**A Fully Symbolic Design and Modeling of Nonlinear Glucose Control with Control System Professional Suite (CSPS) of *Mathematica***

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**Abstract**
In this case study a fully symbolic design and modelling method are presented for blood glucose control of diabetic patiens under intensive care. The analysis is based on a modified two-compartment model proposed by Bergman et al. [1]. The applied feedback control law decoupling even the nonlinear model leads to a fully symbolic solution of the closed loop equations. The effectivity of the applied symbolic procedures being mostly built-in the new version of *Control System Professional Suite (CSPS) Application of Mathematica* - have been demonstrated for controller design in case of a glucose control for treatment of diabetes mellitus. The results are in good agreement with the earlier presented symbolic-numeric analysis by Benyo et al. [7]. This research has been supported by Hungarian National Research Fund, Grants No. OTKA T029830, T042990 and by Hungarian Ministry of Education Grant No. 200/2001.

**Introduction**
Treatment of diabetes mellitus can be represented by outer control loop to replace the partially or totally failing blood-glucose-control system of the human body. To maintain the glucose level in a diabetic under intensive care is currently an actively researched topic in the field of Biomedical Engineering. Many different models and strategies have been designed and applied to the problem Sano [6], Fischer [3], Candas [2], Juhász [4] and Benyó et al. [7]. The authors orientated on Benyó [7], considering as the best appropriate model. Symbolic computation was used to design multivariable modal control based on the space representation of a verified nonlinear model. Computations were carried out and the article was written in Mathematica Version 4.2, and presented as a live worksheet.

**Method**
Insulin-glucose interaction in human body was modelled with a two-compartment nonlinear model :

```
deq1 = p1 X[t] + p2h[t] = X'[t];
deq2 = (p3-X[t])Y[t]+ i[t]+ p4 = Y'[t];
```

The terms *h(t)* and *i(t)* as exogenous insulin and glucose, take the impacts on glucose level into consideration, *X(t)* and Y(t) stand for the concentration of glucose in the plasma and that of the insulin remote from plasma, respectively.

To design the control for this system, it should be linearized. Loading the *CSPS Application,* the linearization will be carried out at the steady state (*X0, Y0, h0, i0*):

$$\dot{x} = \begin{pmatrix} p_1 & 0 \\ -Y0 & p_3 - X0 \end{pmatrix} x + \begin{pmatrix} p_2 & 0 \\ 0 & 1 \end{pmatrix} u$$
$$y = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} x + \begin{pmatrix} 0 & 0 \\ 0 & 0 \end{pmatrix} u$$

or its representation on frequency domain:

```
ControlObjectTF = TransferFunction[s, ControlObjectSS] // Simplify
```

$$\text{TransferFunction}\left[s,\left\{\left\{\frac{p_2}{s-p_1},0\right\},\left\{-\frac{Y0\,p_2}{(s-p_1)(s+X0-p_3)},\frac{1}{s+X0-p_3}\right\}\right\}\right]$$

The steady state values are  The *X[0]=0*, *h[0]=0*, *i[0]=0* and *Y[0]=Y0*. We need to compute *Y0*.
Now, the linearized model is:

```
ControlObjectSS // EquationForm
```

$$\dot{x} = \begin{pmatrix} p_1 & 0 \\ \frac{p_4}{p_3} & p_3 \end{pmatrix} x + \begin{pmatrix} p_2 & 0 \\ 0 & 1 \end{pmatrix} u$$
$$y = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} x + \begin{pmatrix} 0 & 0 \\ 0 & 0 \end{pmatrix} u$$

Introducing *A* and *B* for the matrices as usual, the equilibrium is stable ( $p_1$ and $p_3 < 0$).

Let us consider the $\lambda_1$, $\lambda_2$, as the eigenvalues of the matrix *A-KB*, where *K* is the gain matrix. Then *K* can be computed as:

```
K = Inverse[B].(A-DiagonalMatrix[{λ1, λ2}]) // Simplify; MatrixForm[K]
```

$$\begin{pmatrix} \frac{-\lambda 1 + p_1}{p_2} & 0 \\ \frac{p_4}{p_3} & -\lambda 2 + p_3 \end{pmatrix},$$

Special case of the control, when $\lambda_1 = p_2$ and $\lambda_2 = p_3$. This is a feasible control, because both of the model parameters are negative.

Greater absolute value of $\lambda_1$, $\lambda_2$, make the system reach the steady state faster. So the quality of the control will be improved with the increase of the absolute value of the $\lambda$*'s*, however in real cases, the dynamical performance ability of the actuators can be the bottle-neck. So, we were able to get symbolic results for control design of our system and could draw certain conclusions concerning the control performance, which demonstrate one of the unique features of the *CSPS*. Now, we continue our study with further symbolic computations.

