Properties of the Solutions to “Fractionalized” ODE Systems, with Applications to Processes Arising in the Life Sciences

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Acknowledgement

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Runtime Exploitation of Application Dynamism for Energy-efficient eXascale computing

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European Commission
Horizon 2020
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Goal of the Presentation

The primary goal of this talk is

- not to present new results,
- but to
  - mention some important open problems, and
  - initiate some research work in this respect.

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Frequently Seen Research Approach

Concrete problem
(engineering, physics, chemistry, biology, . . .)

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Classical mathematical model
(integer order derivatives)

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↓

Classical mathematical model
(integer order derivatives)

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Numerical algorithm

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Concrete problem
(engineering, physics, chemistry, biology, ...)

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Classical mathematical model
(integer order derivatives)

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Numerical algorithm

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Simulation results

Frequently Seen Research Approach

Concrete problem
(engineering, physics, chemistry, biology, . . .)

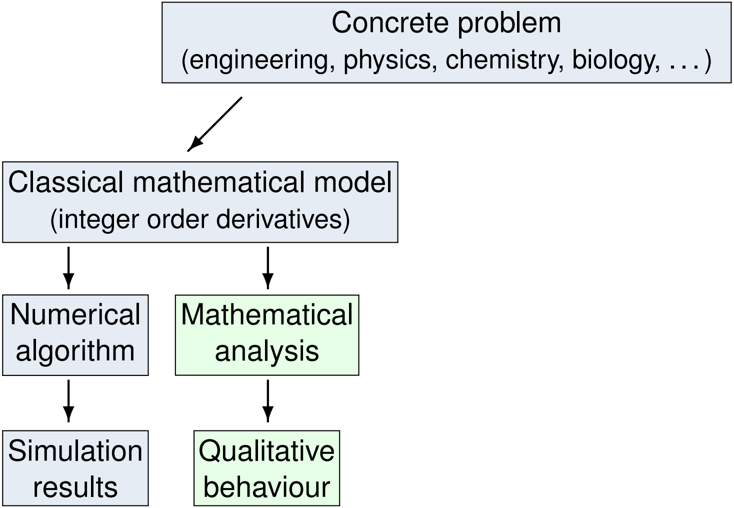
Classical mathematical model
(integer order derivatives)

Numerical algorithm

Mathematical analysis

Simulation results

Frequently Seen Research Approach



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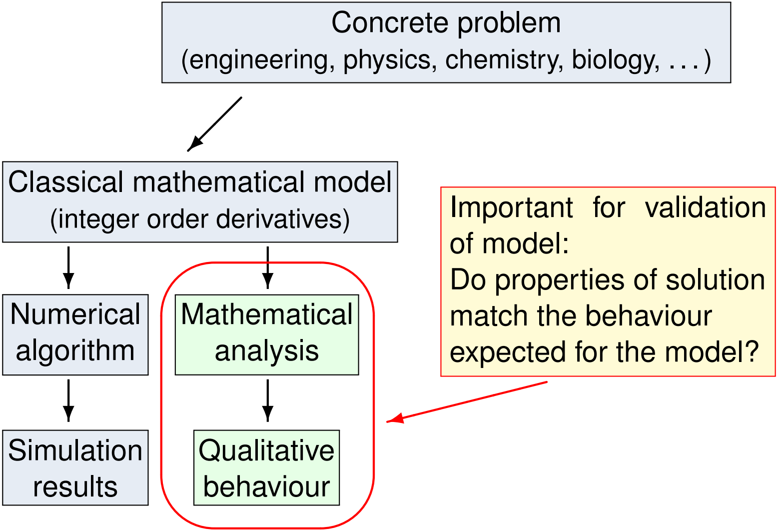

