b_111027b	+6.212	+6.159	+6.260
102	scale_pMK2_090102	+5.987	+5.747	+6.453
103	scale_pMK2_090615d_090922a	+5.884	+5.668	+6.341
104	scale_pMK2_090615d_090922b	+5.980	+5.767	+6.438
105	scale_pMK2_090615d_090922d	+5.774	+5.542	+6.243
106	scale_pMK2_090615d_100416	+6.622	+6.422	+7.082
107	scale_pMK2_090615d_110419	+6.006	+5.806	+6.467
108	scale_pMK2_100241_100428	+6.378	+6.120	+6.841
109	scale_pMK2_100241_100430	+5.806	+5.597	+6.275
110	scale_pMK2_100241_100505	+6.559	+6.327	+7.022
111	scale_pMK2_100504_100512	+6.668	+6.414	+7.151
112	scale_pMK2_100504_100520	+6.876	+6.624	+7.359
113	scale_pMK2_100504_100527	+6.877	+6.627	+7.360
114	scale_pMK2_100517_100610a	+6.466	+6.134	+6.974
115	scale_pMK2_100517_100610b	+6.421	+6.048	+6.935
116	scale_pMK2_100628b_100727	+6.772	+6.504	+7.259
117	scale_pMK2_100628b_100728a	+6.602	+6.315	+7.092
118	scale_pMK2_100628b_100728b	+6.687	+6.422	+7.173
119	scale_pMK2_101029_101103	+6.639	+6.383	+7.124

Table 69: Confidence intervals for the estimated parameter values derived by the profile likelihood $\hat{\theta}$ indicates the estimated optimal parameter value. σ^- and σ^+ indicate 95% point-wise confidence intervals.

	name	$\hat{\theta}$	σ^-	σ^+
120	scale_pMK2_101029_101104	+6.581	+6.314	+7.067
121	scale_pMK2_110317a_110406a	+6.063	+5.707	+6.579
122	scale_pMK2_110317b_110405a	+6.248	+5.892	+6.764
123	scale_pMK2_110317b_110405b	+5.957	+5.602	+6.473
124	scale_pMK2_121024_wb121029	+6.581	+6.350	+7.069
125	scale_pMK2_121031A_wb121105	+6.636	+6.371	+7.112
126	scale_pMK2_121031B_wb121105	+6.260	+6.023	+6.741
127	scale_pMK2_121114A_wb121119	+6.093	+5.830	+6.570
128	scale_pMK2_121114B_wb121119	+6.123	+5.858	+6.599
129	scale_pp38_090615d_090922a	+6.945	+6.805	+7.099
130	scale_pp38_090615d_090922b	+6.743	+6.603	+6.897
131	scale_pp38_090615d_090922d	+6.727	+6.582	+6.881
132	scale_pp38_090615d_100416	+7.839	+7.714	+7.982
133	scale_pp38_090615d_110419	+6.981	+6.859	+7.123
134	scale_pp38_100241_100428	+7.376	+7.230	+7.530
135	scale_pp38_100241_100430	+7.051	+6.870	+7.221
136	scale_pp38_100241_100505	+7.208	+7.053	+7.366
137	scale_pp38_100504_100512	+7.364	+7.196	+7.532
138	scale_pp38_100504_100520	+7.016	+6.729	+7.239
139	scale_pp38_100504_100527	+6.979	+6.723	+7.193
140	scale_pp38_100517_100610a	+6.927	+6.651	+7.162
141	scale_pp38_100517_100610b	+6.927	+6.651	+7.162
142	scale_pp38_100628b_100727	+7.161	+6.953	+7.352
143	scale_pp38_100628b_100728a	+6.984	+6.745	+7.190
144	scale_pp38_100628b_100728b	+6.962	+6.722	+7.170
145	scale_pp38_100708_100715	+6.494	+4.945	+6.900
146	scale_pp38_101029_101103	+7.199	+7.028	+7.368
147	scale_pp38_101029_101104	+6.907	+6.778	+7.053
148	scale_pp38_110317a_110406a	+6.856	+6.698	+7.019
149	scale_pp38_110317b_110405a	+7.273	+7.126	+7.432

