Analyse the Glycose/Insulin - System:
in this paper, the dose should also be optimized

$trunca(M, e) := submatrix(M, 0, e, 0, spalten(M) - 1)$

Project parameters

Dose injection [mg] $D_v := 6$

Duration_injection [min] $\tau := 15$

Infusionrate: (for an infusion pump) $\rho(t, D) := D \cdot e^{-0.05 \cdot (t - \tau)}$

Auxilliary parameters in the system

$$f(t, D) := \begin{cases} D & \text{if } 0 \le t < \tau \\ \rho(t, D) & \text{otherwise} \end{cases}$$

Define the ODE:

$end := 200$ Integration t (in minutes)

Vorgabe

$g'(t) = f(t, D) - m_1 \cdot g(t) - m_2 i(t)$ $g(0) = 0$

$i'(t) = (m_3 \cdot g(t) - m_4 \cdot i(t))$ $i(0) = 0$

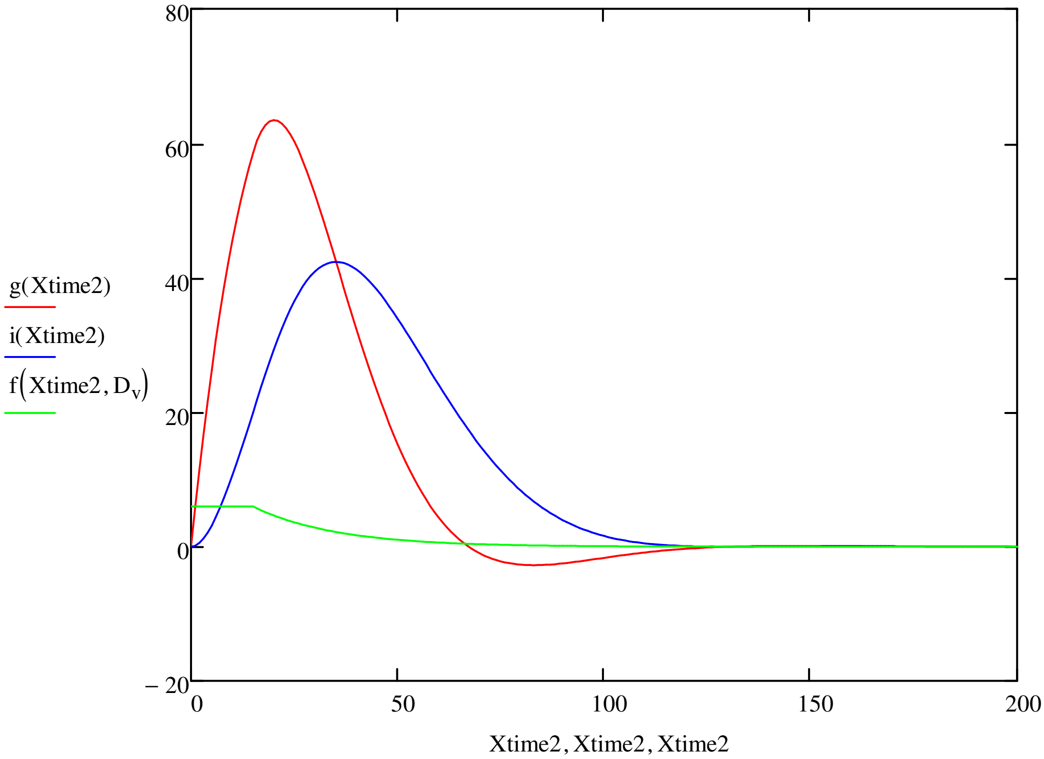
$$Sol(m_1, m_2, m_3, m_4, D) := Gdglösen\left[\begin{pmatrix} g \\ i \end{pmatrix}, t, end\right]$$

$m_1 := 0.05$ $m_2 := 0.05$ $m_3 := 0.05$ $m_4 := 0.05$

$$\begin{pmatrix} g \\ i \end{pmatrix} := Sol(m_1, m_2, m_3, m_4, D_v)$$

Plot the ODE over time:

$Xtime2 := 0 .. 200$



Fit the observed data for Glycose and Insulin:

XY :=

	0	1	2
0	0	77.32	0
1	31.21	165.58	91.51
2	61.53	129.69	104.25
3	90.95	103.57	45.17
4	126.19	91.64	8.11
5	150	74.57	7.79
6			
7			

$$(Xtime\ \ Glc\_concentration\ \ Ins) := \left(XY^{\langle 0\rangle}\ \ XY^{\langle 1\rangle}\ \ XY^{\langle 2\rangle}\right)$$

$Glc := XY^{\langle 1\rangle} - XY_{0,1}$ substracte the treshold at the Glucoseconc.

$\begin{pmatrix} m_1 & m_2 & m_3 & m_4 & D \end{pmatrix} := \begin{pmatrix} 0.035 & 3.6 \cdot 10^{-7} & 4.0 \cdot 10^{-7} & 0.21 & 6 \end{pmatrix}$

Guesses for minerr- from MMA

Vorgabe

$TOL := 10^{-19}$

$\left| \begin{array}{l} \begin{pmatrix} g \\ i \end{pmatrix} \leftarrow Sol(m_1, m_2, m_3, m_4, D) \\ \overrightarrow{g(Xtime)} \end{array} \right. = Glc$

$\left| \begin{array}{l} \begin{pmatrix} g \\ i \end{pmatrix} \leftarrow Sol(m_1, m_2, m_3, m_4, D) \\ \overrightarrow{i(Xtime)} \end{array} \right. = Ins$

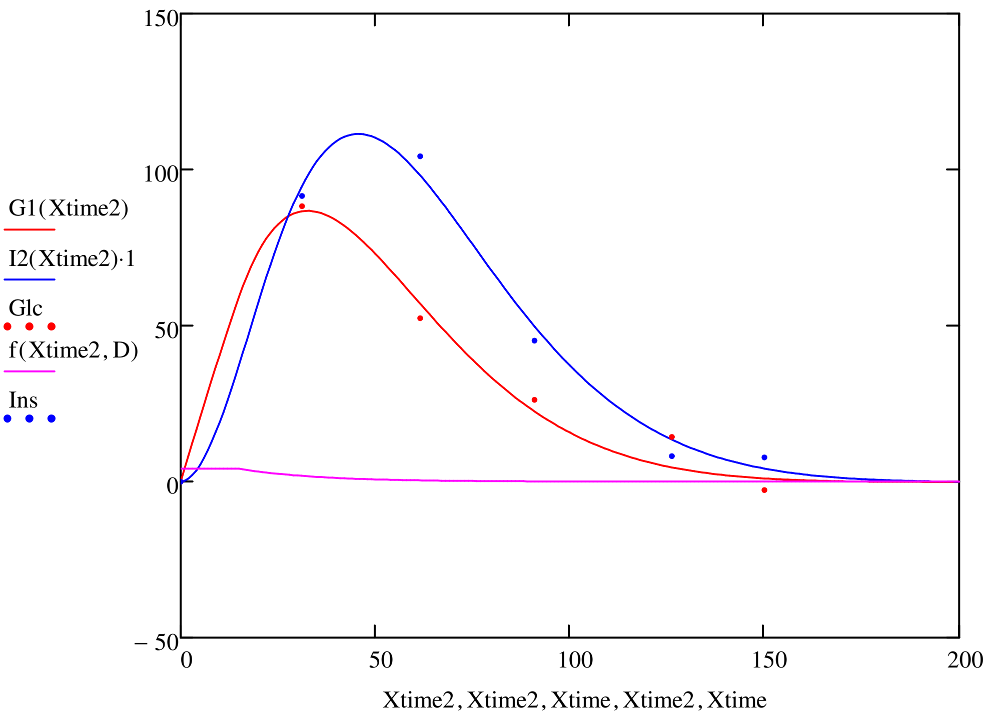
$D > 0$

$\begin{pmatrix} m_1 \\ m_2 \\ m_3 \\ m_4 \\ D \end{pmatrix} := Minfehl(m_1, m_2, m_3, m_4, D)$

