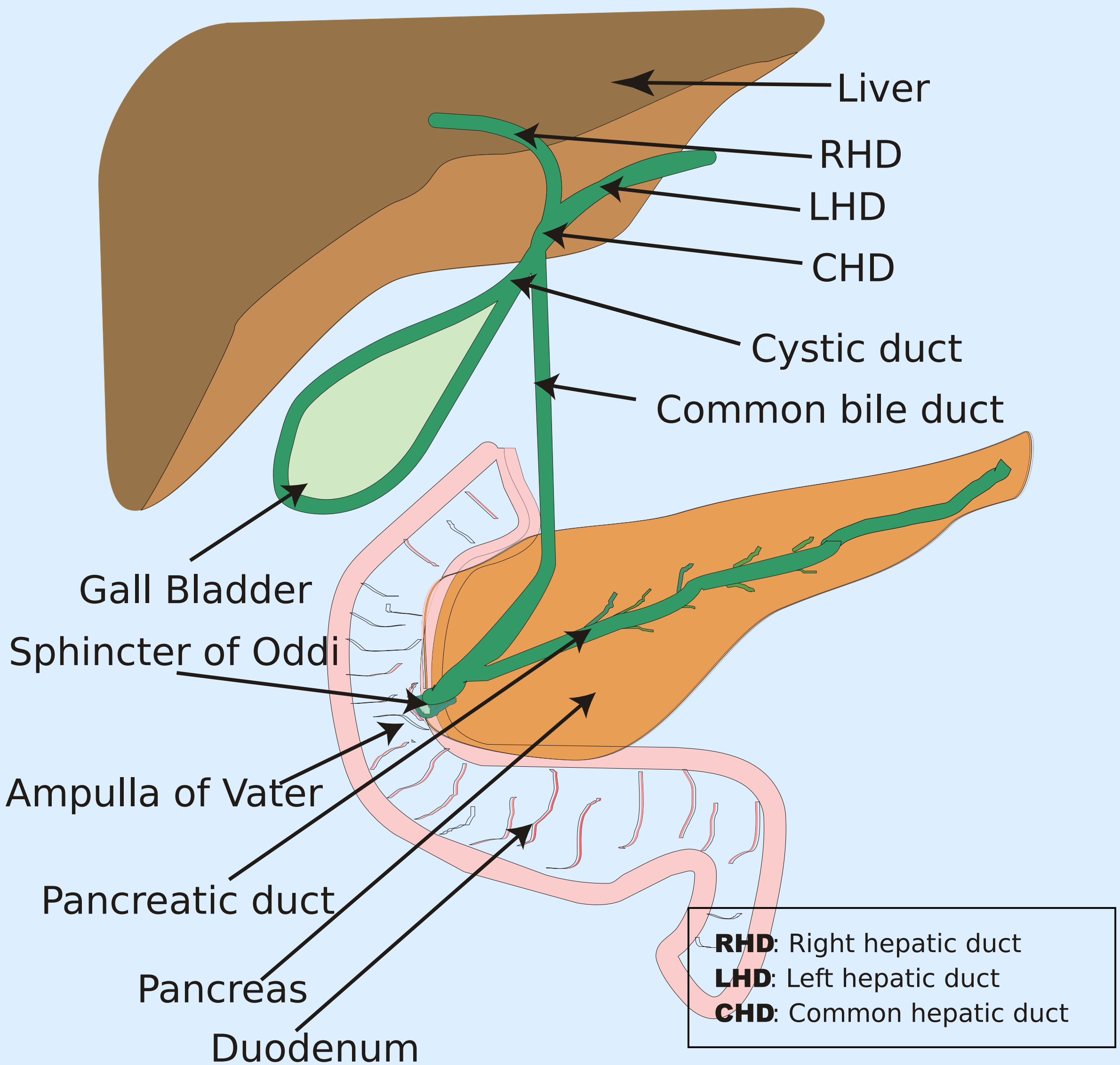
Novosibirsk State Technical University
NETI

15th International Asian School-Seminar
Optimization Problems of Complex Systems
26-30 August 2019

