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BME IIT - Laboratory of Biomedical Engineering

Nonlinear Control Analysis of an ICU Model for Tight Glycaemic Control

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Contents

Motivation

ICU & TGC

- Hypoglycaemia & insulin resistance $\Longrightarrow$ $\nearrow$ morbidity & mortality[1]
- TGC can reduce adverse outcomes [2] (and costs [3])
- Multidimensional problem (avoid hypo, variability, CHO, etc.) [4]
- Repeatability problem [5]
- Variability in ICU patients presents ideal application field for model-based automation of insulin infusions for TGC [6]

$\Downarrow$

ICU Model

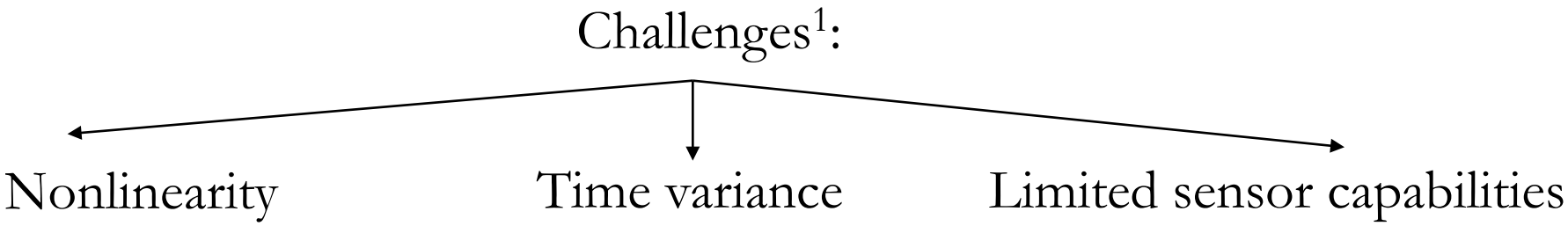
1 – SE Capes et al. (2000). *Lancet*, **355**(9206): 773-778.
2 – J Chase et al. (2008). *Critical Care*, 12:R49.
3 – Van den Berghe et al. (2006). *Crit Care Med*, **34**(3):612-616.
4 – U Pielmeier et al. (2010). *UKACC Conf*, 839-844.
5 – Griesdale et al. (2009) *Can Med Assoc J*, 180(8):821-827.
6 – J Lin et al. (2008). *CMPB*, **89**(2):141-152.

ICU Models

Models[1]

- Minimal model: Bergman-model (1979, 1981)
- ICU: Canterbury-model (2004, 2008, 2010)

  van Herpe-model (2006)



1 – L Kovacs et al. (2010). *UKACC Conf.* 577-582.

Canterbury-model [1]

$$\dot{G}(t) = -p_G G(t) - S_I(t)\left(G(t) + G_E\right)\frac{Q(t)}{1+\alpha_G Q(t)} + P(t)$$

$$\dot{Q}(t) = kI(t) - kQ(t)$$

$$\dot{I}(t) = -\frac{nI(t)}{1+\alpha_I I(t)} + \frac{u_{ex}(t)}{V}$$

- Insulin bounded to interstitial sites
- Insulin losses to the liver and kidneys
- Saturation dynamics
- Insulin sensitivity metric

1 – X.W. Wong et al. (2006). *Med Eng* & *Physics*, 28:665-681.

Redefined Canterbury-model [1]

$$\dot{G}(t) = -p_G G(t) - S_I(t)\frac{G(t)Q(t)}{1+\alpha_G Q(t)} + \frac{P(t) + EGP_b - CNS}{V_G}$$

Actual plasma glucose concentration

$$\dot{Q}(t) = kI(t) - kQ(t)$$

$$\dot{I}(t) = -\frac{nI(t)}{1+\alpha_I I(t)} + \frac{u_{ex}(t)}{V} + \frac{u_{end}(t)}{V}$$

Endogenous insulin production

$$\left.\begin{aligned} \dot{P}_1(t) &= D(t) - d_1 P_1(t) \\ \dot{P}_2(t) &= d_1 P_1(t) - min\{d_2 P_2(t), P_{max}\} \\ P(t) &= \min\{d_2 P_2(t), P_{\max}\} \end{aligned}\right\}$$

Glucose absorption during enteral feeding (in reality are linear f.)

$$u_{end}(t) = k_1 \exp\left(\frac{-k_2 I(t)}{k_3}\right)$$

1 – F. Suhaimi et al. (2010). *UKACC Conf*, 1037-1042.

