

# Control Theory as a Modeling Tool in Physiology

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## I. Cardiovasculat-respiratory modeling

a) The basic model

b) Lower body negative pressure (LBNP)

## II. Modeling the control loops via control theory

1. The linear-quadratic regulator problem

2. Receding horizon control

3. Other possibilities

## III. Some results

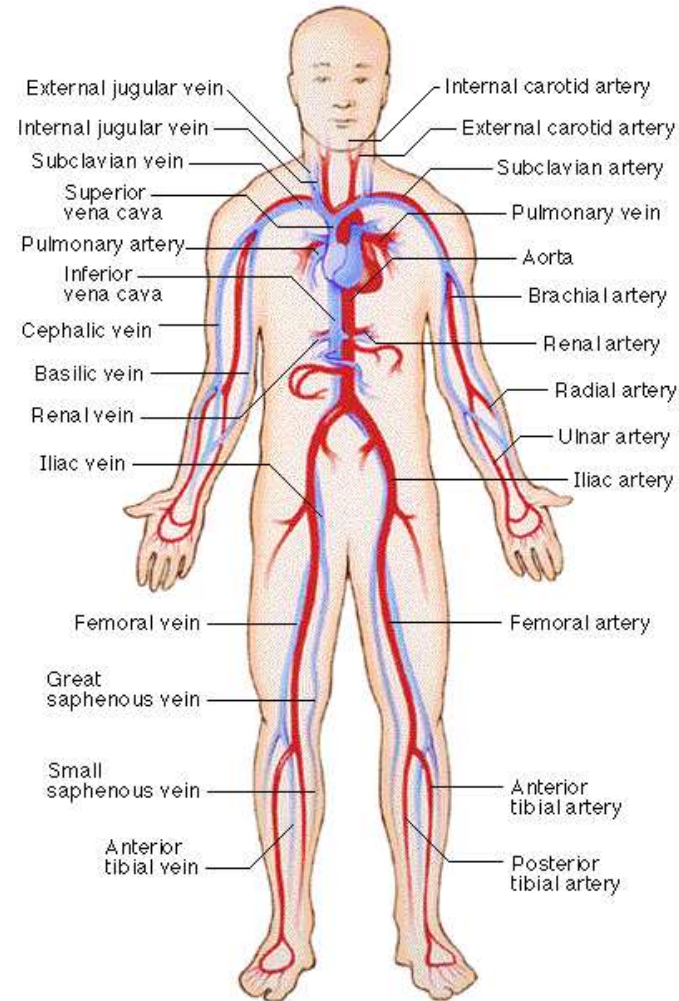
- **Problem:** Reaction of the CVS to an ergometric work-load (bicycle ergometer, 75 Watt for 10 min.)
- **Focus:** Control loops
- **Data:**
  - Heart rate (every 2 sec.),
  - mean arterial systemic pressure (every 2 sec., Finapres)
  - cardiac output of the left ventricle (irregularly, Doppler-echocardiography)

F. K. and R. O. Peer, *A mathematical model for fundamental regulation processes in the cardiovascular system*, J. Math. Biology 31(1993), 611–631