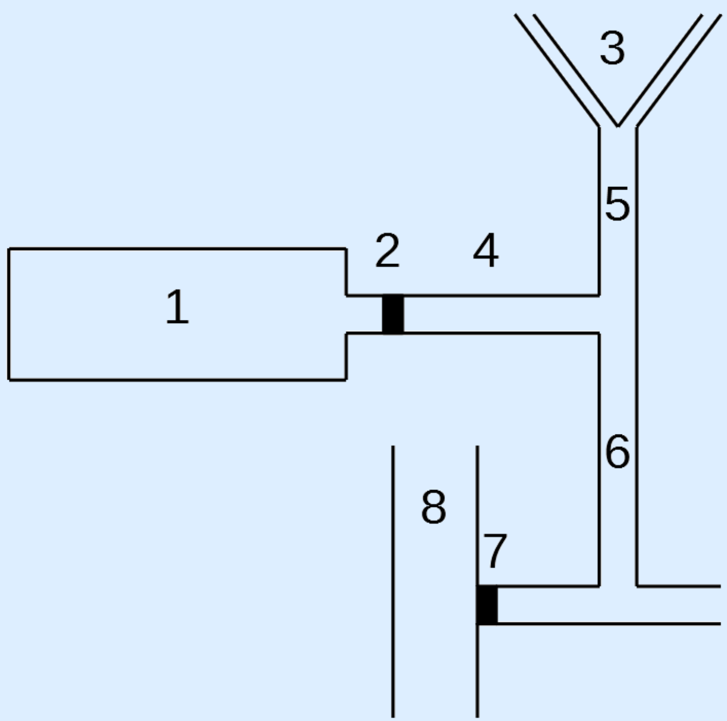
Finding Optimal Solutions on Models of Living Systems