*Nonlinear closed loop model.* The variables of the linearized model represent the deviations from the steady state instead of the total values. Therefore to get the nonlinear closed loop model, one should take into consideration the steady values. So, the control vector is:

```
{h[t], i[t]} = {h0, i0} - K.{X[t]-X0, Y[t]-Y0}
```

$$\left\{-\frac{(-\lambda 1 + p_1)X[t]}{p_2},\ -\frac{p_4 X[t]}{p_3} - (-\lambda 2 + p_3)\left(\frac{p_4}{p_3} + Y[t]\right)\right\}$$

Then our model equations are:

$$p_1 X[t] - (-\lambda 1 + p_1) X[t] = X'[t]$$

$$p_4 - \frac{p_4 X[t]}{p_3} + (p_3 - X[t]) Y[t] - (-\lambda 2 + p_3)\left(\frac{p_4}{p_3} + Y[t]\right) = Y'[t]$$

The solutions of our model equations are:

$$X[t] = e^{t\lambda 1} X0$$

$$Y[t] = \frac{-p_4 + e^{\frac{X0 - e^{t\lambda 1} X0 + t\lambda 1 \lambda 2}{\lambda 1}} (Y0 p_3 + p_4)}{p_3}$$

The control variables:

$$h[t\_] = \frac{e^{t\lambda 1} X0 (\lambda 1 - p_1)}{p_2}$$

$$i[t\_] = \frac{-e^{t\lambda 1} X0 p_4 + e^{\frac{X0 - e^{t\lambda 1} X0 + t\lambda 1 \lambda 2}{\lambda 1}} (\lambda 2 - p_3)(Y0 p_3 + p_4)}{p_3}$$

**Results**

*Numerical simulation of the nonlinear closed loop model.* Let us consider the following numerical values, Juhász et.al. [4]: $p_1$=-0.021151, $p_2$=0.092551, $p_3$=-0.014188, $p_4$ = 0.077947. We consider a *hypoglycaemic* episode with initial values *X0=0.1* and *Y0=2*. Let the eigenvalues be: $\lambda 1 = 0.7 p_1$ and $\lambda 2 = 1.05 p_3$

The dynamic performance of the state variables is shown in Fig. 1. – Fig. 4.

*Simulation without control.* In order to qualify the effect of the control on the dynamical performance, we carry out the simulation without control. This can be done only numerically. The figures (*Fig.1* vs *Fig.4*) clearly show, that the control considerably improves the dynamical performance of the system.

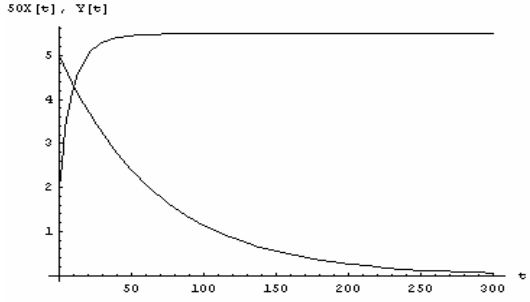


*Fig.1* The state variables in time with control.

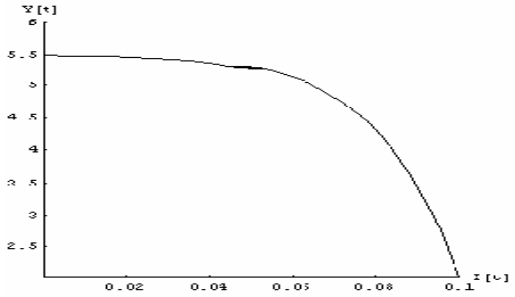


*Fig.2* The state variables on phase plane.

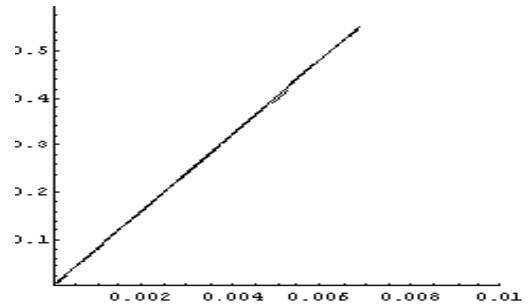


*Fig.3* The control variables on phase plane.

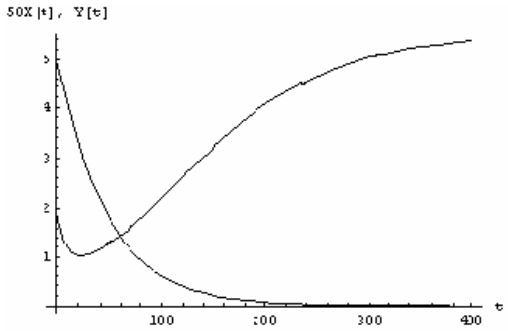


*Fig.4* The state variables in time without control.

**Discussion**

Although, the control design was based on the linearized model, the control could improve considerably the system response. Results show, that it is possible to carry out the design algorithm fully symbolical way. According to the first results, the system is expected – after the necessary further verifications – to provide a useful help to control of blood glucose level in diabetics under intensive care, and to the optimisation process of diabetic administration.

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