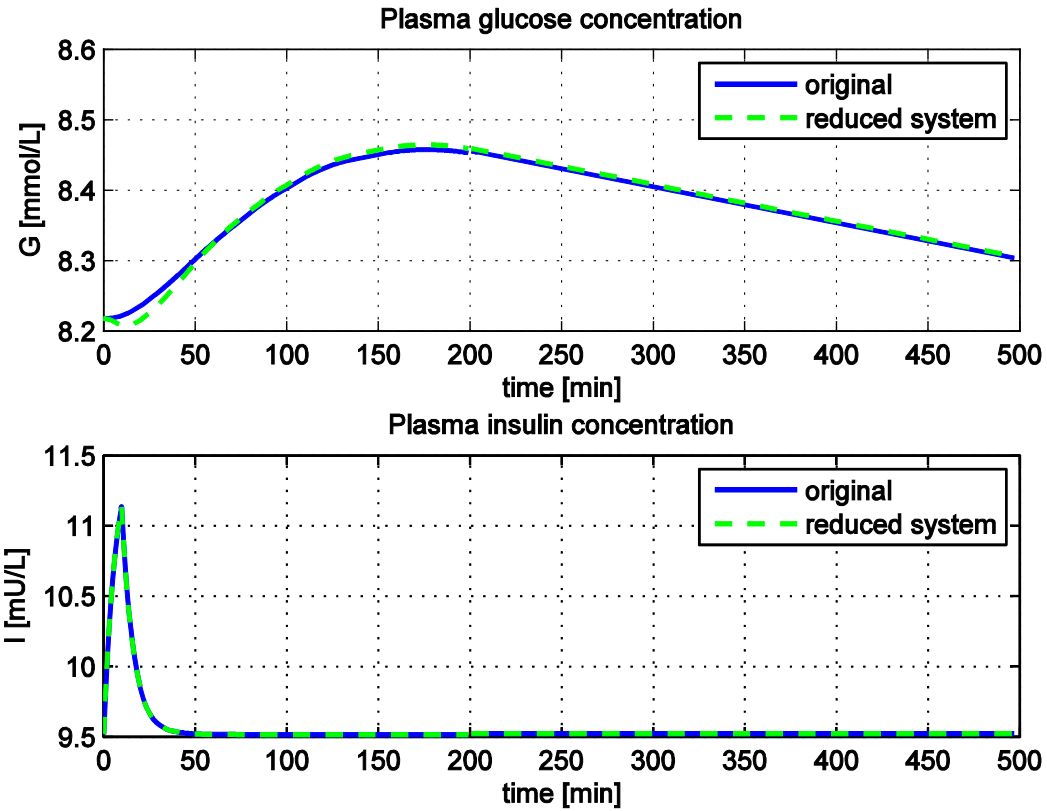
Redefined Canterbury-model [1]

Q(t) is a slow variable [1]:

$$\dot{G}(t) = -$$

$$\dot{I}(t) = -\frac{}{1}$$

$$\frac{GP_b - CNS}{G}$$



1 – E.D. Lehmann, T.A. Deutsch (1992). *J Biomed Eng*, **14**:235-242.

Nonlinear analysis

Reachability

$$\dot{\varsigma}_1 = f_1(\varsigma_1, \varsigma_2) + \sum_{i=1}^{m} g_{1i}(\varsigma_1, \varsigma_2) u_i$$

$$\dot{\varsigma}_2 = f_2(\varsigma_2)$$

$$y_i = h_i(\varsigma_1, \varsigma_2)$$

Increasing the Δ^C distribution by its Lie-derivatives' vector fields, until the rank of the distribution increases.

Observability

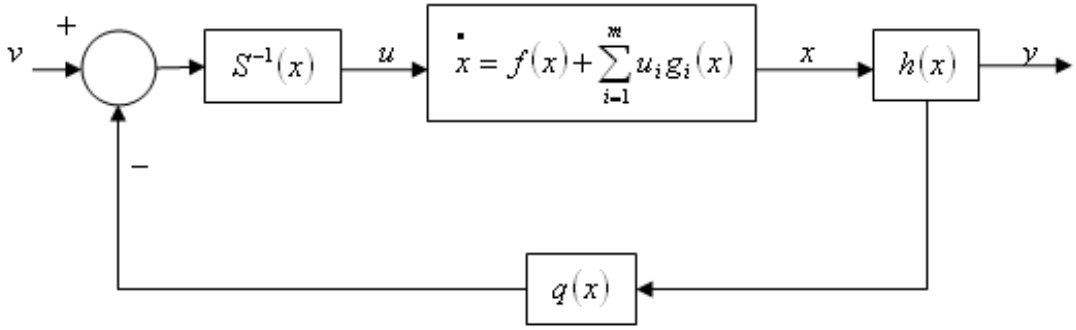
$$\dot{\varsigma}_1 = f_1(\varsigma_1) + \sum_{i=1}^{m} g_{1i}(\varsigma_1) u_i$$