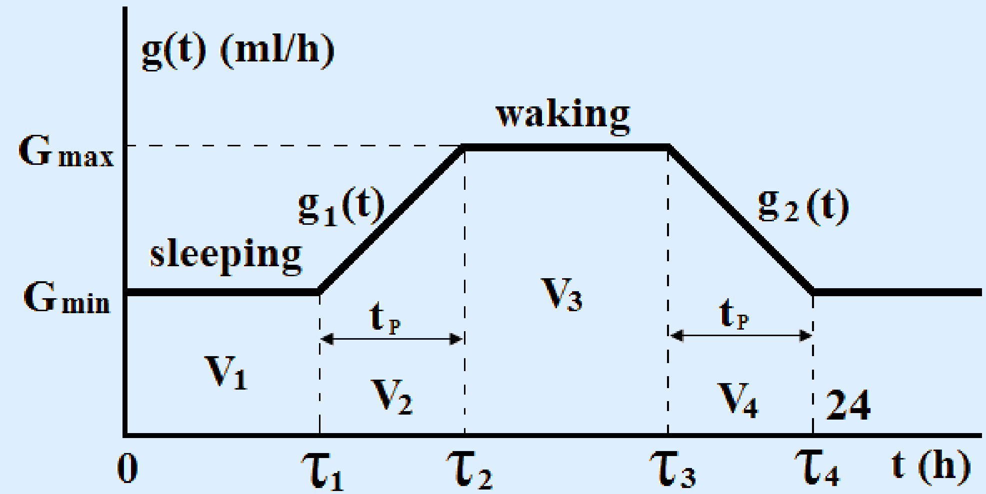
Yury V. Shornikov
Evgeny A. Popov

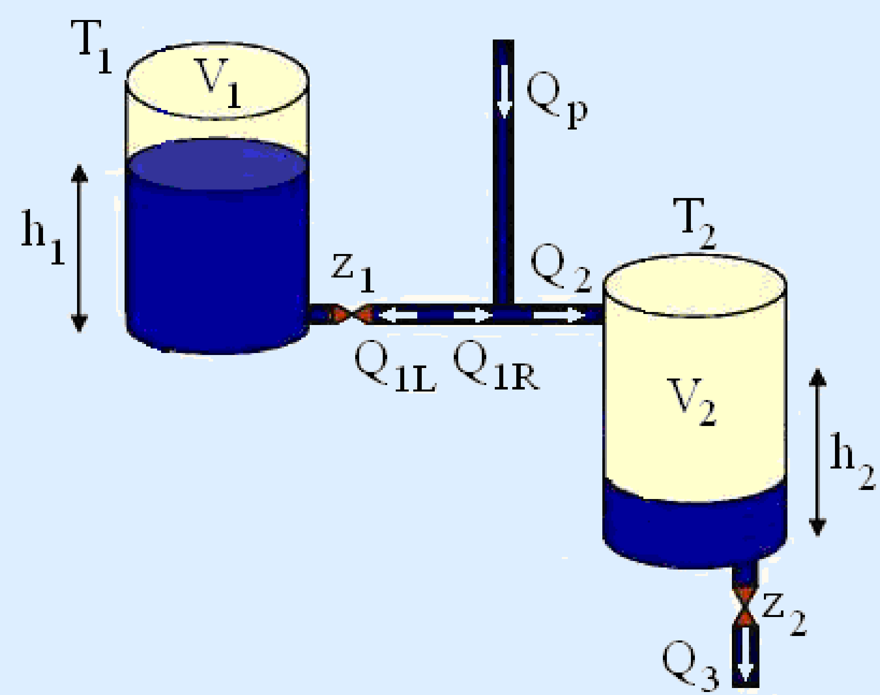
Human Biliary System



Representation as a two tank system







Hybrid Systems

Explicit DAEs with constraints

$$y' = f(x, y, t),$$

$$x = \varphi(x, y, t),$$

$$pr: g(x, y, t) < 0,$$

$$t \in [t_0, t_k], x(t_0) = x_0, y(t_0) = y_0,$$

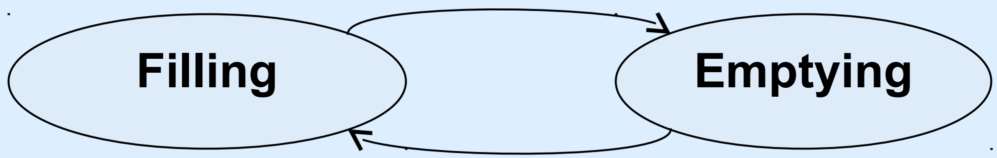
$$\text{where } x \in R^{N_x}, y \in R^{N_y}, t \in R,$$

$$f: R^{N_x} \times R^{N_y} \times R \to R^{N_y},$$

$$\varphi: R^{N_x} \times R^{N_y} \times R \to R^{Nx},$$

$$g: R^{N_x} \times R^{N_y} \times R \to R^{S}.$$

Mathematical Model



$$\begin{cases} x_1{}' = r \cdot g(t) - F_1(x_1), \\ x_2{}' = (1-r) \cdot g(t), \end{cases}$$

$$\begin{cases} x_1{}' = g(t) - F_1(x_1) + F_2(x_2), \\ x_2{}' = -F_2(x_2). \end{cases}$$

where $r \in (0,1)$ is the separation ratio of the synthesized bile flow;

$$F_1(x_1) = \begin{cases} k_1 \cdot x_1, x_1 < x_1^*, \\ F_1^*, x_1 \geq x_1^*, \end{cases}$$

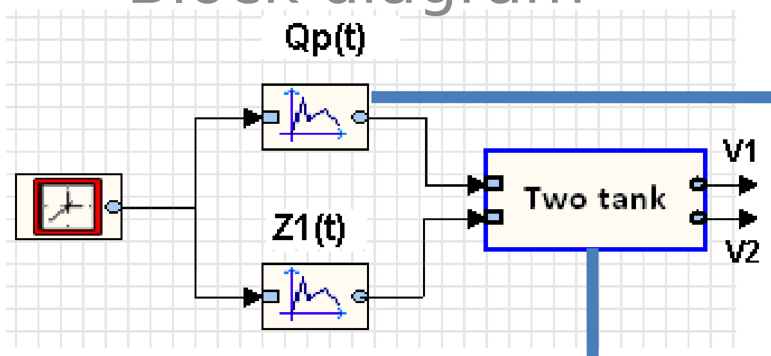
is the flow through the sphincter of Oddi;

$$F_2(x_2) = \begin{cases} k_2 \cdot x_2, x_2 < x_2^*, \\ F_2^*, x_2 \geq x_2^*. \end{cases}$$