Table 70: Confidence intervals for the estimated parameter values derived by the profile likelihood $\hat{\theta}$ indicates the estimated optimal parameter value. σ^- and σ^+ indicate 95% point-wise confidence intervals.

	name	$\hat{\theta}$	σ^-	σ^+
150	scale_pp38_110317b_110405b	+7.205	+7.058	+7.364
151	scale_pp38_121024_wb121029	+7.977	+7.776	+8.167
152	scale_pp38_121031A_wb121105	+6.949	+6.736	+7.143
153	scale_pp38_121031B_wb121105	+7.080	+6.848	+7.280
154	scale_pp38_121114A_wb121119	+6.760	+6.551	+6.952
155	scale_pp38_121114B_wb121119	+6.627	+6.318	+6.851
156	sd_BSA_MK2ges	-1.456	-1.639	-1.203
157	sd_BSA_p38ges	-1.951	-2.134	-1.697
158	sd_MK2ges_au	-1.333	-1.422	-1.230
159	sd_kal_intstd_MK2ges	-1.042	-1.285	-0.767
160	sd_kal_intstd_p38ges	-1.456	-1.647	-1.167
161	sd_kal_intstd_pMK2	-1.438	-1.623	-1.176
162	sd_kal_intstd_pp38	-1.860	-2.051	-1.582
163	sd_p38ges_au	-1.431	-1.521	-1.327
164	sd_pMK2_au	-0.950	-0.975	-0.924
165	sd_pMK2_mk2ko_au	-0.502	-0.557	-0.441
166	sd_pMK2_phosphaInh_au	-0.923	-0.998	-0.838
167	sd_pp38_au	-0.836	-0.860	-0.810
168	sd_pp38_mk2ko_au	-0.700	-0.748	-0.648
169	sd_pp38_phosphaInh_au	-0.805	-0.880	-0.720

Table 71: Confidence intervals for the estimated parameter values derived by the profile likelihood $\hat{\theta}$ indicates the estimated optimal parameter value. σ^- and σ^+ indicate 95% point-wise confidence intervals.

	name	θ_{min}	$\hat{\theta}$	θ_{max}	log	non-log $\hat{\theta}$	fitted
1	V	-5	-0.0355	+3	1	$+9.21 \cdot 10^{-01}$	1
2	conc_MK2ges_kalibrator	-5	-0.5154	+8	1	$+3.05 \cdot 10^{-01}$	1
3	conc_p38ges_kalibrator	-5	+0.1990	+8	1	$+1.58 \cdot 10^{+00}$	1
4	il1b_sat	-5	-0.1761	+3	1	$+6.67 \cdot 10^{-01}$	1
5	init_MK2	-5	+0.9087	+3	1	$+8.10 \cdot 10^{+00}$	1
6	init_p38	-5	-0.4486	+3	1	$+3.56 \cdot 10^{-01}$	1
7	intstd_pro_MK2gesKalibrator	-5	-0.1723	+8	1	$+6.73 \cdot 10^{-01}$	1
8	intstd_pro_p38gesKalibrator	-5	+1.9015	+8	1	$+7.97 \cdot 10^{+01}$	1
9	intstd_pro_pMK2Kalibrator	-5	+0.4163	+8	1	$+2.61 \cdot 10^{+00}$	1
10	intstd_pro_pp38Kalibrator	-5	+1.7415	+8	1	$+5.51 \cdot 10^{+01}$	1
11	mk2_act_p38	-5	+0.6908	+3	1	$+4.91 \cdot 10^{+00}$	1
12	mk2_dea	-5	-0.1355	+3	1	$+7.32 \cdot 10^{-01}$	1
13	mkp_prod_pp38	-5	-2.0642	+3	1	$+8.63 \cdot 10^{-03}$	1
14	offset_BSA_MK2ges	-5	+7.5103	+1e+01	1	$+3.24 \cdot 10^{+07}$	1
15	offset_BSA_p38ges	-5	+7.5837	+1e+01	1	$+3.83 \cdot 10^{+07}$	1
16	offset_MK2ges_100421_111026a	-5	+6.0165	+9	1	$+1.04 \cdot 10^{+06}$	1
17	offset_MK2ges_100504_111027a	-5	+6.0246	+9	1	$+1.06 \cdot 10^{+06}$	1
18	offset_MK2ges_100504_111027b	-5	+6.0340	+9	1	$+1.08 \cdot 10^{+06}$	1
19	offset_MK2ges_100628b_111027b	-5	+6.0567	+9	1	$+1.14 \cdot 10^{+06}$	1
20	offset_gel_pMK2_090102	-5	+4.3320	+9	1	$+2.15 \cdot 10^{+04}$	1
21	offset_gel_pMK2_090615d_090922a	-5	+4.4434	+9	1	$+2.78 \cdot 10^{+04}$	1
22	offset_gel_pMK2_090615d_090922b	-5	+4.4709	+9	1	$+2.96 \cdot 10^{+04}$	1
23	offset_gel_pMK2_090615d_090922d	-5	+4.5096	+9	1	$+3.23 \cdot 10^{+04}$	1
24	offset_gel_pMK2_090615d_100416	-5	-5.0000	+9	1	$+1.00 \cdot 10^{-05}$	1

