Simulace procesů se dvěma časovými škálami pomocí Equation-Based Modeling
(*How to transform an ODE system describing slow-fast phenomena to a PDE based model and solve it using COMSOL Multiphysics*)

Štěpán Papáček

JU v ČB/ÚTIA - AV ČR, v.v.i.,
with special support of Marie G. Papáčková (MFF UK Praha).

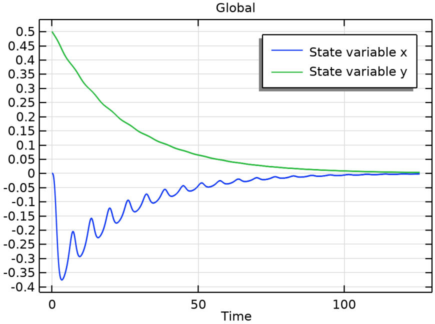
Konference COMSOL Multiphysics, ČR 2022

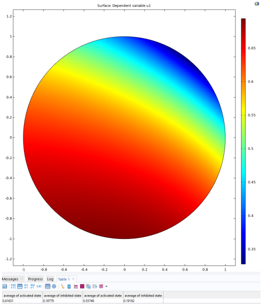
Zaječí, 27.5.2022

Remembering COMSOL conference 2021:

Transformace ODR s harmonickým buzením na PDR

Efficient Solution of a Parameter Estimation Problem using Equation-Based Modeling in COMSOL





It was one encouraging example *"how to transform ODEs into PDEs"*.

And now for something not completely different. . .

How to transform ODEs into PDEs ?

Exosystem as the harmonic input signal generator → ODEs are transformed to a **stationary PDE system** (2) .

Defining harmonic input $u(t)$ (with angular frequency ω) as follows: $u(t) = K(1 - \cos(\omega t)) = K(1 - w_2)$, where $\mathbf{w}(t) = [\sin(\omega t), \cos(\omega t)]^T$. Then, the input signal can be generated by an external autonomous system, so-called **EXO SYSTEM**:

$$\dot{\mathbf{w}}(t) = \begin{bmatrix} \dot{w}_1 \\ \dot{w}_2 \end{bmatrix} = \omega \begin{bmatrix} 0 & 1 \\ -1 & 0 \end{bmatrix} \begin{bmatrix} w_1 \\ w_2 \end{bmatrix} = \omega \ S \ \mathbf{w}, \tag{1}$$

and further

$$\dot{x} = \nabla x(w(t)) \ \dot{w}(t) = \omega \nabla x(w) S w = \big[\mathcal{A} + u(w)\mathcal{B}\big] x(w), \tag{2}$$

where $\nabla x := [\nabla x_1, \nabla x_2, \nabla x_3]^T$, and $\nabla x_i = [\frac{\partial x_i}{\partial w_1}, \frac{\partial x_i}{\partial w_2}]$.

Outline

1. Introduction – Motivation
2. ODE & Slow-fast decomposition – Preliminaries
3. Case study & COMSOL Model - Equation-Based Modeling
4. Conclusion – Future prospects

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- Let us solve an *(ill-posed) inverse problem* of **PARAMETER ESTIMATION**!
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E.g., if a (quasi) periodic behaviour is expected...
How to identify the dynamics evolving in *slow time*?

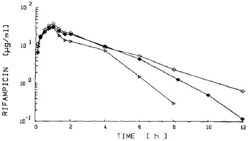

Fig. 2. Rifampicin serum concentration-time curves from patient 4 following intravenous administration of 600 mg rifampicin on day 1 (◇), day 8 (◆) and day 22 (▷)

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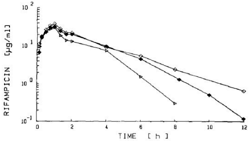

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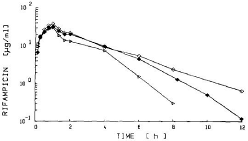

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- **COMSOL Multipysics (Equation-Based Modeling)** can help !!!