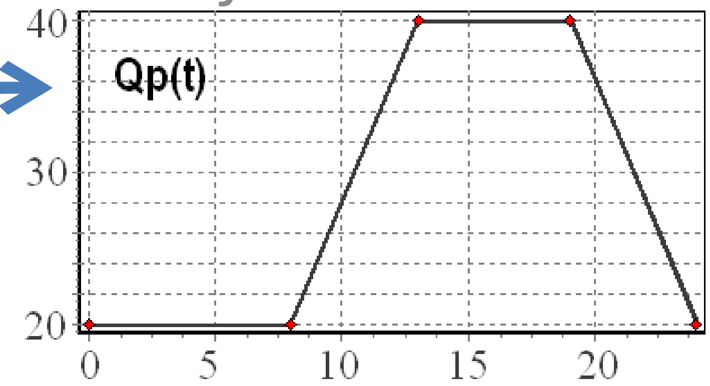
is the flow through the sphincter of Lutkens.

Computer Model

Block diagram



Daily bile secretion



Textual model

```
p=0.9;        Z2=1;
Q1max=105;    Q2max=130;  // bandwidth of valves
a1=226;       a2=30;      // flow rates
r1=0.2;       r2=0.3;
R1=2;         R2=0.4;
V1=100;       V2=2;       // initial conditions
macro Q1L= p*Qp*(1-Z1);
macro Q1R= max(0, min(a1*Pi*pow(r1, 2)*
                 sqrt(2*g*V1/(Pi*pow(R1, 2))), Q1max))*Z1;
macro Q2 = (1-p)*Qp*(1-Z1)+Qp*Z1;
macro Q3 = max(0, min(a2*Pi*pow(r2, 2)*
                 sqrt(2*g*V2/(Pi*pow(R2, 2))), Q2max))*Z2;
V1'=Q1L-Q1R;
V2'=Q1R+Q2-Q3;            // liquid levels in tanks
```

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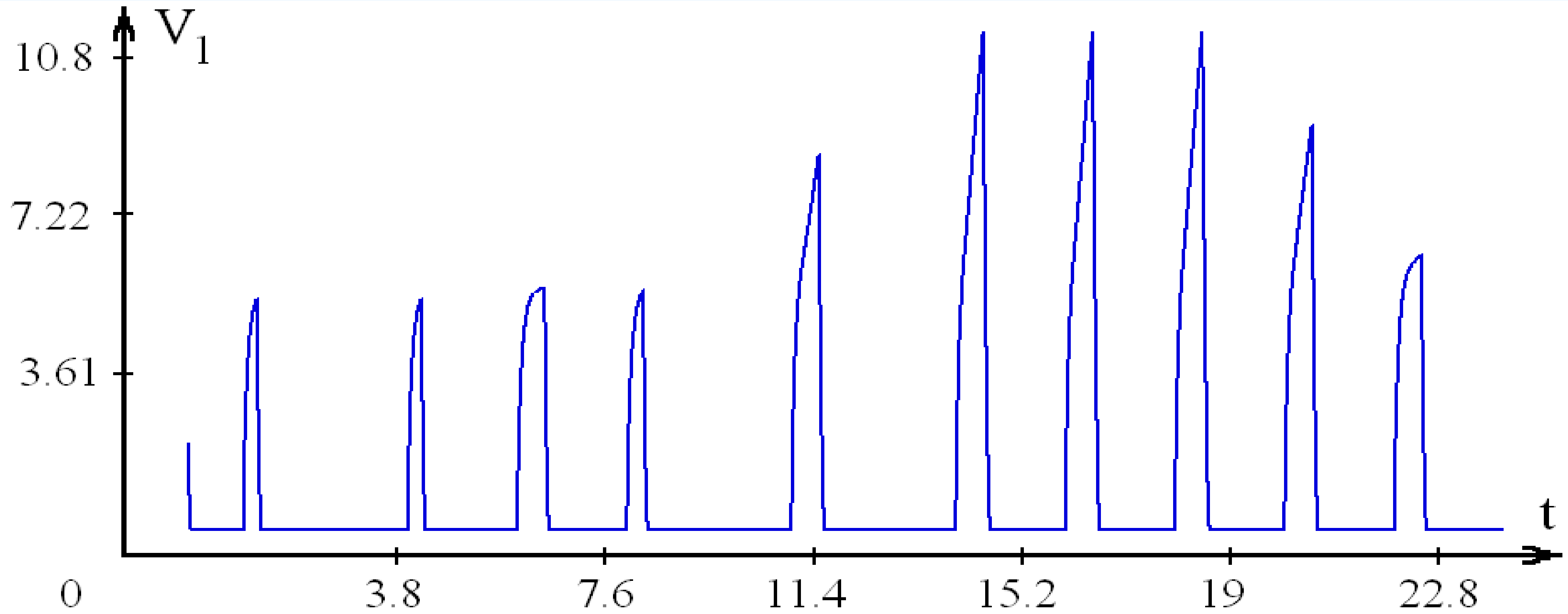
Daily Bile Level in the Gallbladder