Table 72: Estimated parameter values
$\hat{\theta}$ indicates the estimated value of the parameters. θ_{min} and θ_{max} indicate the upper and lower bounds for the parameters. The log-column indicates if the value of a parameter was log-transformed. If log = 1 the non-log-column indicates the non-logarithmic value of the estimate. The fitted-column indicates if the parameter value was estimated (1), was temporarily fixed (0) or if its value was fixed to a constant value (2).

2.6 Multi-experiment fit without inhibitor experiments

In Figure 6 in the main part of this article we made quantitative predictions with the model to determine the effect of different inhibitors. For these prediction we used a parameter set which was obtained by a fit without the inhibitor experiments described in Section 2.2.26–2.2.32, since these experiments were used for validating the prediction. All other experiments were implemented like described in Section 2.

In total 137 parameters are estimated from the experimental data, yielding a value of the objective function $-2\log(L) = -1843.76$ for a total of 1408 data points. The model parameter were estimated by maximum likelihood estimation applying the MATLAB lsqnonlin algorithm. In Table 72 – 77 the estimated parameter values are given. Parameters highlighted in red color indicate parameter values close to their bounds. The parameter name prefix init_ indicates the initial value of a dynamic variable. The parameter name prefix offset_ indicates a offset of the experimental data. The parameter name prefix scale_ indicates a scaling factor of the experimental data. The parameter name prefix sd_ indicates the magnitude of the measurement noise for a specific measurement.