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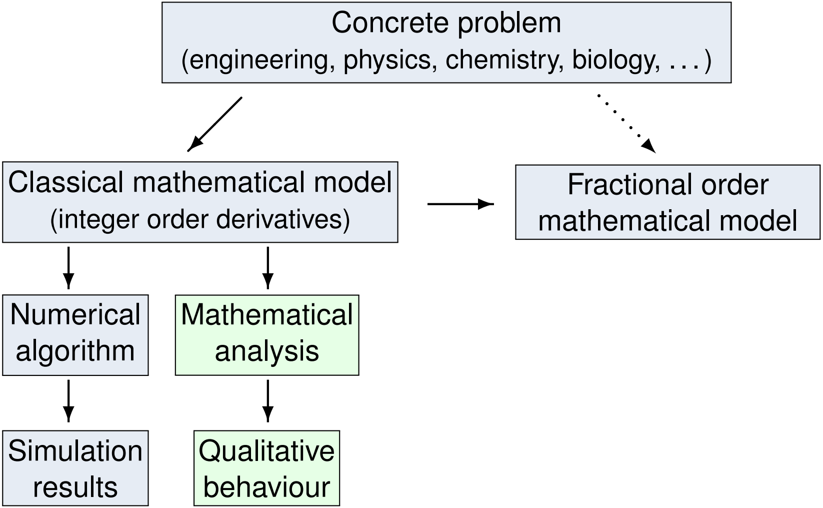

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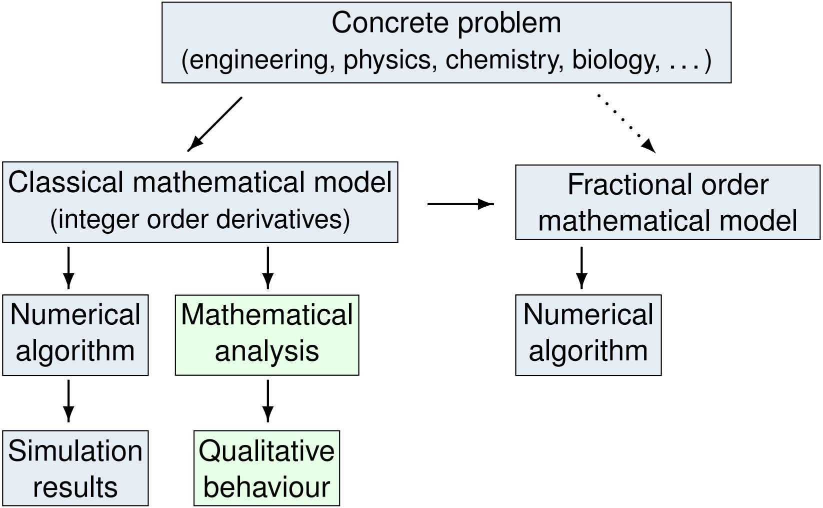

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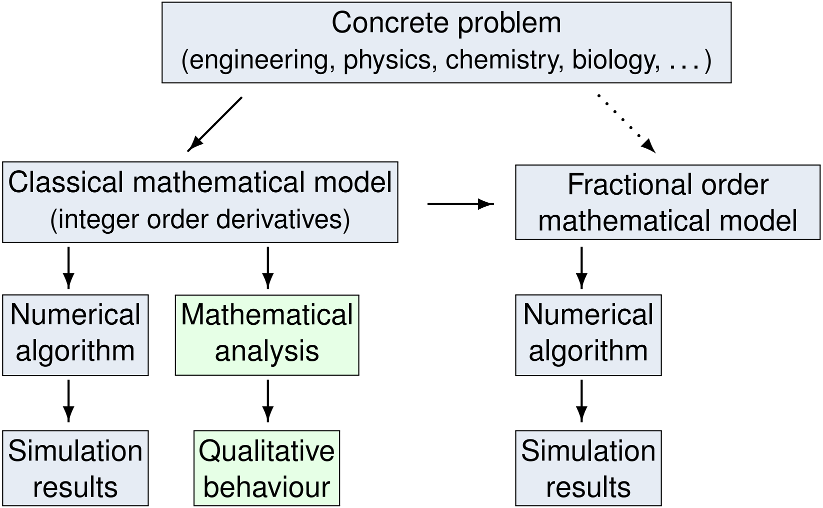