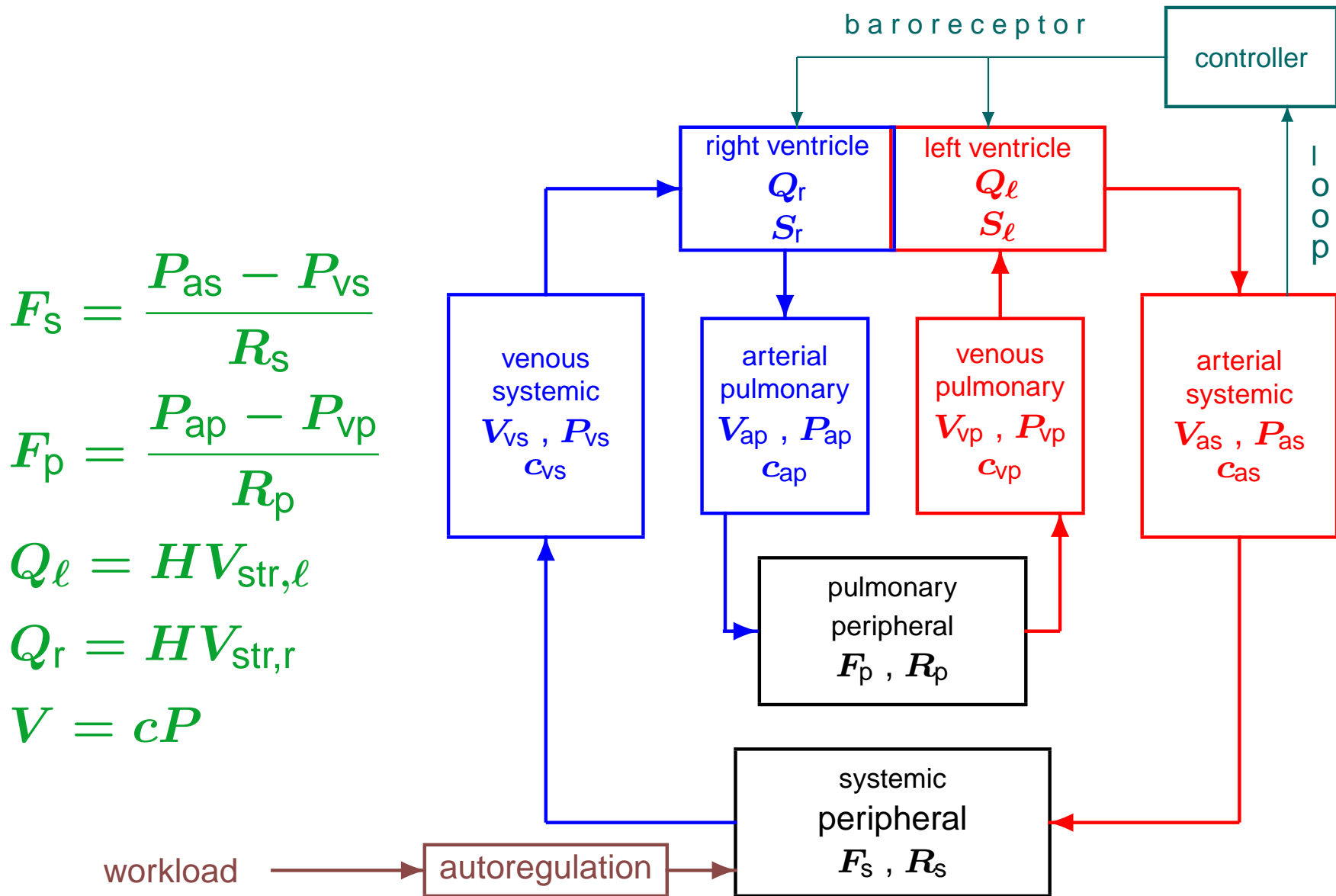
# The basic model

## Model structure:

compartmental model  
non-pulsatile flow  
autoregulation  
barorezeptor-loop



# The basic model



$$F_s = \frac{P_{as} - P_{vs}}{R_s}$$

$$F_p = \frac{P_{ap} - P_{vp}}{R_p}$$

$$Q_l = HV_{str,l}$$

$$Q_r = HV_{str,r}$$

$$V = cP$$

# Model equations

$$c_{as}\dot{P}_{as} = Q_\ell - F_s,$$

$$Q_\ell = H \frac{c_\ell P_{vp} a_\ell(H) S_\ell}{a_\ell(H) P_{as} + k_\ell(H) S_\ell}$$

$$c_{vs}\dot{P}_{vs} = F_s - Q_r,$$

$$k_\ell(H) = e^{-(c_\ell R_\ell)^{-1} t_d(H)}, \quad a_\ell(H) = 1 - k_\ell(H)$$

$$c_{ap}\dot{P}_{ap} = Q_r - F_p,$$

$$c_{vp}\dot{P}_{vp} = F_p - Q_\ell,$$

$$\ddot{S}_\ell + \gamma_\ell \dot{S}_\ell + \alpha_\ell S_\ell = \beta_\ell H,$$

$$\ddot{S}_r + \gamma_r \dot{S}_r + \alpha_r S_r = \beta_r H,$$

$$\dot{R}_s = \frac{1}{K} \left( A_{\text{pesk}} (F_s C_{a,O_2} - M) - (P_{as} - P_{vs}) \right),$$

