Robust Tight Glycaemic Control of ICU Patients

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Motivation

ICU & TGC

- Hypoglycaemia & insulin resistance ⟹ ↗ 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]

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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)

Challenges[1]:

Nonlinearity | Time variance | Limited sensor capabilities

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

Canterbury-model [1]

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

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

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

- 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

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

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

Endogenous insulin production

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

$$\dot{P}_1(t) = D(t) - d_1 P_1(t)$$

$$\dot{P}_2(t) = d_1 P_1(t) - min\{d_2 P_2(t), P_{max}\}$$

$$P(t) = \min\{d_2 P_2(t), P_{\max}\}$$

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

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

Aim of robust H_∞ control

Basic control requirements:

stability & performance ← uncertainty

good command following

disturbance rejection

⇓

Nominal Performance & Robust Stability

⇓

H_∞ – minimization in „worst case”

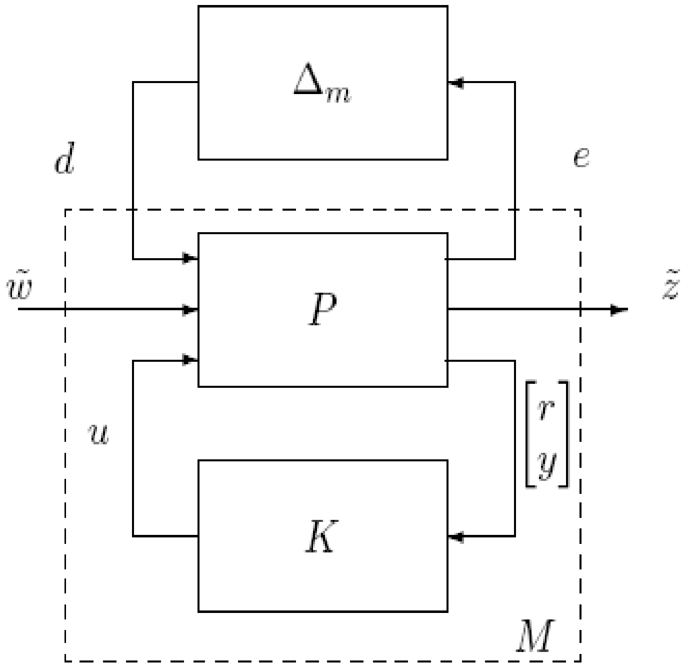
Rationalism (exact formulation)

+ Empiricism (based on expertise)

μ-Synthesis method

M (P-K) structure

$$\begin{bmatrix} e \\ \tilde{z} \end{bmatrix} = \begin{bmatrix} M_{11} & M_{12} \\ M_{21} & M_{22} \end{bmatrix} \begin{bmatrix} d \\ \tilde{w} \end{bmatrix}$$