	name	θ_{min}	$\hat{\theta}$	θ_{max}	log	non-log $\hat{\theta}$	fitted
25	offset_gel_pMK2_090615d_110419	-5	-5.0000	+9	1	$+1.00 \cdot 10^{-05}$	1
26	offset_gel_pMK2_100241_100428	-5	+5.8363	+9	1	$+6.86 \cdot 10^{+05}$	1
27	offset_gel_pMK2_100241_100430	-5	-5.0000	+9	1	$+1.00 \cdot 10^{-05}$	1
28	offset_gel_pMK2_100241_100505	-5	+5.8573	+9	1	$+7.20 \cdot 10^{+05}$	1
29	offset_gel_pMK2_100504_100512	-5	+5.7732	+9	1	$+5.93 \cdot 10^{+05}$	1
30	offset_gel_pMK2_100504_100520	-5	+5.9229	+9	1	$+8.37 \cdot 10^{+05}$	1
31	offset_gel_pMK2_100504_100527	-5	+5.8879	+9	1	$+7.72 \cdot 10^{+05}$	1
32	offset_gel_pMK2_100517_100610a	-5	+5.9020	+9	1	$+7.98 \cdot 10^{+05}$	1
33	offset_gel_pMK2_100517_100610b	-5	+5.9976	+9	1	$+9.95 \cdot 10^{+05}$	1
34	offset_gel_pMK2_100628b_100727	-5	+5.9898	+9	1	$+9.77 \cdot 10^{+05}$	1
35	offset_gel_pMK2_100628b_100728a	-5	+5.9154	+9	1	$+8.23 \cdot 10^{+05}$	1
36	offset_gel_pMK2_100628b_100728b	-5	+5.8492	+9	1	$+7.07 \cdot 10^{+05}$	1
37	offset_gel_pMK2_110317a_110406a	-5	+3.0145	+9	1	$+1.03 \cdot 10^{+03}$	1
38	offset_gel_pMK2_110317b_110405a	-5	+3.0962	+9	1	$+1.25 \cdot 10^{+03}$	1
39	offset_gel_pMK2_110317b_110405b	-5	+2.8479	+9	1	$+7.05 \cdot 10^{+02}$	1
40	offset_gel_pp38_090615d_090922a	-5	-5.0000	+9	1	$+1.00 \cdot 10^{-05}$	1
41	offset_gel_pp38_090615d_090922b	-5	-5.0000	+9	1	$+1.00 \cdot 10^{-05}$	1
42	offset_gel_pp38_090615d_090922d	-5	-5.0000	+9	1	$+1.00 \cdot 10^{-05}$	1
43	offset_gel_pp38_090615d_100416	-5	+5.1148	+9	1	$+1.30 \cdot 10^{+05}$	1
44	offset_gel_pp38_090615d_110419	-5	-5.0000	+9	1	$+1.00 \cdot 10^{-05}$	1
45	offset_gel_pp38_100241_100428	-5	+5.7109	+9	1	$+5.14 \cdot 10^{+05}$	1
46	offset_gel_pp38_100241_100430	-5	+5.7172	+9	1	$+5.21 \cdot 10^{+05}$	1
47	offset_gel_pp38_100241_100505	-5	+5.6817	+9	1	$+4.81 \cdot 10^{+05}$	1
48	offset_gel_pp38_100504_100512	-5	+5.5770	+9	1	$+3.78 \cdot 10^{+05}$	1
49	offset_gel_pp38_100504_100520	-5	+5.7941	+9	1	$+6.22 \cdot 10^{+05}$	1

Table 73: Estimated parameter values
$\hat{\theta}$ indicates the estimated value of the parameters. θ_{min} and θ_{max} indicate the upper and lower bounds for the parameters. The log-column indicates if the value of a parameter was log-transformed. If log = 1 the non-log-column indicates the non-logarithmic value of the estimate. The fitted-column indicates if the parameter value was estimated (1), was temporarily fixed (0) or if its value was fixed to a constant value (2).