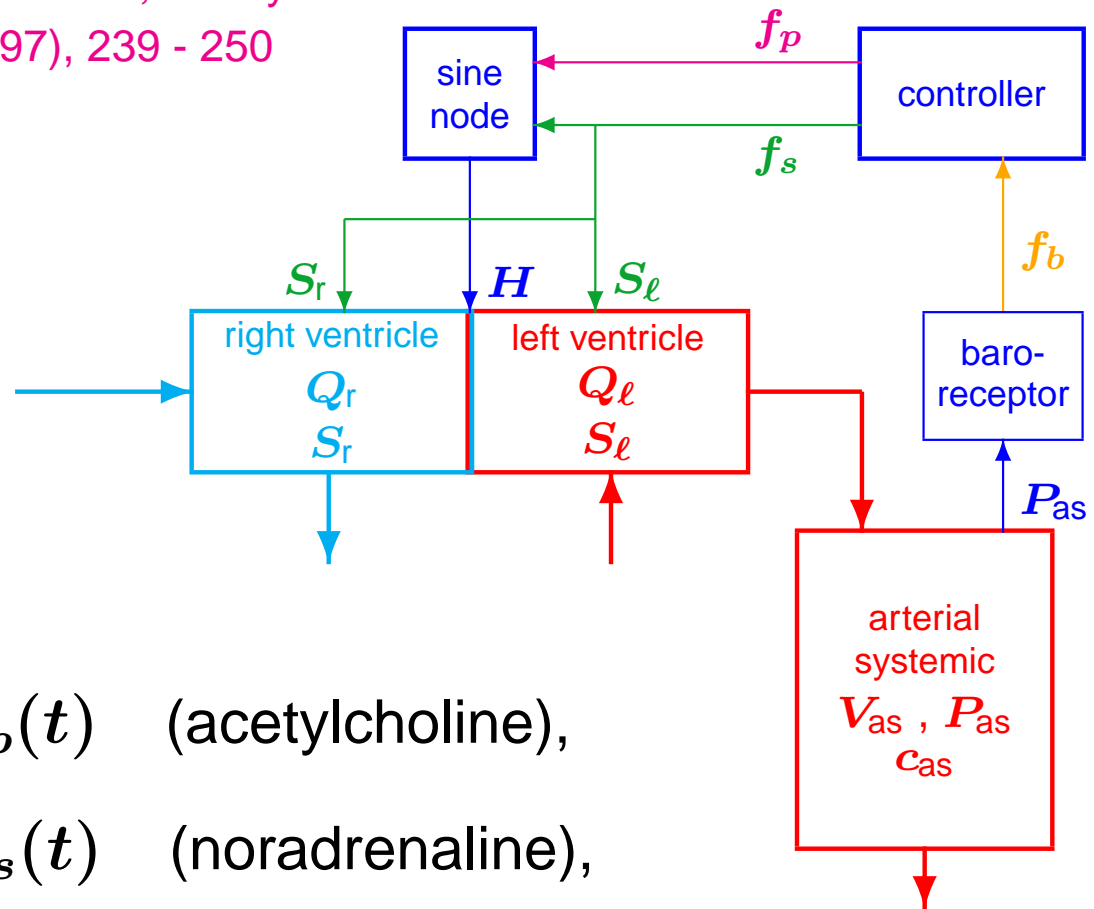
$$\dot{H} = u(t) \quad \dots \text{baroreceptor loop !}$$

$$\dot{x}(t) = \mathcal{F}(x(t), q) + Bu(t)$$

# Baroreceptor-loop

F.K., S. Lafer & R. O. Peer, *A model for the cardiovascular system under an ergometric workload*, Surveys on Mathematics for Industry 7 (1997), 239 - 250

b a r o r e c e p t o r



l  
o  
o  
p

$$\dot{f}_b = g(P_{as}),$$

$$(\dot{f}_s, \dot{f}_p)^\top = F(f_b),$$

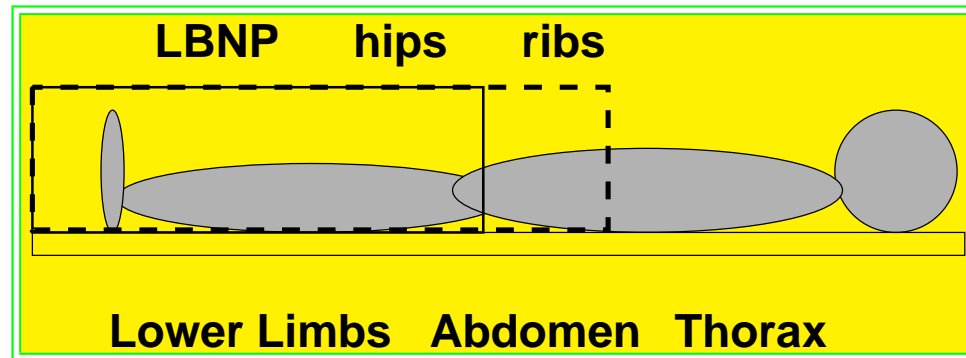
$$\dot{C}_{ac} = -\tau_{ac}C_{ac} + f_p(t) \quad (\text{acetylcholine}),$$

$$\dot{C}_{na} = -\tau_{na}C_{na} + f_s(t) \quad (\text{noradrenaline}),$$

$$\dot{H} = h(C_{ac}, C_{na})$$

$$\ddot{S}_l + \gamma_l \dot{S}_l + \alpha_l S_l = \beta_l f_s, \quad \ddot{S}_r + \gamma_r \dot{S}_r + \alpha_r S_r = \beta_r f_s$$

## Lower body negative pressure:



M. Fink, J.J. Batzel & F. K., *Aspects of control of the cardiovascular-respiratory system during orthostatic stress induced by lower body negative pressure*, *Math. Biosciences* 206 (2007), 273–308