Conservative solution for RS

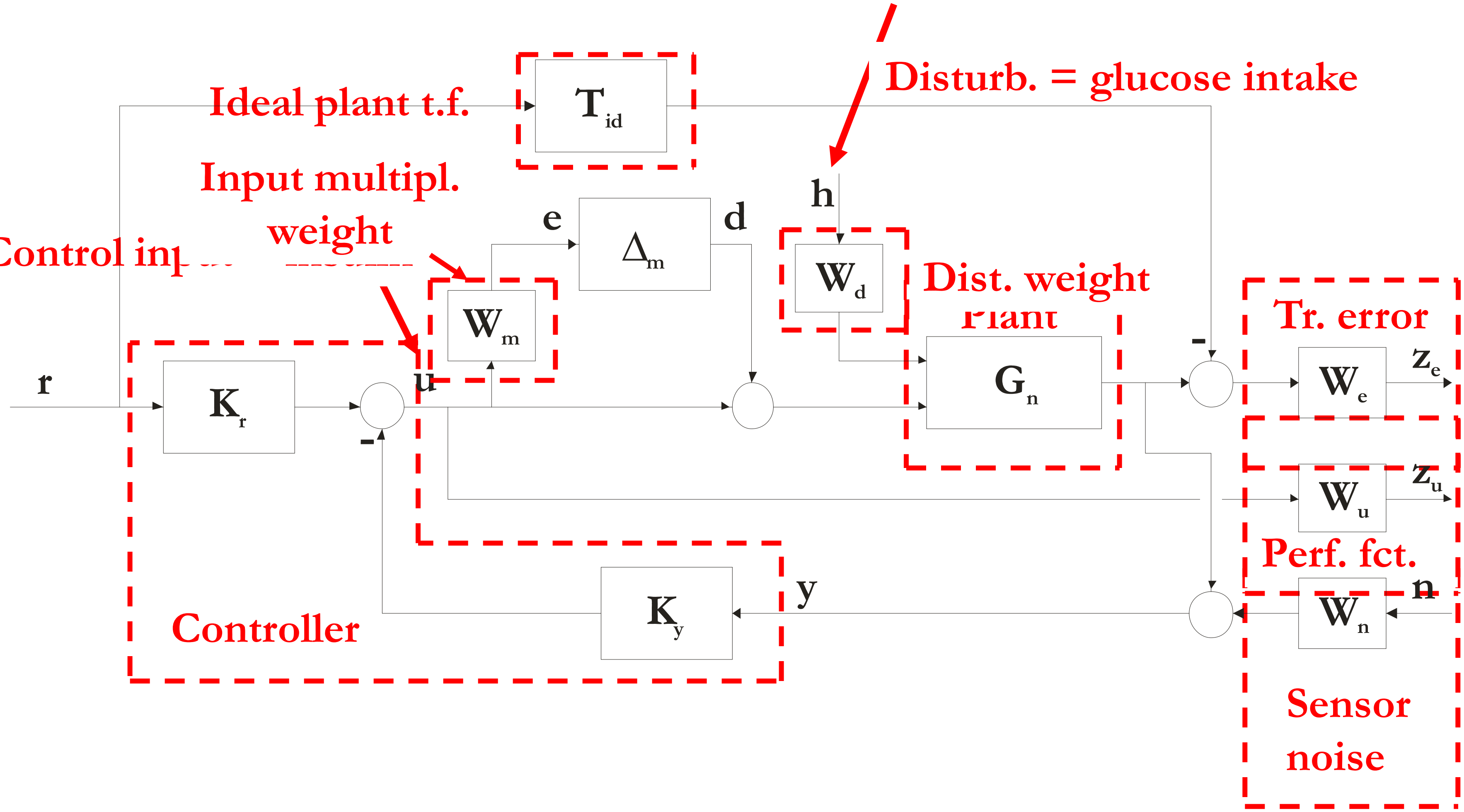
$$\left\| M_{\Delta} \right\|_{\infty} < \gamma$$