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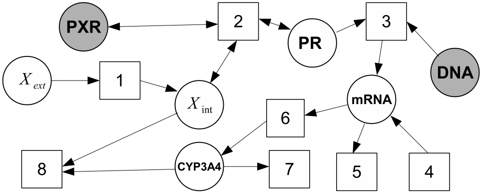
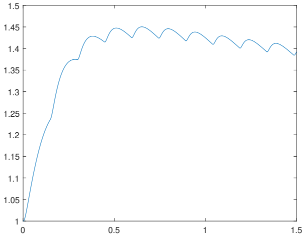
Drug *rifampicin* metabolism and the PXR-mediated XME induction process





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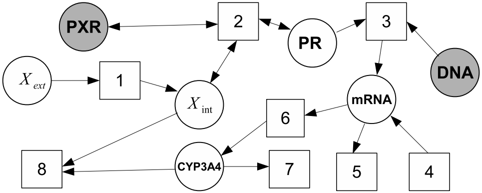

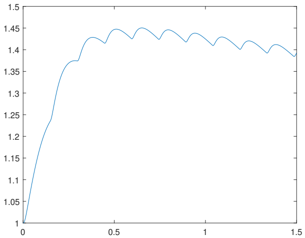

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J. D. Tebbens, C. Matonoha, A. Matthios, Š. Papáček: On parameter estimation in an *in vitro* compartmental model for drug-induced enzyme production in pharmacotherapy. Applications of Mathematics, 64 (2019), 253-277.

Method of multiple scales (MMS) for *slow-fast* ODEs

Two time-scales: fast t and slow ϵt. The WKB method.

- General IVP (n-order ODE): Dynamics of state variables $y \in \mathbb{R}$ is:

$$\frac{\mathrm{d}^n\, y(p,t,\epsilon t)}{\mathrm{d}t^n} = f\left(\frac{\mathrm{d}^{n-1}\, y(p,t,\epsilon t)}{\mathrm{d}t^{n-1}}, \ldots, y(p,t,\epsilon t)\right), \tag{3}$$

  with the corresponding initial conditions, $p \in \mathbb{R}^q$ and $\epsilon \ll 1$.

- For some systems, so-called *secular terms* invalidate the solution when $t = O(1/\epsilon)$.
- The WKB method: we look for a solution of the form $y = y(\theta, \tau, \epsilon, p)$, $\theta = \frac{1}{\epsilon}\varphi(\epsilon t)$ and $\tau = \epsilon t$, where we require y to be 2π-periodic function of the 'fast' variable θ, i.e. $y(\theta, \tau, \epsilon, p) = y(\theta + 2\pi, \tau, \epsilon, p)$.
- By the chain rule, Eq. (4), we can transform the ODE (3) into a PDE ....

$$\frac{\mathrm{d}\,(\bullet)}{\mathrm{d}t} = \varphi_\tau \frac{\partial(\bullet)}{\partial\theta} + \epsilon \frac{\partial(\bullet)}{\partial\tau}. \tag{4}$$

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J. Kevorkian, J.D. Cole, Multiple Scale and Singular Perturbation Methods, Springer, New York, 1996.

https://en.wikipedia.org/wiki/Multiple-scale-analysis

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(one simple) Two time-scale process #2:

Initial value problem of a pendulum with slowly changing length

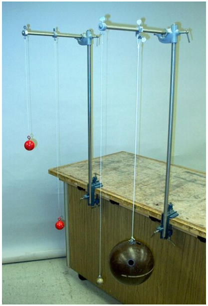
Using (4) the ODE (5) is transformed → PDE with two 'almost independent' time variables (defining the computational domain).