	name	θ_{min}	$\hat{\theta}$	θ_{max}	log	non-log $\hat{\theta}$	fitted
50	offset_gel_pp38_100504_100527	-5	+5.7762	+9	1	$+5.97 \cdot 10^{+05}$	1
51	offset_gel_pp38_100517_100610a	-5	+5.7544	+9	1	$+5.68 \cdot 10^{+05}$	1
52	offset_gel_pp38_100517_100610b	-5	+5.7544	+9	1	$+5.68 \cdot 10^{+05}$	1
53	offset_gel_pp38_100628b_100727	-5	+5.7679	+9	1	$+5.86 \cdot 10^{+05}$	1
54	offset_gel_pp38_100628b_100728a	-5	+5.7073	+9	1	$+5.10 \cdot 10^{+05}$	1
55	offset_gel_pp38_100628b_100728b	-5	+5.7172	+9	1	$+5.21 \cdot 10^{+05}$	1
56	offset_gel_pp38_100708_100715	-5	+5.7012	+9	1	$+5.03 \cdot 10^{+05}$	1
57	offset_gel_pp38_110317a_110406a	-5	+3.9779	+9	1	$+9.50 \cdot 10^{+03}$	1
58	offset_gel_pp38_110317b_110405a	-5	+4.3273	+9	1	$+2.12 \cdot 10^{+04}$	1
59	offset_gel_pp38_110317b_110405b	-5	+4.3363	+9	1	$+2.17 \cdot 10^{+04}$	1
60	offset_kal_intstd_MK2ges	-5	+5.8403	+8	1	$+6.92 \cdot 10^{+05}$	1
61	offset_kal_intstd_p38ges	-5	+5.4935	+8	1	$+3.11 \cdot 10^{+05}$	1
62	offset_kal_intstd_pMK2	-5	+5.6360	+8	1	$+4.33 \cdot 10^{+05}$	1
63	offset_kal_intstd_pp38	-5	+5.7537	+8	1	$+5.67 \cdot 10^{+05}$	1
64	offset_p38ges_100421_111026a	-5	+6.0465	+9	1	$+1.11 \cdot 10^{+06}$	1
65	offset_p38ges_100504_111027a	-5	+5.9651	+9	1	$+9.23 \cdot 10^{+05}$	1
66	offset_p38ges_100504_111027b	-5	+5.9732	+9	1	$+9.40 \cdot 10^{+05}$	1
67	offset_p38ges_100628b_111027b	-5	+5.8417	+9	1	$+6.94 \cdot 10^{+05}$	1
68	p38_act_basal	-5	-3.7704	+3	1	$+1.70 \cdot 10^{-04}$	1
69	p38_act_il1b	-5	-1.9120	+3	1	$+1.22 \cdot 10^{-02}$	1
70	p38_dea_const	-5	-5.0000	+3	1	$+1.00 \cdot 10^{-05}$	1
71	p38_dea_mkp	-5	+1.4862	+3	1	$+3.06 \cdot 10^{+01}$	1
72	scale_BSA_MK2ges	-5	+8.2940	+1e+01	1	$+1.97 \cdot 10^{+08}$	1
73	scale_BSA_p38ges	-5	+8.2408	+1e+01	1	$+1.74 \cdot 10^{+08}$	1
74	scale_MK2ges_100421_111026a	-5	+6.1602	+9	1	$+1.45 \cdot 10^{+06}$	1

Table 74: Estimated parameter values
$\hat{\theta}$ indicates the estimated value of the parameters. θ_{min} and θ_{max} indicate the upper and lower bounds for the parameters. The log-column indicates if the value of a parameter was log-transformed. If log = 1 the non-log-column indicates the non-logarithmic value of the estimate. The fitted-column indicates if the parameter value was estimated (1), was temporarily fixed (0) or if its value was fixed to a constant value (2).