$$\dot{\varsigma}_2 = f_2(\varsigma_1, \varsigma_2) + \sum_{i=1}^{m} g_{2i}(\varsigma_1, \varsigma_2) u_i$$

$$y_i = h_i(\varsigma_1)$$

Expending the O observable subspace with Lie-derivatives, until the rank of the $d\Delta^O$ co-distribution increases.

Input-output linearization



Nonlinear analysis - results

Name of the model	Dimension	Reachability	Observability
Canterbury-model	3	3	2

G(t), Q(t), I(t)

plasma glucose can be easily measured

plasma insulin can be estimated by knowing insulin input

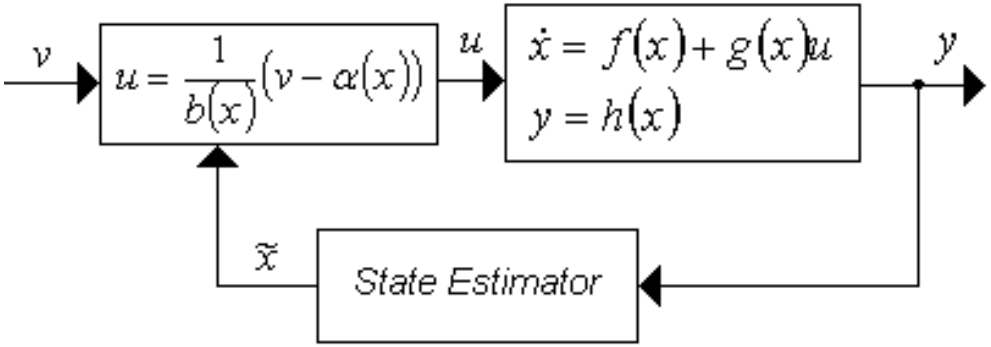
Nonlinear analysis - results

Exact linearization

$$a(x) = L_f^2 h(x) = \left(\left(\frac{S_I I \alpha_G}{(1+\alpha_G I)^2} - \frac{S_I}{1+\alpha_G I} \right) \left(u_{enb} - \frac{nI}{1+\alpha_I I} \right) - \left(p_G + \frac{S_I I}{1+\alpha_G I} \right)^2 \right) G - \left(p_G + \frac{S_I I}{1+\alpha_G I} \right) \left(\frac{EGB_b + CNS}{V_G} \right)$$

$$b(x) = L_g L_f^1 h(x) = \frac{-S_I G}{(1+\alpha_G I)^2 V_I}$$

$$u_{ex} = \frac{1}{b(x)} (u - \alpha(x))$$



LPV Modeling

Nonlinear model based design technique (extension of LTI systems) [1,2]

$$\dot{x}(t) = A(\rho(t))x(t) + B(\rho(t))u(t)$$
$$y(t) = C(\rho(t))x(t) + D(\rho(t))u(t)$$

$\varrho(t)$ should be known by measurement or computation

2 well-known techniques:

- affine type: a part of the ϱ(t) are equal with the $x(t)$ states
- polytope type: the validity of the model is caught inside a polytope region $\Longrightarrow$ linear combination of linear models

$$\Sigma(t) \subset \{\Sigma_1, \ldots, \Sigma_2\} = \left\{ \sum_{i=1}^{j} \alpha_i \Sigma_i : \alpha_i \geq 0, \sum_{i=1}^{j} \alpha_i = 1 \right\} \qquad \Sigma_i = \begin{bmatrix} A_i & B_i \\ C_i & D_i \end{bmatrix}$$

1 – F Wu et al. (2000). *Int J Control*, **73**(12): 1104-1114.
2 – W Tan (1997). Applications of Linear Parameter-Varying Control Theory. *MSc. thesis, Berkeley*.