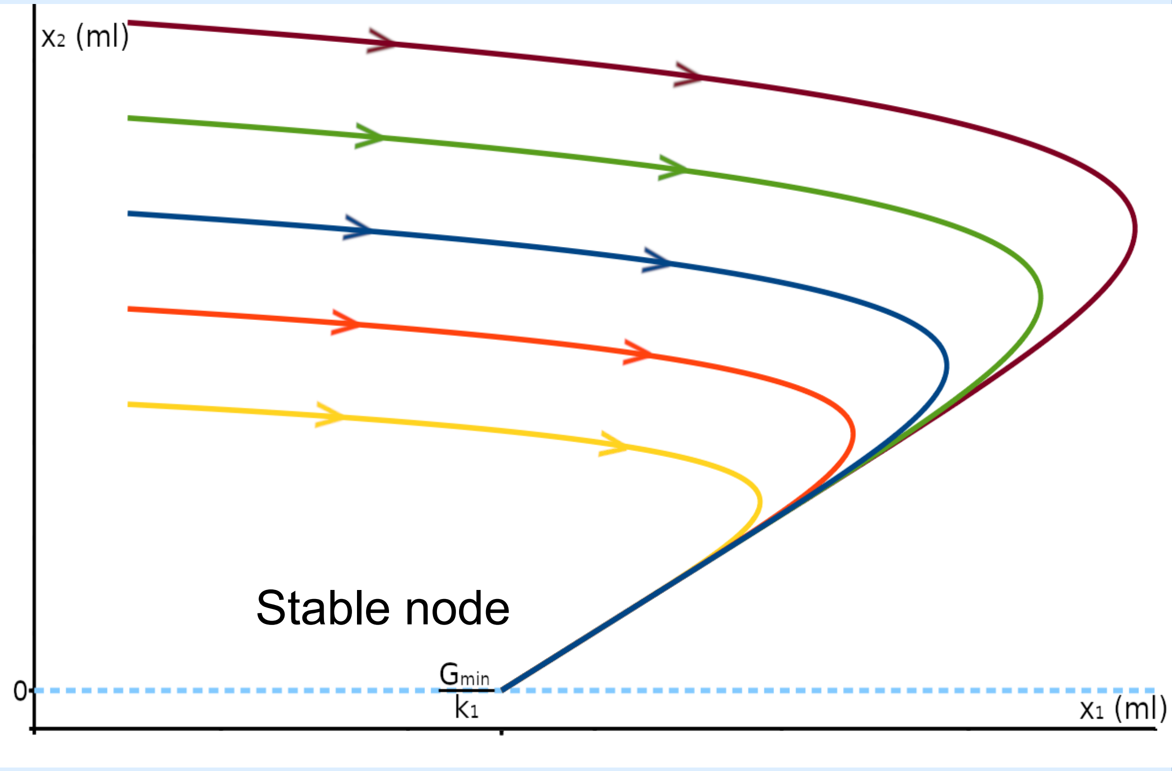


Parametrization

In the Filling mode for $t \in [0, \tau_1]$:

$$g(t) = G_{min}, \text{ so}$$

$$\begin{cases} x_1' = G_{min} - k_1 \cdot x_1 + k_2 \cdot x_2, \\ x_2' = -k_2 \cdot x_2. \end{cases}$$