	name	θ_{min}	$\hat{\theta}$	θ_{max}	log	non-log $\hat{\theta}$	fitted
75	scale_MK2ges_100504_111027a	-5	+6.1439	+9	1	$+1.39 \cdot 10^{+06}$	1
76	scale_MK2ges_100504_111027b	-5	+6.0320	+9	1	$+1.08 \cdot 10^{+06}$	1
77	scale_MK2ges_100628b_111027b	-5	+6.1495	+9	1	$+1.41 \cdot 10^{+06}$	1
78	scale_kal_intstd_MK2ges	-5	+4.8516	+8	1	$+7.11 \cdot 10^{+04}$	1
79	scale_kal_intstd_p38ges	-5	+4.8285	+8	1	$+6.74 \cdot 10^{+04}$	1
80	scale_kal_intstd_pMK2	-5	+5.0046	+8	1	$+1.01 \cdot 10^{+05}$	1
81	scale_kal_intstd_pp38	-5	+4.5825	+8	1	$+3.82 \cdot 10^{+04}$	1
82	scale_p38ges_100421_111026a	-5	+6.2892	+9	1	$+1.95 \cdot 10^{+06}$	1
83	scale_p38ges_100504_111027a	-5	+5.5919	+9	1	$+3.91 \cdot 10^{+05}$	1
84	scale_p38ges_100504_111027b	-5	+6.1935	+9	1	$+1.56 \cdot 10^{+06}$	1
85	scale_p38ges_100628b_111027b	-5	+6.2115	+9	1	$+1.63 \cdot 10^{+06}$	1
86	scale_pMK2_090102	-5	+6.2348	+9	1	$+1.72 \cdot 10^{+06}$	1
87	scale_pMK2_090615d_090922a	-5	+6.1258	+9	1	$+1.34 \cdot 10^{+06}$	1
88	scale_pMK2_090615d_090922b	-5	+6.2227	+9	1	$+1.67 \cdot 10^{+06}$	1
89	scale_pMK2_090615d_090922d	-5	+6.0273	+9	1	$+1.06 \cdot 10^{+06}$	1
90	scale_pMK2_090615d_100416	-5	+6.8723	+9	1	$+7.45 \cdot 10^{+06}$	1
91	scale_pMK2_090615d_110419	-5	+6.2569	+9	1	$+1.81 \cdot 10^{+06}$	1
92	scale_pMK2_100241_100428	-5	+6.6119	+9	1	$+4.09 \cdot 10^{+06}$	1
93	scale_pMK2_100241_100430	-5	+6.0558	+9	1	$+1.14 \cdot 10^{+06}$	1
94	scale_pMK2_100241_100505	-5	+6.7923	+9	1	$+6.20 \cdot 10^{+06}$	1
95	scale_pMK2_100504_100512	-5	+6.9011	+9	1	$+7.96 \cdot 10^{+06}$	1
96	scale_pMK2_100504_100520	-5	+7.1115	+9	1	$+1.29 \cdot 10^{+07}$	1
97	scale_pMK2_100504_100527	-5	+7.1107	+9	1	$+1.29 \cdot 10^{+07}$	1
98	scale_pMK2_100517_100610a	-5	+6.7011	+9	1	$+5.02 \cdot 10^{+06}$	1
99	scale_pMK2_100517_100610b	-5	+6.6560	+9	1	$+4.53 \cdot 10^{+06}$	1

Table 75: Estimated parameter values
$\hat{\theta}$ indicates the estimated value of the parameters. θ_{min} and θ_{max} indicate the upper and lower bounds for the parameters. The log-column indicates if the value of a parameter was log-transformed. If log = 1 the non-log-column indicates the non-logarithmic value of the estimate. The fitted-column indicates if the parameter value was estimated (1), was temporarily fixed (0) or if its value was fixed to a constant value (2).

	name	θ_{min}	$\hat{\theta}$	θ_{max}	log	non-log $\hat{\theta}$	fitted
100	scale_pMK2_100628b_100727	-5	+7.0085	+9	1	$+1.02 \cdot 10^{+07}$	1
101	scale_pMK2_100628b_100728a	-5	+6.8339	+9	1	$+6.82 \cdot 10^{+06}$	1
102	scale_pMK2_100628b_100728b	-5	+6.9200	+9	1	$+8.32 \cdot 10^{+06}$	1
103	scale_pMK2_110317a_110406a	-5	+6.3046	+9	1	$+2.02 \cdot 10^{+06}$	1
104	scale_pMK2_110317b_110405a	-5	+6.4894	+9	1	$+3.09 \cdot 10^{+06}$	1
105	scale_pMK2_110317b_110405b	-5	+6.1989	+9	1	$+1.58 \cdot 10^{+06}$	1
106	scale_pp38_090615d_090922a	-5	+6.9203	+9	1	$+8.32 \cdot 10^{+06}$	1
107	scale_pp38_090615d_090922b	-5	+6.7180	+9	1	$+5.22 \cdot 10^{+06}$	1
108	scale_pp38_090615d_090922d	-5	+6.7097	+9	1	$+5.13 \cdot 10^{+06}$	1
109	scale_pp38_090615d_100416	-5	+7.8228	+9	1	$+6.65 \cdot 10^{+07}$	1
110	scale_pp38_090615d_110419	-5	+6.9631	+9	1	$+9.19 \cdot 10^{+06}$	1
111	scale_pp38_100241_100428	-5	+7.3503	+9	1	$+2.24 \cdot 10^{+07}$	1
112	scale_pp38_100241_100430	-5	+7.0281	+9	1	$+1.07 \cdot 10^{+07}$	1
113	scale_pp38_100241_100505	-5	+7.1786	+9	1	$+1.51 \cdot 10^{+07}$	1
114	scale_pp38_100504_100512	-5	+7.3291	+9	1	$+2.13 \cdot 10^{+07}$	1
115	scale_pp38_100504_100520	-5	+6.9982	+9	1	$+9.96 \cdot 10^{+06}$	1
116	scale_pp38_100504_100527	-5	+6.9526	+9	1	$+8.97 \cdot 10^{+06}$	1
117	scale_pp38_100517_100610a	-5	+6.9070	+9	1	$+8.07 \cdot 10^{+06}$	1
118	scale_pp38_100517_100610b	-5	+6.9070	+9	1	$+8.07 \cdot 10^{+06}$	1
119	scale_pp38_100628b_100727	-5	+7.1211	+9	1	$+1.32 \cdot 10^{+07}$	1
120	scale_pp38_100628b_100728a	-5	+6.9446	+9	1	$+8.80 \cdot 10^{+06}$	1
121	scale_pp38_100628b_100728b	-5	+6.9203	+9	1	$+8.32 \cdot 10^{+06}$	1
122	scale_pp38_100708_100715	-5	+6.5461	+9	1	$+3.52 \cdot 10^{+06}$	1
123	scale_pp38_110317a_110406a	-5	+6.8041	+9	1	$+6.37 \cdot 10^{+06}$	1
124	scale_pp38_110317b_110405a	-5	+7.2159	+9	1	$+1.64 \cdot 10^{+07}$	1