$ERR = 16.077$

$\begin{pmatrix} m_1 \\ m_2 \\ m_3 \\ m_4 \\ D \end{pmatrix} = \begin{pmatrix} -3.477 \times 10^{-3} \\ 0.021 \\ 0.121 \\ 0.085 \\ 4.127 \end{pmatrix}$

$\begin{pmatrix} G1 \\ I2 \end{pmatrix} := Sol(m_1, m_2, m_3, m_4, D)$



Calculation of the standard deviation with the Fisher's Info Matrix:

$\mathrm{diff} := 0.0000001$

Calculate the Products of the Sensi-Matrice

$$\mathrm{Adj}(\mathrm{diff}, i, n) := \left| \begin{array}{l} a \leftarrow 0 \\ a_{n-1} \leftarrow 0 \\ a \leftarrow a + 1 \\ a_i \leftarrow a_i + \mathrm{diff} \\ a \end{array} \right.$$

To use this for different analyses, you need to porivde the endpoint and also parameterize the parameter values (rather than use the current worksheet values).

$$\mathrm{Derivs}(\mathrm{pars}, \mathrm{diff}, \mathrm{endpoint}) := \left| \begin{array}{l} \text{for } i \in 0..4 \\ \quad \left| \begin{array}{l} \begin{pmatrix} Am_1 \\ Am_2 \\ Am_3 \\ Am_4 \\ AD \end{pmatrix} \leftarrow \overrightarrow{(\mathrm{pars} \cdot \mathrm{Adj}(\mathrm{diff}, i, 5))} \\ \begin{pmatrix} AG1 \\ AI1 \end{pmatrix} \leftarrow \mathrm{Sol}(Am_1, Am_2, Am_3, Am_4, AD) \\ \begin{pmatrix} Am_1 \\ Am_2 \\ Am_3 \\ Am_4 \\ AD \end{pmatrix} \leftarrow \overrightarrow{(\mathrm{pars} \cdot \mathrm{Adj}(-\mathrm{diff}, i, 5))} \\ \begin{pmatrix} AG2 \\ AI2 \end{pmatrix} \leftarrow \mathrm{Sol}(Am_1, Am_2, Am_3, Am_4, AD) \\ Xt \leftarrow \mathrm{trunca}(\mathrm{Xtime}, \mathrm{endpoint}) \\ D^{\langle i \rangle} \leftarrow \overrightarrow{\dfrac{AG1(Xt) - AG2(Xt)}{2 \cdot \mathrm{diff} \cdot \mathrm{pars}_i}} \end{array} \right. \\ D \end{array} \right.$$

Central differences are used for changing the parameters:

This looks for the first Parameter (m_1) as follows:

$$Adj(-diff, 0, 5) = \begin{pmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \end{pmatrix} \quad Adj(diff, 0, 5) = \begin{pmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \end{pmatrix}$$

Parameterchange for m1 **left** from the central point

$$\overrightarrow{\left[\begin{pmatrix} m_1 \\ m_2 \\ m_3 \\ m_4 \\ D \end{pmatrix} \cdot Adj(-diff, 0, 5)\right]} = \begin{pmatrix} -3.477 \times 10^{-3} \\ 0.021 \\ 0.121 \\ 0.085 \\ 4.127 \end{pmatrix}$$