Less conserv. solution for RP by μ

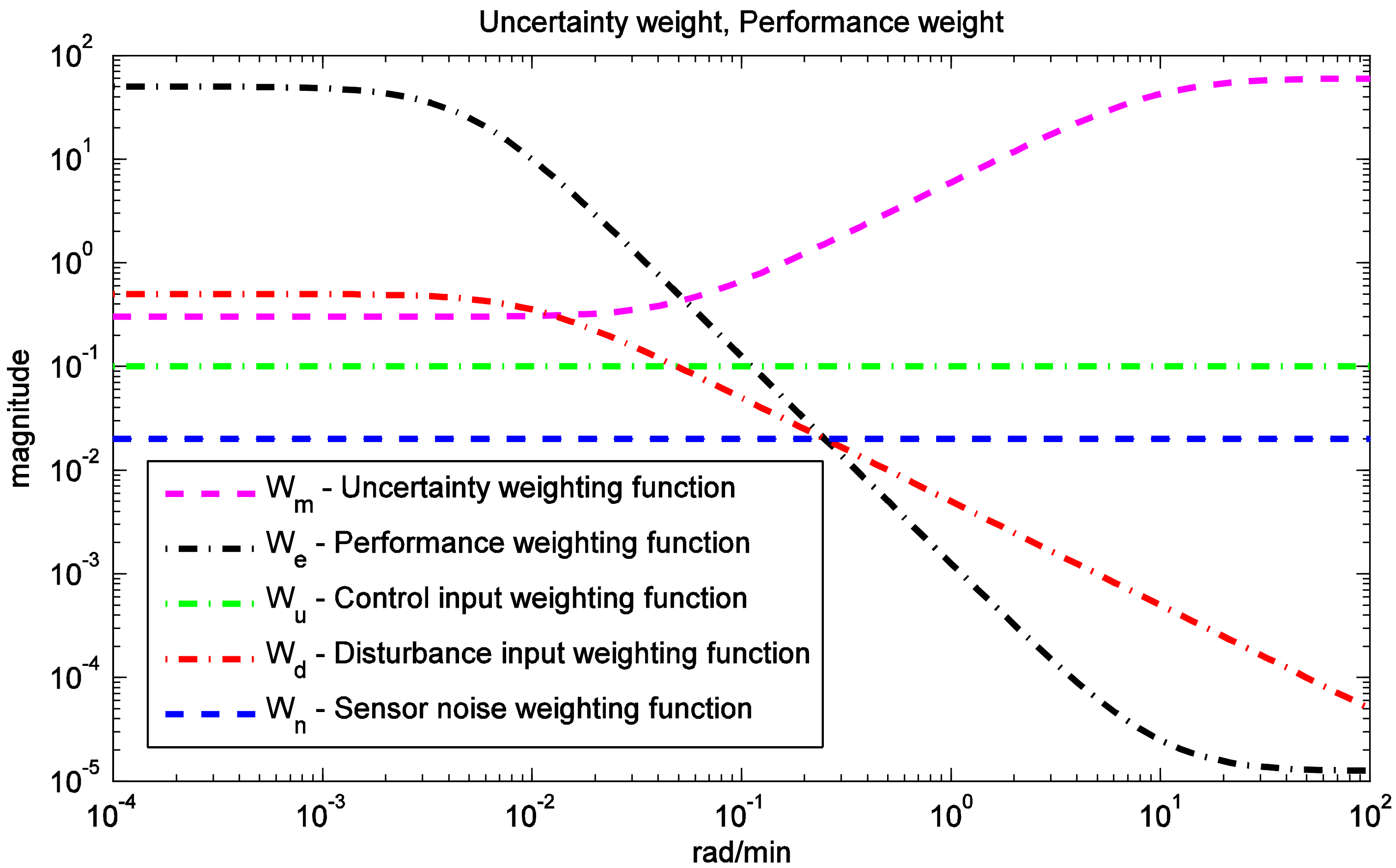
$$\left\| \mu(M) \right\|_{\infty} < 1$$