$$G_{min} \rightarrow max$$

$$max(x_1(t)) \leq x_1^*,$$

$$k_1 = 5, k_2 = 0.7, x_1(t_0) = 0.5, x_2(t_0) = 10.$$

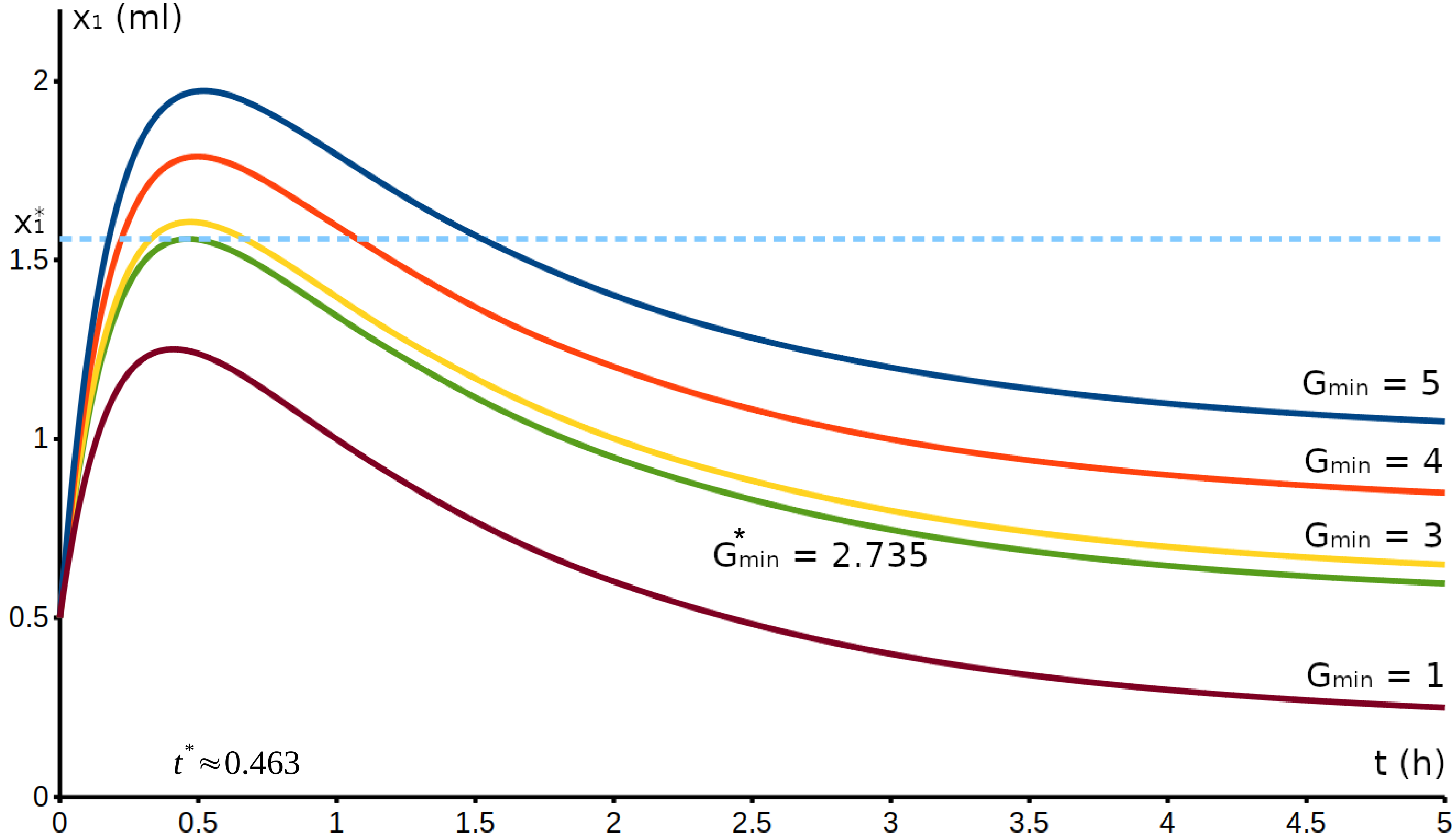
Computer Model

```
// Parameters
const K1 = 5;
const K2 = 0.7;

// Varied parameter
const G1 = 5.0;
const G2 = 4.0;
const G3 = 3.0;
const G4 = 2.735;
const G5 = 1.0;

// Varied biliary system
for i = 1:5
{
   x1[i]' = G[i] - K1 * x1[i] + K2 * x2[i];
   x1[i](t0) = 0.5;
   x2[i]' = -K2 * x2[i];
   x2[i](t0) = 10.0;
}
```