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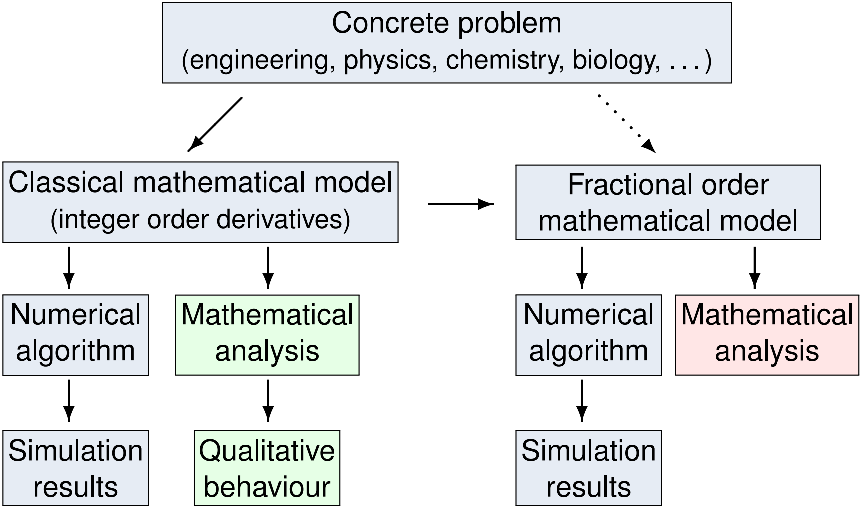

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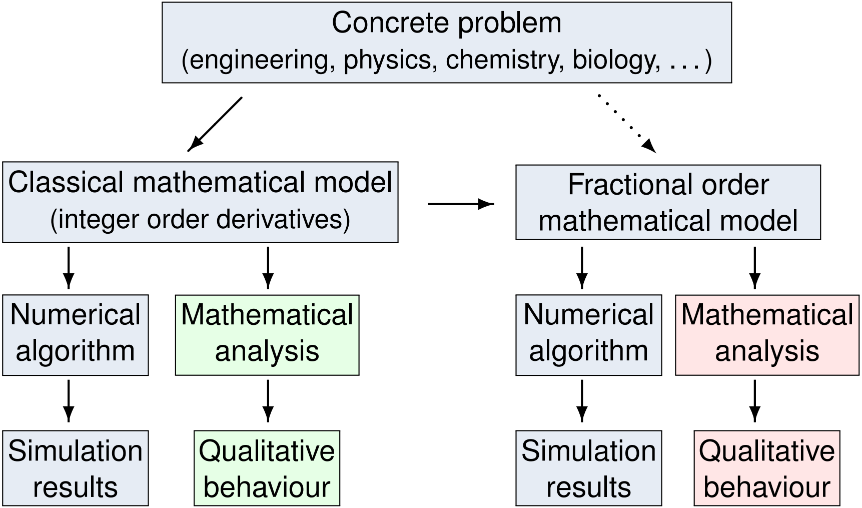

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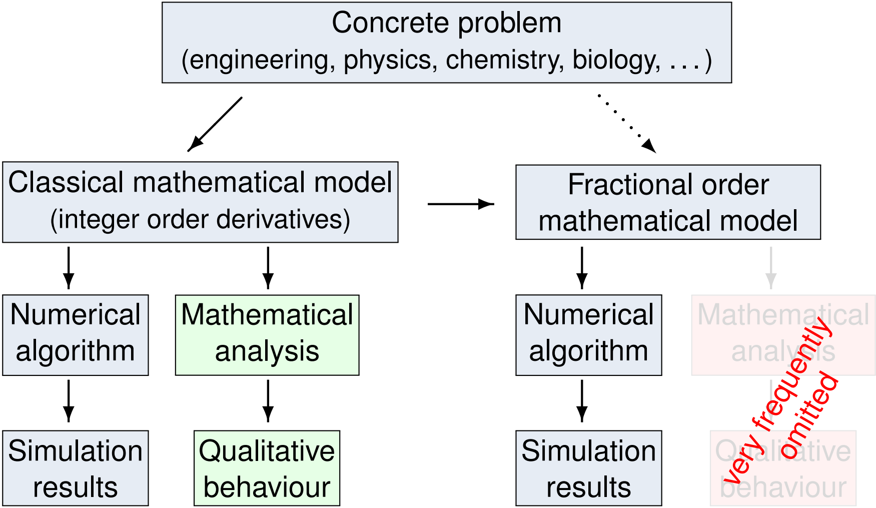