Cardiovascular part:

$$c_{as,up} \dot{P}_{as,up} = Q_\ell - F_a - F_{s,up},$$

$$c_{as,lo} \dot{P}_{as,lo} = F_a - F_{s,lo} - c_{as,lo} \dot{P}_{LBNP},$$

$$c_{vs,lo} \dot{P}_{vs,lo} = F_{s,lo} - F_v - c_{vs,lo} \dot{P}_{LBNP} \\ - \dot{c}_{vs,lo} (P_{vs,lo} + P_{LBNP}) - \dot{V}_u, \text{ (ribs case)}$$

$$c_{vs,up} \dot{P}_{vs,up} = F_v - Q_r + F_{s,up} - \dot{V}_u, \text{ (hips case)}$$

$$c_{ap} \dot{P}_{ap} = Q_r - F_p,$$

$$c_{vp} \dot{P}_{vp} = F_p - Q_\ell.$$

Capacitance ...  $V = f(P)$ , Compliance ...  $c = f'(P)$

unstressed volume ...  $V_u = f(0)$

Special case:  $V = cP + V_u$

Respiratory part:

$$V_{A,\text{CO}_2} \dot{P}_{a,\text{CO}_2} = 863 F_p (C_{v,\text{CO}_2} - C_{a,\text{CO}_2}) + \dot{V}_A (P_{i,\text{CO}_2} - P_{a,\text{CO}_2}),$$

$$V_{A,\text{O}_2} \dot{P}_{a,\text{O}_2} = 863 F_p (C_{v,\text{O}_2} - C_{a,\text{O}_2}) + \dot{V}_A (P_{i,\text{O}_2} - P_{a,\text{O}_2}),$$

$$V_{T,\text{CO}_2} \dot{C}_{v,\text{CO}_2} = MR_{\text{CO}_2} + F_s (C_{a,\text{CO}_2} - C_{v,\text{CO}_2}),$$

$$V_{T,\text{O}_2} \dot{C}_{v,\text{O}_2} = -MR_{\text{O}_2} + F_s (C_{a,\text{O}_2} - C_{v,\text{O}_2}),$$

$$\dot{H} = u_1(t),$$

$$\ddot{V}_A = u_2(t),$$

$$\dot{V}_u = u_3(t),$$

$$\dot{A}_{\text{pesk}} = u_4(t).$$

→  $V_u$ ... unstressed volume

→  $R_s = A_{\text{pesk}} C_{v,O_2}$

# Optimal control (basic model)

Choose  $u(t)$  such that:

$$J(u(\cdot), x^{\text{rest}}) = \int_0^{\infty} (q_{\text{as}}^2 (P_{\text{as}}(t) - P_{\text{as}}^{\text{exer}})^2 + u(t)^2) dt \rightarrow \min$$

$$x(0) = x^{\text{rest}}$$

$$\implies \quad u(t) = K(x(t) - x^{\text{exer}}), \quad K = -B^T X,$$

$$XA + A^T X - XBB^T X + C^T C = 0,$$

where  $A = (\partial \mathcal{F} / \partial)(x^{\text{exer}}, q)$ ,  $B = \text{col}(0, \dots, 1)$ ,  
 $C = (q_{\text{as}}, 0, \dots, 0)$ .

$u(t)$  is the optimal control for the linearized system

$$\dot{x}(t) = Ax(t) + Bu(t), \quad y(t) = Cx(t).$$

# Optimal controls (LBNP)

$$\int_0^{\infty} \left( q_a (P_{as,up}(t) - P_{as,up}^f)^2 + q_v (P_{vs,up}(t) - P_{vs,up}^f)^2 \right. \\ \left. + q_{CO_2} (P_{a,CO_2}(t) - P_{a,CO_2}^f)^2 + q_{O_2} (P_{a,O_2}(t) - P_{a,O_2}^f)^2 \right. \\ \left. + q_1 u_1(t)^2 + q_2 u_2(t)^2 + q_3 u_3(t)^2 + q_4 u_4(t)^2 \right) dt$$

→ 0

# Receding horizon control

Choose  $t_{\text{start}} < t_{\text{end}}$  and consider the problem:

$$\min_u J(x, u) = \int_{t_{\text{start}}}^{t_{\text{end}}} \left( q_{as}^2 (P_{as}(t) - P_{as}^{\text{exer}})^2 + u(t)^2 \right) dt$$
$$+ \frac{\alpha_c}{2} (P_{as}(t_{\text{end}}) - P_{as}^{\text{exer}})^2$$

subject to

$$\dot{x}(t) = \mathcal{F}(x(t), u(t)), \quad t \in (t_{\text{start}}, t_{\text{end}}),$$

$$x(t_{\text{start}}) = x_0,$$

Choose new  $t_{\text{start}}$  and  $t_{\text{end}}$ , where in general  $t_{\text{start}}^{\text{new}} < t_{\text{start}}^{\text{old}}$ .