Parameterchange for m1 **right** from the central point

$$\overrightarrow{\left[\begin{pmatrix} m_1 \\ m_2 \\ m_3 \\ m_4 \\ D \end{pmatrix} \cdot Adj(diff, 0, 5)\right]} = \begin{pmatrix} -3.477 \times 10^{-3} \\ 0.021 \\ 0.121 \\ 0.085 \\ 4.127 \end{pmatrix}$$

$$DerivM := Derivs\left[\begin{pmatrix} m_1 \\ m_2 \\ m_3 \\ m_4 \\ D \end{pmatrix}, diff, letzte(Xtime)\right]$$

$$FisherInfoMat := DerivM^T \cdot DerivM$$

$$FisherInfoMat = \begin{pmatrix} 1.336 \times 10^7 & 1.778 \times 10^7 & 3.029 \times 10^6 & -3.844 \times 10^6 & -7.934 \times 10^4 \\ 1.778 \times 10^7 & 2.516 \times 10^7 & 4.286 \times 10^6 & -5.753 \times 10^6 & -9.01 \times 10^4 \\ 3.029 \times 10^6 & 4.286 \times 10^6 & 7.303 \times 10^5 & -9.802 \times 10^5 & -1.535 \times 10^4 \\ -3.844 \times 10^6 & -5.753 \times 10^6 & -9.802 \times 10^5 & 1.386 \times 10^6 & 1.671 \times 10^4 \\ -7.934 \times 10^4 & -9.01 \times 10^4 & -1.535 \times 10^4 & 1.671 \times 10^4 & 662.745 \end{pmatrix}$$

$$\text{geninv(FisherInfoMat)} = \begin{pmatrix} 1.154\times10^{-3} & 34.83 & -204.428 & -1.889\times10^{-3} & 0.032 \\ 34.82 & -1.206\times10^{9} & 7.078\times10^{9} & -67.443 & 602.002 \\ -204.367 & 7.078\times10^{9} & -4.154\times10^{10} & 395.844 & -3.533\times10^{3} \\ -1.889\times10^{-3} & -67.46 & 395.944 & 3.13\times10^{-3} & -0.051 \\ 0.032 & 602.287 & -3.535\times10^{3} & -0.051 & 0.869 \end{pmatrix}$$

$$\text{diag(geninv(FisherInfoMat))} = \begin{pmatrix} 1.154\times10^{-3} \\ -1.206\times10^{9} \\ -4.154\times10^{10} \\ 3.13\times10^{-3} \\ 0.869 \end{pmatrix}$$

The Square-Root from a neg. number results in a complex number! (See σ_{m2} and σ_{m3})

The 2nd and 3rd items of this matrix is very dependent of diff! In MMA the deviations are made from the symbolically solution of the ODE-solution, so there is a exact solution!

$\text{num\_of\_Params} := 5$

$\text{degree\_of\_freedom} := \text{letzte(Xtime)} + 1 - \text{num\_of\_Params}$

$$\text{SSEa} := \sum_{i=0}^{\text{letzte(Xtime)}} \left[\left(\text{Glc}_i - \text{G1}\left(\text{Xtime}_i\right)\right)^2\right] \qquad \text{SSEa} = 147.937 \qquad \sqrt{\text{SSEa}} = 12.163$$

$$\text{SSEb} := \sum_{i=0}^{\text{letzte(Xtime)}} \left[\left(\text{Ins}_i - \text{I2}\left(\text{Xtime}_i\right)\right)^2\right] \qquad \text{SSEb} = 110.53 \qquad \sqrt{\text{SSEb}} = 10.513$$

$$\text{SSE} := \sqrt{\text{SSEa} + \text{SSEb}} \qquad \text{SSE} = 16.077$$

$$\begin{pmatrix} \sigma_{m1} \\ \sigma_{m2} \\ \sigma_{m3} \\ \sigma_{m4} \\ \sigma_{D} \end{pmatrix} := \sqrt{\frac{SSEa}{degree\_of\_freedom}} \cdot \sqrt{diag(geninv(FisherInfoMat))}$$

$$\begin{pmatrix} \sigma_{m1} \\ \sigma_{m2} \\ \sigma_{m3} \\ \sigma_{m4} \\ \sigma_{D} \end{pmatrix} = \begin{pmatrix} 0.413 \\ 4.224i \times 10^{5} \\ 2.479i \times 10^{6} \\ 0.68 \\ 11.339 \end{pmatrix}$$