Table 76: Estimated parameter values
$\hat{\theta}$ indicates the estimated value of the parameters. θ_{min} and θ_{max} indicate the upper and lower bounds for the parameters. The log-column indicates if the value of a parameter was log-transformed. If log = 1 the non-log-column indicates the non-logarithmic value of the estimate. The fitted-column indicates if the parameter value was estimated (1), was temporarily fixed (0) or if its value was fixed to a constant value (2).

	name	θ_{min}	$\hat{\theta}$	θ_{max}	log	non-log $\hat{\theta}$	fitted
125	scale_pp38_110317b_110405b	-5	+7.1489	+9	1	$+1.41 \cdot 10^{+07}$	1
126	sd_BSA_MK2ges	-5	-1.4574	+9	1	$+3.49 \cdot 10^{-02}$	1
127	sd_BSA_p38ges	-5	-1.9516	+8	1	$+1.12 \cdot 10^{-02}$	1
128	sd_MK2ges_au	-5	-1.3342	+3	1	$+4.63 \cdot 10^{-02}$	1
129	sd_kal_intstd_MK2ges	-5	-0.9796	+8	1	$+1.05 \cdot 10^{-01}$	1
130	sd_kal_intstd_p38ges	-5	-1.4582	+8	1	$+3.48 \cdot 10^{-02}$	1
131	sd_kal_intstd_pMK2	-5	-1.4415	+8	1	$+3.62 \cdot 10^{-02}$	1
132	sd_kal_intstd_pp38	-5	-1.8626	+8	1	$+1.37 \cdot 10^{-02}$	1
133	sd_p38ges_au	-5	-1.4321	+3	1	$+3.70 \cdot 10^{-02}$	1
134	sd_pMK2_au	-5	-0.9382	+3	1	$+1.15 \cdot 10^{-01}$	1
135	sd_pMK2_mk2ko_au	-5	-0.5025	+3	1	$+3.14 \cdot 10^{-01}$	1
136	sd_pp38_au	-5	-0.8710	+3	1	$+1.35 \cdot 10^{-01}$	1
137	sd_pp38_mk2ko_au	-5	-0.7018	+3	1	$+1.99 \cdot 10^{-01}$	1

Table 77: Estimated parameter values
$\hat{\theta}$ indicates the estimated value of the parameters. θ_{min} and θ_{max} indicate the upper and lower bounds for the parameters. The log-column indicates if the value of a parameter was log-transformed. If log = 1 the non-log-column indicates the non-logarithmic value of the estimate. The fitted-column indicates if the parameter value was estimated (1), was temporarily fixed (0) or if its value was fixed to a constant value (2).

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