qALPV

Affine dependency:

$$A(\rho) = A_0 + \rho_1 A_1 + \ldots + \rho_N A_N$$
$$B(\rho) = B_0 + \rho_1 B_1 + \ldots + \rho_N B_N$$
$$C(\rho) = C_0 + \rho_1 C_1 + \ldots + \rho_N C_N$$
$$D(\rho) = D_0 + \rho_1 D_1 + \ldots + \rho_N D_N$$

$$\Sigma(t) = \left\{ \Sigma_0 + \sum_{i=1}^{N} \rho_i \Sigma_i : \rho_i \in \left[\underline{\rho}_i \ \overline{\rho}_i\right], \dot{\rho}_i \in \left[\underline{\dot{\rho}}_i \ \overline{\dot{\rho}}_i\right] \right\} \qquad \Sigma_i = \begin{bmatrix} A_i & B_i \\ C_i & D_i \end{bmatrix}$$

Three possibilities:

- Jacobi linearization
- state transformation
- function substitution

qALPV → Results

Canterbury-model

$$\dot{G}(t) = -p_G G(t) - S_I(t)\frac{G(t)I(t)}{1+\alpha_G I(t)} + \frac{P(t) + EGP_b - CNS}{V_G}$$

$$\dot{I}(t) = -\frac{nI(t)}{1+\alpha_I I(t)} + \frac{u_{ex}(t)}{V} + \frac{u_{end}(t)}{V}$$

$$\rho(t) = \begin{bmatrix} \rho_1(t) \\ \rho_2(t) \end{bmatrix} = \begin{bmatrix} S_I(t)\dfrac{I(t)}{1+\alpha_G I(t)} \\ \dfrac{1}{1+\alpha_I I(t)} \end{bmatrix}$$

Can be calculated

qALPV → Results

Canterbury-model

$$\dot{G}(t) = -p_G G(t) - S_I(t)\frac{G(t)I(t)}{1+\alpha_G I(t)} + \frac{P(t) + EGP_b - CNS}{V_G}$$

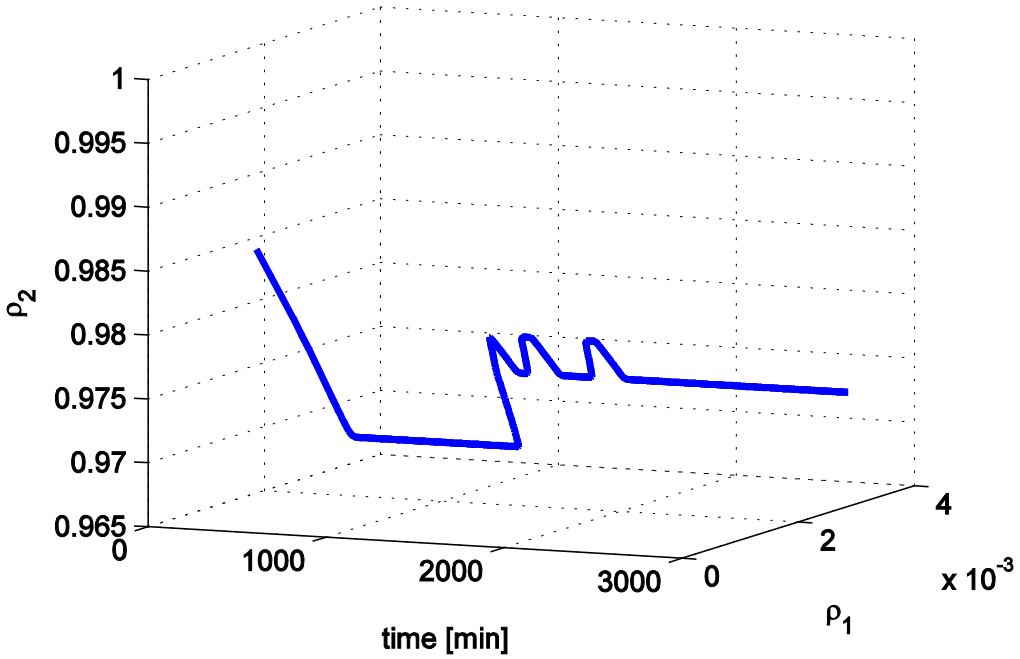
$$\dot{I}(t) = -\frac{nI(t)}{1+\alpha_I I(t)} + \frac{u_{ex}(t)}{V} + \frac{u_{end}(t)}{V}$$

$$A(\rho(t)) = A_0 + A_1\rho_1(t) + A_2\rho_2(t) =$$

$$= \begin{bmatrix} p_G & 0 \\ 0 & 0 \end{bmatrix} + \begin{bmatrix} -1 & 0 \\ 0 & 0 \end{bmatrix}\rho_1(t) + \begin{bmatrix} 0 & 0 \\ 0 & -n \end{bmatrix}\rho_2(t)$$