M. Mutsaers, M. Bachar, J. J. Batzel, F. K. & S. Volkwein, *Receding horizon controller for the baroreceptor loop in a model for the cardiovascular system*, *Cardiovascular Eng.* 8 (2007)

# A nonlinear feedback law



$$\dot{x}(t) = f(x(t)) + g(x(t))u(t), \quad t \geq 0,$$

$$x(0) = 0,$$

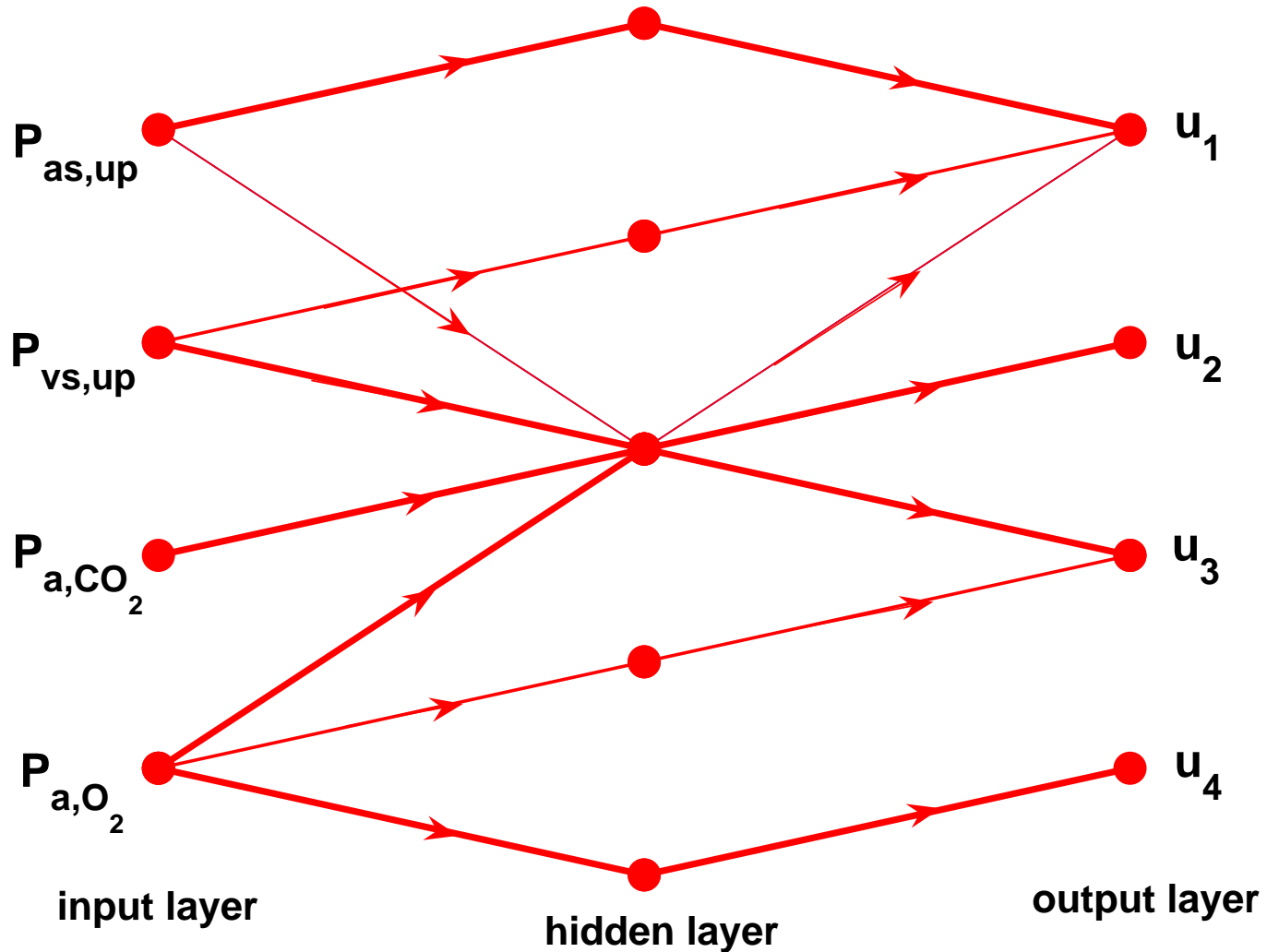
$$y(t) = h(x(t)).$$

A nonlinear, stabilizing feedback law:

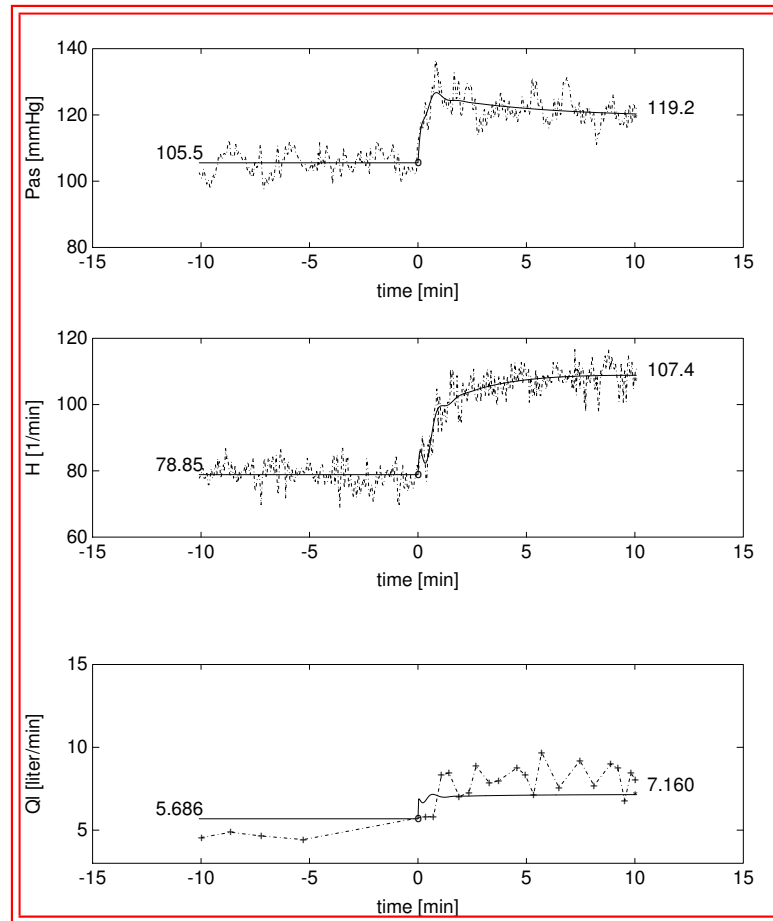
$$u(t) = F(x(t))$$

A. Isidori: *Nonlinear Systems Theory*, 3rd ed., Springer Verlag, Berlin 1995.

## Neural network:

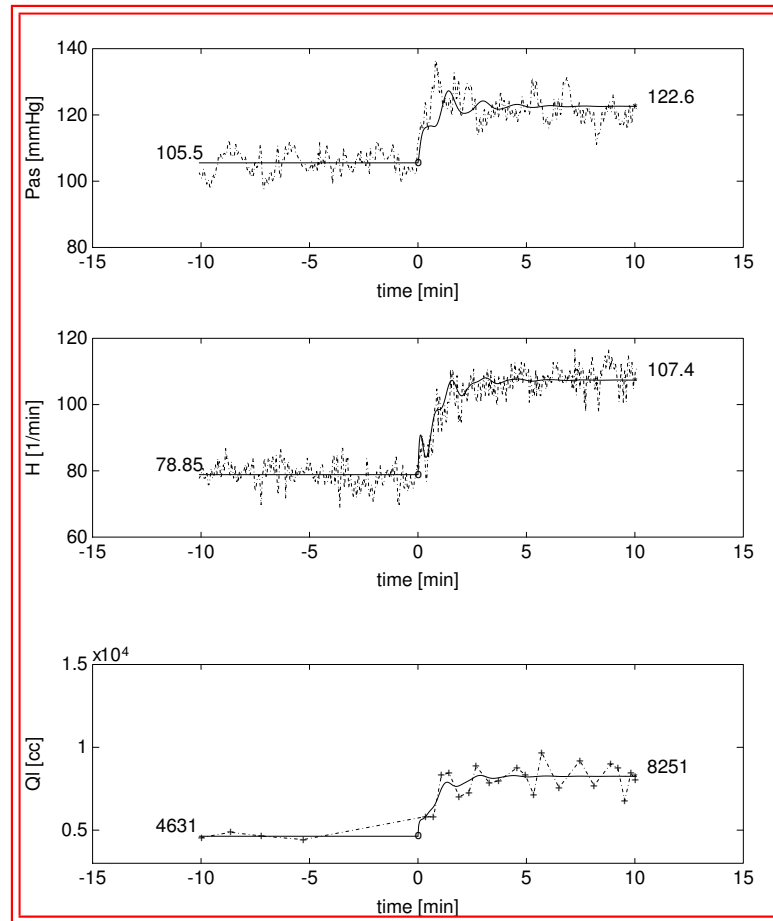


# Results for LQR



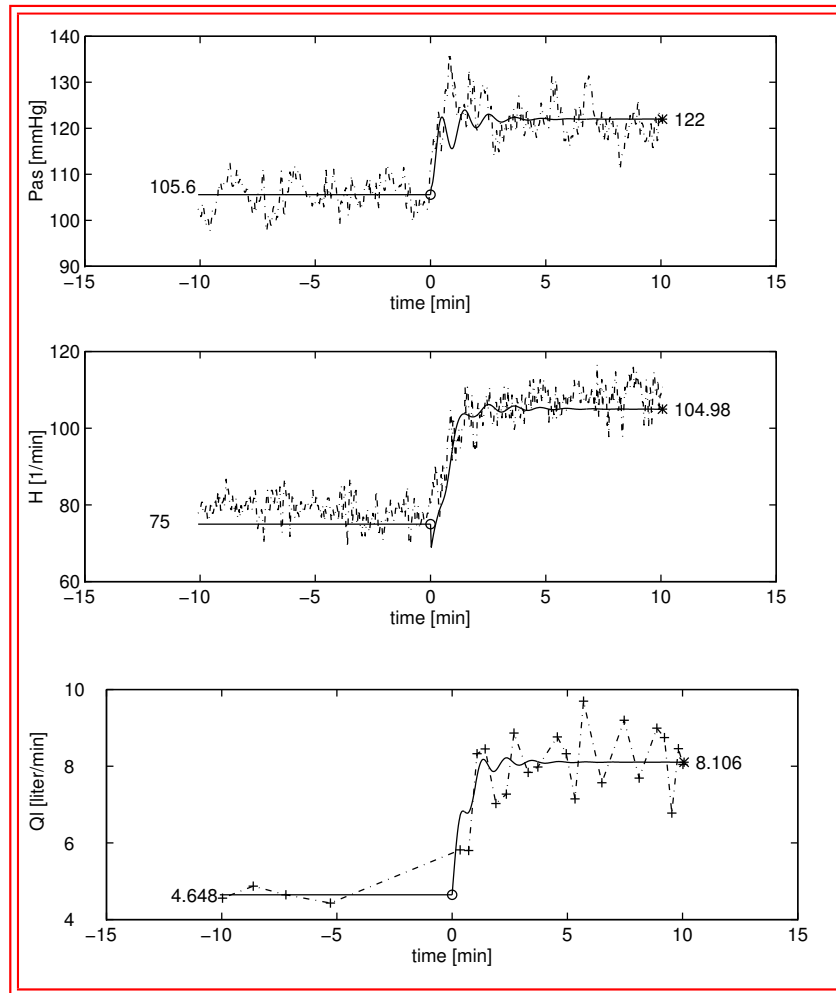
Measurements (dot-dashed) for  $P_{as}$ ,  $H$ ,  $Q_l$  and model-output (solid). Parameter identification was done only with measurements for  $P_{as}$  and  $h$ .

# Results for LQR



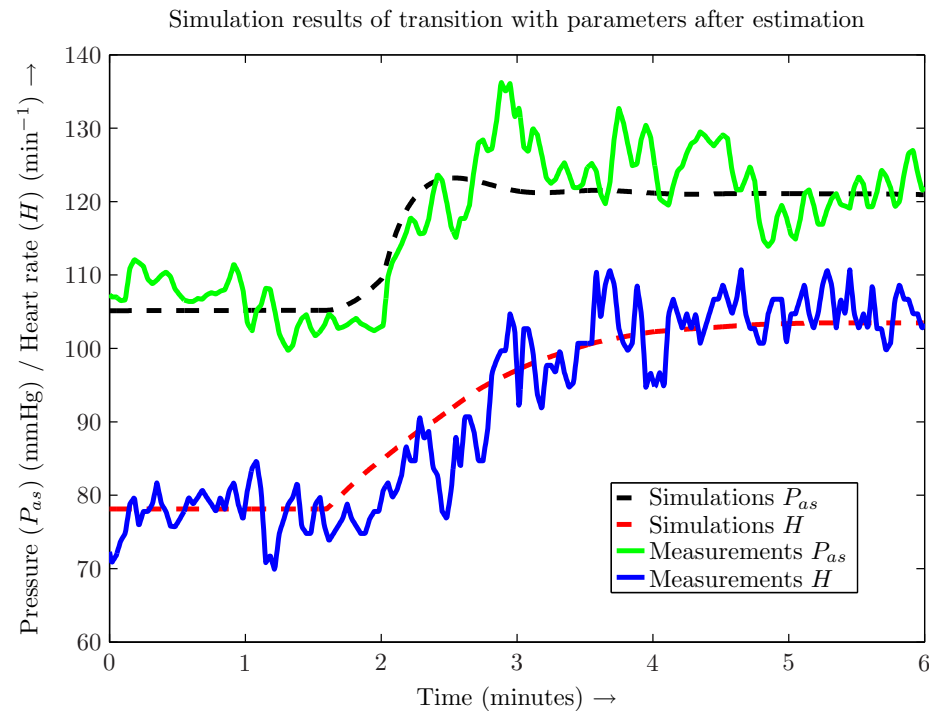
Measurements (dot-dashed) for  $P_{as}$ ,  $H$ ,  $Q_l$  and model-output (solid). Parameter identification was done with all measurements.