$$\mu_{\Delta}(M) = \frac{1}{min_{\Delta}(\overline{\sigma}\{\Delta\} : \Delta \in \Delta, det(I + \Delta M) = 0)}$$

Closed-loop interconnection



Weighting functions



Robust performance results

Iteration	1	2	3
Controller order	11	11	13
D-scale order	0	0	2
γ achieved	1.563	1.014	1.005
Peak value of μ	0.763	0.692	0.727

LPV Modeling

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

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

$\rho(t)$ 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 ⟹ 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

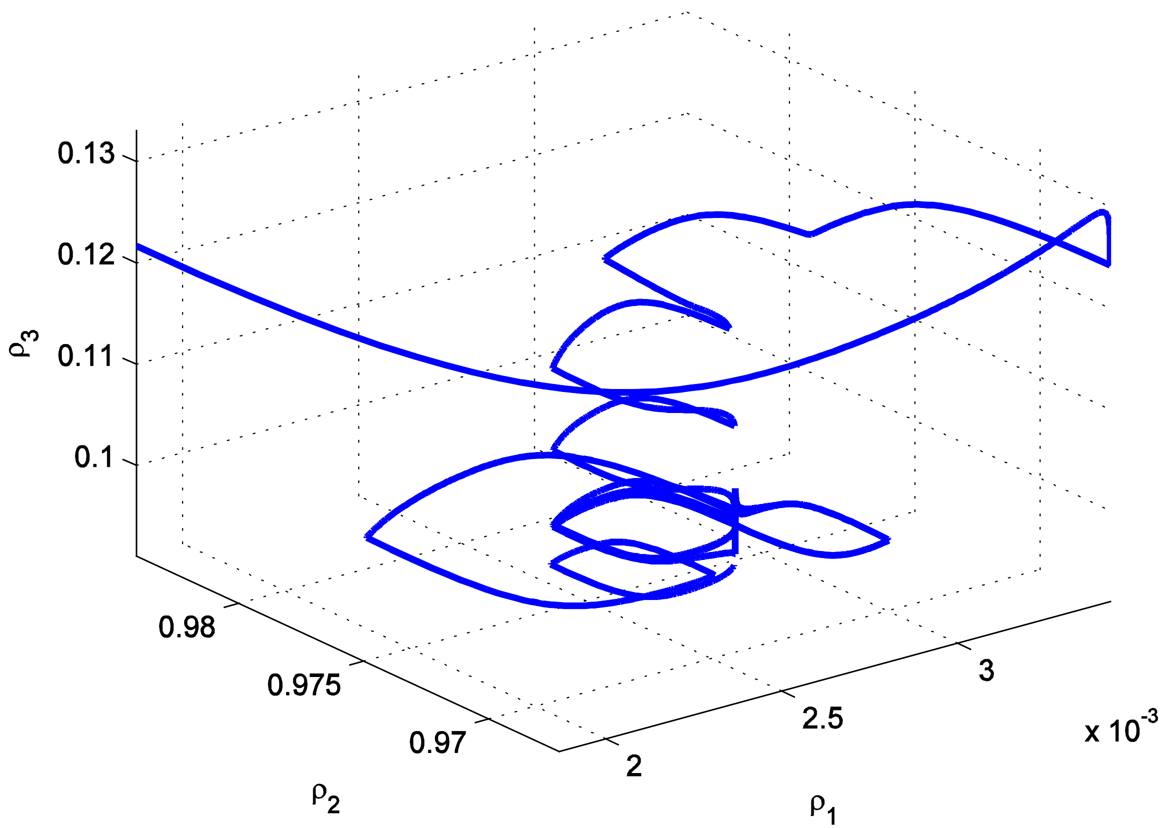
qALPV → Canterbury-model

$$\rho(t) = \begin{bmatrix} \rho_1(t) \\ \rho_2(t) \\ \rho_3(t) \end{bmatrix} = \begin{bmatrix} \frac{S_I(t)Q(t)}{1+\alpha_G Q(t)} \\ \frac{1}{1+\alpha_I I(t)} \\ \frac{1}{G(t)} \end{bmatrix}$$

Can be calculated

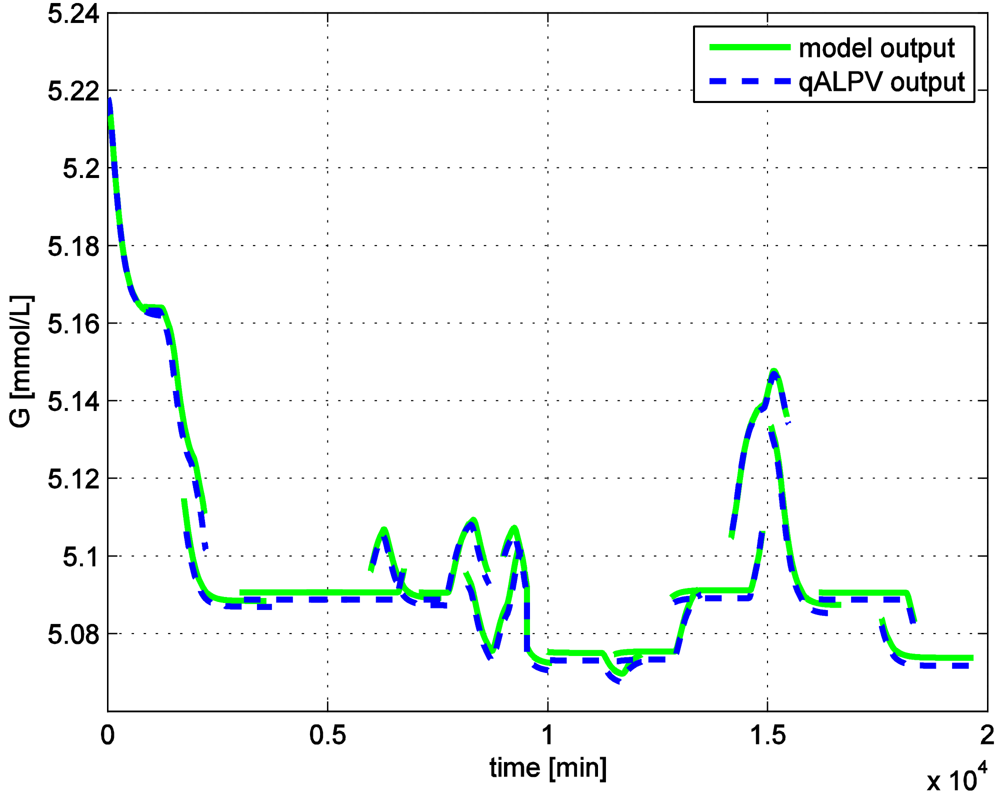
Measured

qALPV → Results



Results

Real clinical dataset [1]



1 – J. Chase et al. (2008). *J Diab Sci* & *Techn*, **24**(4): 584-594.

Conclusions

- Frequently used ICU model:
  - linear robust μ-synthesis method
  - qALPV + μ-synthesis method
- Nonlinear model based robust control more general
- Further work
  - other ICU Canterbury-models
  - more simulations on real dataset
  - in-silico validations

Thank you for your attention!

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