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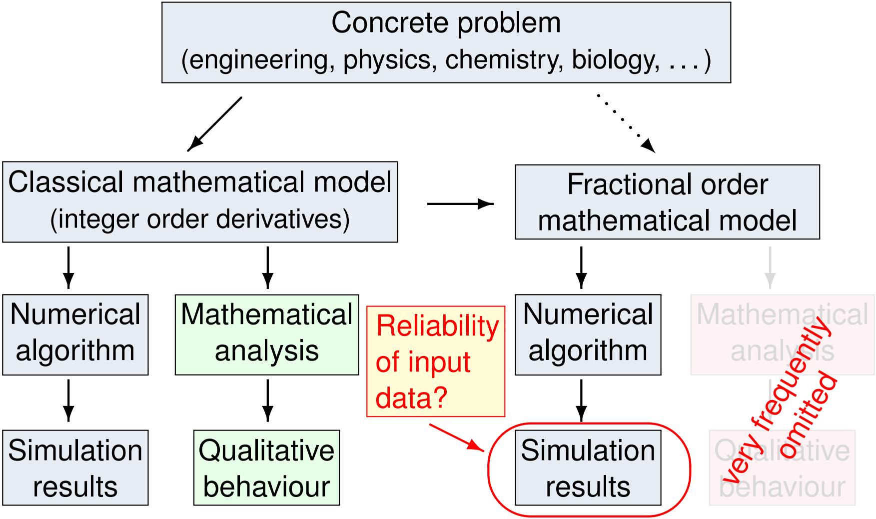

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Dengue Fever

- Most important arthropod-borne viral disease of humans
- Transmitted from human to human via bites of (female) mosquitoes
  (mainly *Aedes aegypti* but also, e.g., *Aedes albopictus*)
- Endemic in many parts of the region from 35° N to 35° S
- Approx. 2.5 billion people living in the affected countries
- Likely to spread even further, e.g. to central and even northern Europe, in the coming decades

(World Health Organization, 2009)

SIR Model

- Human population is decomposed into 3 groups (susceptible, infected, recovered)
- Mosquito population is decomposed into 2 groups (susceptible, infected)

$$
\begin{aligned}
D^1 \; S_\mathrm{h} &= \mu_\mathrm{h}(N_\mathrm{h} - S_\mathrm{h}) - \frac{\beta_\mathrm{h} b}{N_\mathrm{h} + m} S_\mathrm{h} I_\mathrm{m} \\
D^1 \; I_\mathrm{h} &= \frac{\beta_\mathrm{h} b}{N_\mathrm{h} + m} S_\mathrm{h} I_\mathrm{m} - (\mu_\mathrm{h} + \gamma) I_\mathrm{h} \\
D^1 \; R_\mathrm{h} &= \gamma I_\mathrm{h} - \mu_\mathrm{h} R_\mathrm{h} \\
D^1 \; S_\mathrm{m} &= A - \frac{\beta_\mathrm{m} b}{N_\mathrm{h} + m} S_\mathrm{m} I_\mathrm{h} - \mu_\mathrm{m} S_\mathrm{m} \\
D^1 \; I_\mathrm{m} &= \frac{\beta_\mathrm{m} b}{N_\mathrm{h} + m} S_\mathrm{m} I_\mathrm{h} - \mu_\mathrm{m} I_\mathrm{m}
\end{aligned}
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D_*^{\alpha_h} S_h &= \mu_h (N_h - S_h) - \frac{\beta_h b}{N_h + m} S_h I_m \\
D_*^{\alpha_h} I_h &= \frac{\beta_h b}{N_h + m} S_h I_m - (\mu_h + \gamma) I_h \\
D_*^{\alpha_h} R_h &= \gamma I_h - \mu_h R_h \\
D_*^{\alpha_m} S_m &= A - \frac{\beta_m b}{N_h + m} S_m I_h - \mu_m S_m \\
D_*^{\alpha_m} I_m &= \frac{\beta_m b}{N_h + m} S_m I_h - \mu_m I_m
\end{aligned}
$$

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Parameters in Integer Order Model

Example equation from SIR model:

$$D^1 \quad I_m = \frac{\beta_m b}{N_h + m} S_m I_h - \mu_m I_m$$

Unknown functions:

- I_m — # of infected mosquitoes
- S_m — # of susceptible mosquitoes
- I_h — # of infected humans

Parameters in Integer Order Model

Example equation from SIR model:

$$D^1 \quad I_m = \frac{\beta_m b}{N_h + m} S_m I_h - \mu_m I_m$$

Parameters:

- μ_m — per capita mortality rate of mosquitoes
- b — biting rate (avg. # of bites per mosquito per day)
- N_h — total # of humans
- m — # of alternative blood sources for mosquitoes
- β_m — transmission probability (human $\rightarrow$ mosquito)

Parameters in Integer Order Model

Example equation from SIR model:

$$D^1 \quad I_\mathrm{m} = \frac{\beta_\mathrm{m} b}{N_\mathrm{h} + m} S_\mathrm{m} I_\mathrm{h} - \mu_\mathrm{m} I_\mathrm{m}$$

Typical values (Cape Verde outbreak, 2009):

- $\mu_\mathrm{m} = 0.1\,\mathrm{d}^{-1}$
- $b = 0.7\,\mathrm{d}^{-1}$
- $N_\mathrm{h} = 56\,000$
- $m = 0$
- $\beta_\mathrm{m} = 0.36$

Parameters in Integer Order Model

Example equation from SIR model:

$$D^1 \quad I_{\mathrm{m}} = \frac{\beta_{\mathrm{m}} b}{N_{\mathrm{h}} + m} S_{\mathrm{m}} I_{\mathrm{h}} - \mu_{\mathrm{m}} I_{\mathrm{m}}$$

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$$\left.\begin{array}{l} \bullet\ \ N_{\mathrm{h}} = 56\,000 \\ \bullet\ \ m = 0 \\ \bullet\ \ \beta_{\mathrm{m}} = 0.36 \end{array}\right\} \text{dimensionless}$$

Parameters in Fractional Order Model

Example equation from SIR model:

$$D_*^{\alpha_{\mathrm{m}}} I_{\mathrm{m}} = \frac{\beta_{\mathrm{m}} b}{N_{\mathrm{h}} + m} S_{\mathrm{m}} I_{\mathrm{h}} - \mu_{\mathrm{m}} I_{\mathrm{m}}$$

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- $\beta_m = 0.36$

Mismatch of dimensions between LHS ($\text{time}^{-\alpha_m}$) and RHS (time^{-1})!

Handling of Parameters for Fractionalized ODEs

Fundamental Message

Parameters known to be valid for integer-order models need to be very carefully transferred to fractional generalizations of models.

Possible solution:

$$D_*^{\alpha_m} I_m = \frac{\beta_m b^{\alpha_m}}{N_h + m} S_m I_h - \mu_m^{\alpha_m} I_m$$

Properties:

- Resolves dimensional mismatch
- Analog approach can be used for other equations of model

Handling of Parameters for Fractionalized ODEs

Fundamental Message

Parameters known to be valid for integer-order models need to be very carefully transferred to fractional generalizations of models.

Possible solution:

$$D_*^{\alpha_m} I_m = \frac{\beta_m b^{\alpha_m}}{N_h + m} S_m I_h - \mu_m^{\alpha_m} I_m$$

Questions:

- Does technical meaning of b match its use in equation?
- Would an alternative approach be more appropriate?
  If yes, which one?

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FDE Model for Fermentation Process

Manufacturing of bio-ethanol:

- Biological reactive system
- End product used, e.g., as fuel for combustion engines
- Reactor contains
  - biomass (bacteria)
    concentration $b(t)$ at time t; $0 < b(0) =: b_0$ known
  - subtrate (sugar)
    concentration $s(t)$ at time t; $0 < s(0) =: s_0$ known
  - end product (ethanol)
    concentration $e(t)$ at time t; $0 = e(0) =: e_0$

FDE Model for Fermentation Process

Evolution of component concentrations during the process:

- Bacteria reproduce (rate $\sim b(t)s(t)$)

(Toledo-Hernandez et al., 2014)

FDE Model for Fermentation Process

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Evolution of component concentrations during the process:

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FDE Model for Fermentation Process

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Evolution of component concentrations during the process:

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- Bacteria consume substrate; rate $\sim b(t)s(t)$

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- Bacteria convert substrate into ethanol; rate $\sim b(t)s(t)$

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$\beta, \sigma, \epsilon \in (0, 1]$, hence rates are of fractional order, i.e. parameters c, b, k, p have unit time^{-r}, $r \in (0, 1]$

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$$\begin{aligned} D_*^\beta b(t) &= cb(t)s(t) - mb(t), & b(0) &= b_0 \\ D_*^\sigma s(t) &= -kb(t)s(t), & s(0) &= s_0 \\ D_*^\epsilon e(t) &= pb(t)s(t), & e(0) &= 0 \end{aligned}$$