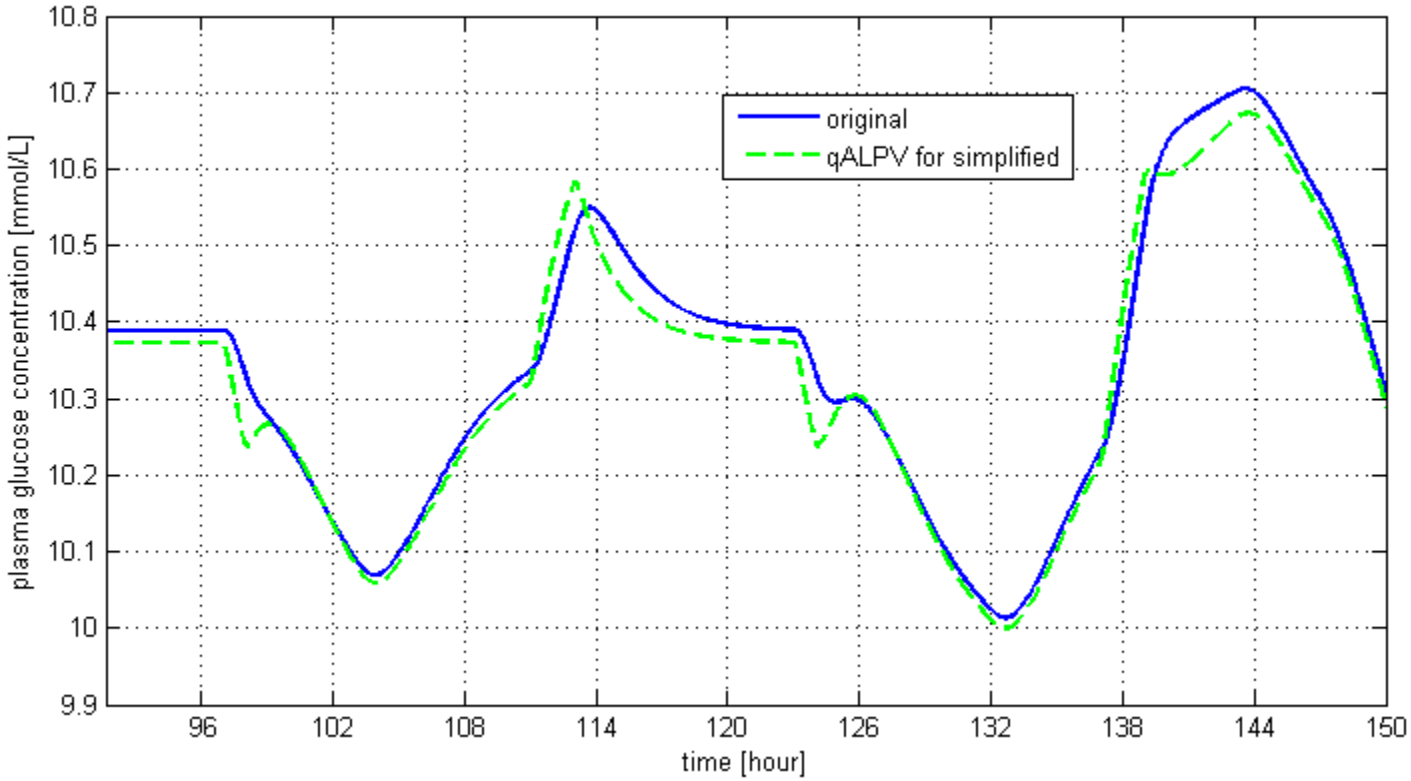
$$B_1 = \begin{bmatrix} 0 \\ \frac{1}{V} \end{bmatrix}, B_2 = \begin{bmatrix} 1 \\ 0 \end{bmatrix}, C = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}.$$

qALPV → Results



Scheduling parameter		By measurement	Theoretical bound
ρ_1	$\underline{\rho}_1$	0.0019	0 (if I $\rightarrow$ 0)
	$\overline{\rho}_1$	0.0034	0.0146 (if I $\rightarrow \infty$)
ρ_2	$\underline{\rho}_2$	0.9672	0 (if I $\rightarrow \infty$)
	$\overline{\rho}_2$	0.9841	1 (I $\rightarrow$ 0)

qALPV vs. nonlinear system



Conclusions

- Nonlinear control analysis roadmap of a frequently used ICU model
- Nonlinear analysis
- qALPV investigation and formulation
- Further work:
  - ➢ robust control method (H_∞) + new Canterbury-model (2010)
  - ➢ simulations of different real-life scenarios (per patient management)

Thank you for your attention!

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