ODE describing the position y (an angle) is following

$$\frac{\mathrm{d}^2\, y(t, \epsilon t)}{\mathrm{d}t^2} + \omega^2\, y = 0, \qquad (5)$$

with I.C. : $y(0) = 1\,,\ \dot{y}(0) = 0,$

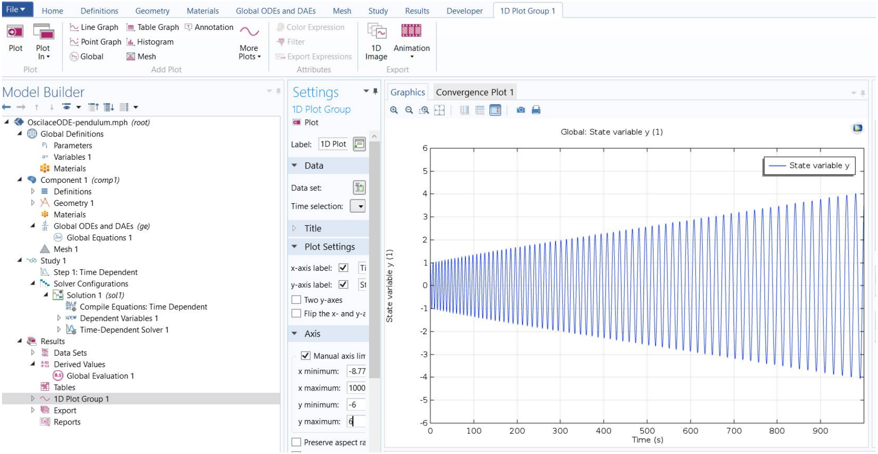
and $\boxed{\omega^2 = \frac{g}{l(\epsilon t)}}$ where $l = l_0(1 + \epsilon t)$.



Eventually, let us start with COMSOL Multiphysics!

1^{st} step: The Global **ODEs** and DAEs (ge) interface

under the **Mathematics** branch



2^{nd} step: **PDE** interface – the **Mathematics** branch

Coefficient Form PDE - General Form PDE - Weak Form PDE

Periodic behavior in fast time ($t \equiv x$) $\rightarrow$ 1D element $[0, 2\pi]$ with periodic BC.
Slow time ($\tau \equiv \epsilon x$) 'runs' from 0 to $T_f = \epsilon \cdot t_{final}$, only (comput. time saving...).
Initial value for y (a function of x), Initial time derivative $\frac{\partial y}{\partial \tau}$, etc.

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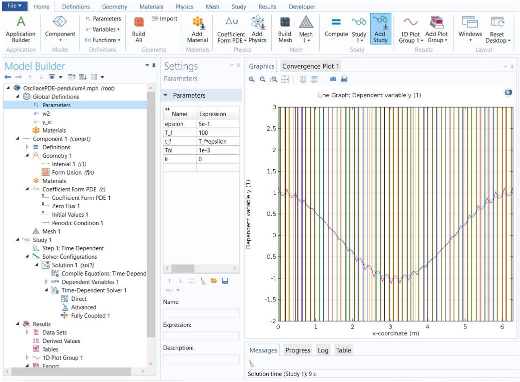

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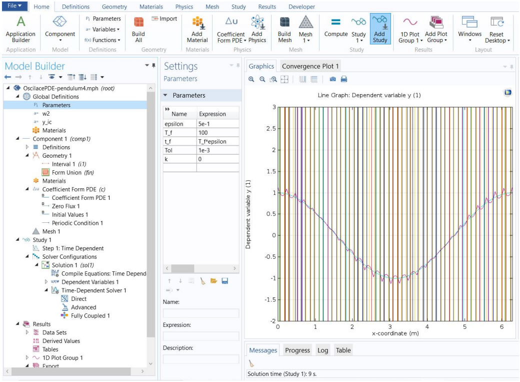

Obviously not successful attempt! The solution $y(x, \tau)$ is to be expected as a perturbation-series: $y(x, \tau) = Y_0(x, \tau) + \epsilon Y_1(x, \tau) + \mathcal{O}(\epsilon^2) \rightarrow$ at least 2 PDEs …

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- *Do roka a do dne :)*

Conclusion – Questions?

Thanks for your kind attention!

„Až si příště bude někdo stěžovat, že jste udělali chybu, tak mu řekněte, že je to možná dobře. Protože bez nedokonalostí a chyb bych neexistoval ani já ani vy."

– Stephen Hawking (1942-2018)