# Results for nonlinear feedback



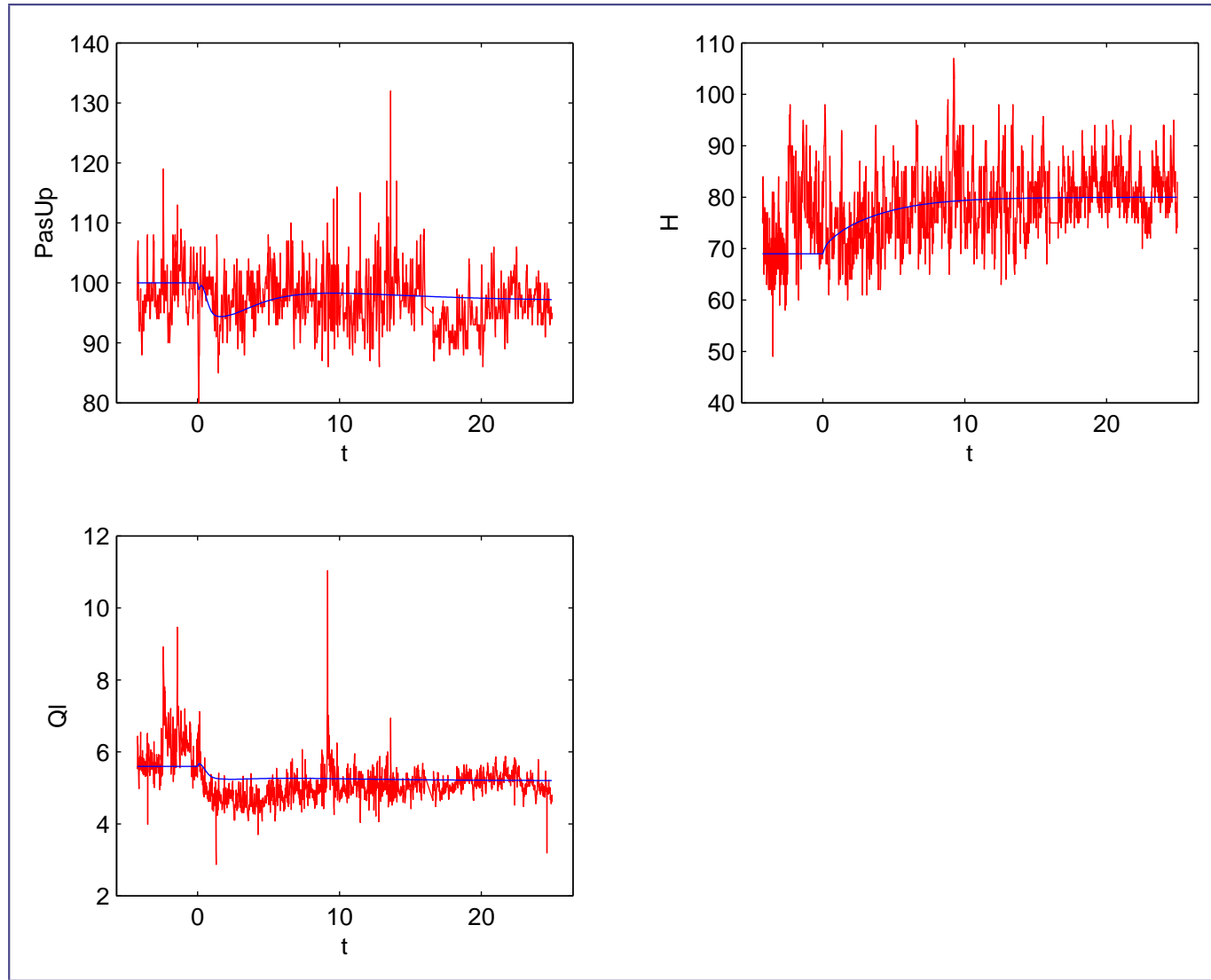
Measurements (dot-dashed) for  $P_{as}$ ,  $H$ ,  $Q_{\ell}$  and model-output (solid). Parameters are the same as those obtained for LQR using all measurements.

# Results for receding horizon control



Measurements and model output for  $P_{as}$  and  $H$ . Parameters are the same as for previous slide except for the control parameters and  $c_\ell$ ,  $c_r$  which were identified anew.

# Results – hips case



# Results – ribs case