Simulation Results



Comparison with the Closed-Form Solution

The partial solution is

$$x_1(t) = \left(x_1^0 - \frac{G_{min}}{k_1} - \frac{k_2 x_2^0}{k_1 - k_2}\right) e^{-k_1 t} + \frac{k_2 x_2^0}{k_1 - k_2} e^{-k_2 t} + \frac{G_{min}}{k_1},$$

$$x_2(t) = x_2^0 e^{-k_2 t}.$$

$$t^* = \frac{\ln\left(\frac{A_2 k_2}{A_1 k_1}\right)}{k_2 - k_1} \approx 0.464\, h,$$

where $A_1 = x_1^0 - \frac{G_{min}}{k_1} - \frac{k_2 x_2^0}{k_1 - k_2}, A_2 = \frac{k_2 x_2^0}{k_1 - k_2}.$

$$t^{*\,\text{(simulation)}} \approx 0.463\, h.$$

ISMA

Modeling languages:

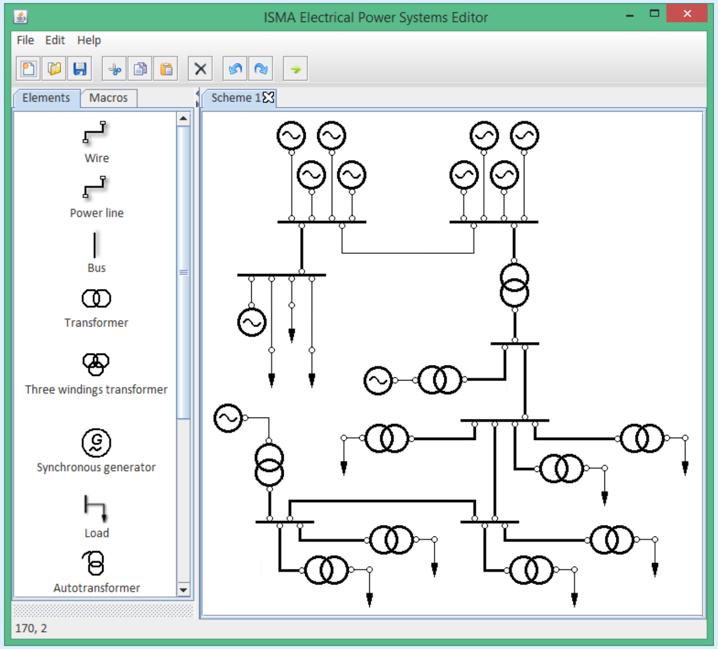
- Textual general-purpose language LISMA;
- Block-textual diagrams;
- Harel statecharts;
- Domain-specific languages.

```
h1’ = (1 / S) * (Qp – Q1 – Q2 – V3 * Q3);
h2’ = (1 / S) * (Q2 + V3 * Q3 – V4 * Q4);

state st1 (h1 <= hv3) {
    V3 = 0;
} from init, st2;

state st2 (h1 > hv3) {
    V3 = 1;
} from init, st1;
```

```
C2H6=k1=>CH3+CH3;
CH3+C2H6=k2=>CH4+C2H5;
```



ISMA's Library of Numerical Methods

Method (p, m)*	Description
DISPF (5, 6)	Stability control. For ODEs of moderate and low stiffness
RADAU5 (3, 3)	Stiff ODEs
DISPF1_RADAU5	The adaptive method DISPF combined with RADAU5 with stiffness control. For very stiff ODEs
DP78ST (8, 13)	Stability control, variable order and stepsize, high accuracy. For ODEs of moderate stiffness. Based on the Dormand-Prince method
RKF78ST (7, 13)	The same. Based on the Runge-Kutta-Fehlberg method
RK2ST (2, 2) RK3ST (2, 3)	Explicit methods with stability control for simulating nonstiff ODEs
DISPS1	Algorithm of variable order with adaptive stability regions
MK22 (2, 2) MK21 (2, 2)	Frozen Jacobian matrix. For stiff ODEs.

* *p* denotes the order and *m* stands for the number of stages of a method.

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