$\beta, \sigma, \epsilon \in (0, 1]$, hence rates are of fractional order,
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Fractional System and Integer Order Counterpart

$$
\begin{aligned}
D_*^{\beta} b(t) &= \quad cb(t)s(t) - mb(t), \quad & b(0) = b_0 \qquad (1)\\
D_*^{\sigma} s(t) &= -kb(t)s(t), & s(0) = s_0 \qquad (2)\\
D_*^{\epsilon} e(t) &= \quad pb(t)s(t), & e(0) = 0 \qquad (3)
\end{aligned}
$$

$$c > 0, \quad m \geq 0, \quad k > 0, \quad p > 0$$

$$b_0 > 0, \qquad s_0 > 0$$

D_*^{α} denotes the Caputo operator of order α.

Fractional System and Integer Order Counterpart

$$
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D_*^{\beta} b(t) &= cb(t)s(t) - mb(t), & b(0) &= b_0 & (1)\\
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\end{aligned}
$$

$$c > 0, \quad m \geq 0, \quad k > 0, \quad p > 0$$

$$b_0 > 0, \qquad s_0 > 0$$

System is only partially coupled:
Function e appears only in Eq. (3) but not in Eqs. (1) and (2).

Fractional System and Integer Order Counterpart

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\begin{aligned}
D_*^{\beta} b(t) &= cb(t)s(t) - mb(t), & b(0) &= b_0 & (1)\\
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D_*^{\epsilon} e(t) &= pb(t)s(t), & e(0) &= 0 & (3)
\end{aligned}
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$$c > 0, \quad m \geq 0, \quad k > 0, \quad p > 0$$

$$b_0 > 0, \qquad s_0 > 0$$

$\Rightarrow$ Solve in two steps:

(a) Solve subsystem (1) & (2) for b and s,

(b) solve (3) for e.

Fractional System and Integer Order Counterpart

$$
\begin{aligned}
D^1 b(t) &= \quad cb(t)s(t) - mb(t), \quad & b(0) = b_0 \qquad (1)\\
D^1 s(t) &= -kb(t)s(t), & s(0) = s_0 \qquad (2)\\
D^1 e(t) &= \quad pb(t)s(t), & e(0) = 0 \qquad (3)
\end{aligned}
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Behaviour of Solutions as t Varies (1)

Integer order case:

- Solution exists for all $t \geq 0$
  $\Rightarrow$ Process can run for arbitrarily long interval of time
- All components of solution are nonnegative
  $\Rightarrow$ Negative concentrations do not make sense

Method of proof:

- Substitution $b(t) = \exp(-(B(t))\ \ )$, $s(t) = \exp(-(S(t))\ \ )$
- Use chain rule to rewrite differential equation

Behaviour of Solutions as t Varies (1)

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Method of proof:

- Substitution $b(t) = E_\beta\ (-(B(t))^\beta)$, $s(t) = E_\sigma\ (-(S(t))^\sigma)$?
- Use chain rule to rewrite differential equation

Behaviour of Solutions as t Varies (2)

Integer order case:

- Function s is monotone decreasing
  $\Rightarrow$ Substrate is consumed but not replaced
- Function e is monotone increasing
  $\Rightarrow$ Ethanol is produced but not consumed

Method of proof:

Differential equation yields info about sign of $D^1 s$ and $D^1 e$

$\Rightarrow$ monotonicity follows directly

Behaviour of Solutions as t Varies (2)

Fractional order case:

- Function s is monotone decreasing
  $\Rightarrow$ Substrate is consumed but not replaced **?**
- Function e is monotone increasing
  $\Rightarrow$ Ethanol is produced but not consumed **?**

Method of proof:

Differential equation yields info about sign of $D_*^\sigma s$ and $D_*^\epsilon e$

$\Rightarrow$ monotonicity not necessarily asserted

(Al-Refai 2012; Di. 2016)

Behaviour of Solutions as t Varies (3)

Integer order case:

- Function b is monotone increasing if $m = 0$
  $\Rightarrow$ Bacteria reproduce but do not die
- Function b is monotone decreasing for $t > T^*$ if $m > 0$
  $\Rightarrow$ After certain point in time, mortality $>$ reproduction

Method of proof:

Differential equation yields info about sign of $D^1 b$

$\Rightarrow$ monotonicity follows directly

Behaviour of Solutions as t Varies (3)

Fractional order case:

- Function b is monotone increasing if $m = 0$?
  $\Rightarrow$ Bacteria reproduce but do not die
- Function b is monotone decreasing for $t > T^*$ if $m > 0$?
  $\Rightarrow$ After certain point in time, mortality $>$ reproduction

Method of proof:

Differential equation yields info about sign of $D_*^\beta b$

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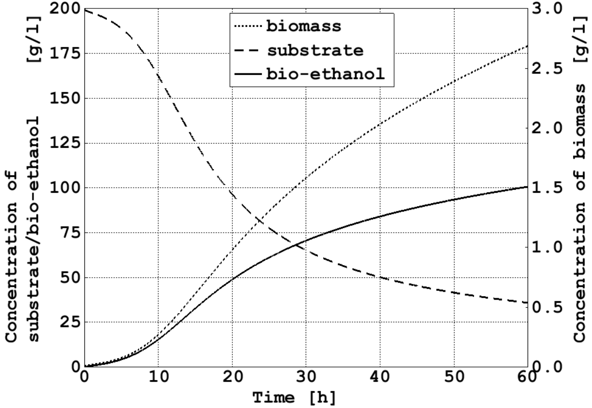
(Al-Refai 2012; Di. 2016)

Behaviour of Solutions as t Varies



Evolution of components of solution for fractional order model with $m = 0$

Behaviour of Solutions as t Varies (4)

Integer order case:

- $\lim_{t\to\infty} b(t) = 0$ if $m > 0$; $\lim_{t\to\infty} b(t) = b_0 + s_0 c/k$ if $m = 0$
  $\Rightarrow$ Bacteria die out if mortality > 0; saturation otherwise
- $\lim_{t\to\infty} s(t) = 0$
  $\Rightarrow$ Substrate is consumed completely

Method of proof:

- Substitution $b(t) = \exp(-(B(t))\ \ )$, $s(t) = \exp(-(S(t))\ \ )$
- Use chain rule to rewrite differential equation
- Use results given above

Behaviour of Solutions as t Varies (4)

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- $\lim_{t\to\infty} b(t) = 0$ if $m > 0$; $\lim_{t\to\infty} b(t) = b_0 + s_0 c/k$ if $m = 0$ **?**
  $\Rightarrow$ Bacteria die out if mortality > 0; saturation otherwise
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  $\Rightarrow$ Substrate is consumed completely **?**

Method of proof:

- Substitution $b(t) = E_\beta\left(-(B(t))^\beta\right)$, $s(t) = E_\sigma\left(-(S(t))^\sigma\right)$ **?**
- Use chain rule to rewrite differential equation
- Use results given above

Behaviour of Solutions as t Varies (5)

Integer order case:

- $\lim_{t\to\infty} e(t)$ exists
  $\Rightarrow$ Limited amount of ethanol can be produced
- $\lim_{t\to\infty} e(t)$ is independent of b_0
  $\Rightarrow$ Production depends only on initial amount of substrate

Method of proof:

- Substitution $b(t) = \exp(-(B(t))\ \ )$, $s(t) = \exp(-(S(t))\ \ )$
- Use chain rule to rewrite differential equation
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Behaviour of Solutions as t Varies (5)

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- Substitution $b(t) = E_\beta\left(-(B(t))^\beta\right)$, $s(t) = E_\sigma\left(-(S(t))^\sigma\right)$ **?**
- Use chain rule to rewrite differential equation
- Use results given above

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Behaviour of Solutions as Initial Value b_0 Varies

Integer order case ($m = 0$):

For $b_0 < \tilde{b}_0$ (higher initial concentration of bacteria),

- $b(b_0, s_0; t) < b(\tilde{b}_0, s_0; t)$ for all $t > 0$
  $\Rightarrow$ Persisently higher number of bacteria during process
- $e(b_0, s_0; t) < e(\tilde{b}_0, s_0; t)$ for all $t > 0$
  $\Rightarrow$ Faster production of ethanol
- Under certain additional conditions,
  $s(b_0, s_0; t) > s(\tilde{b}_0, s_0; t)$ for all $t > 0$
  $\Rightarrow$ Faster consumption of substrate

Method of proof:

- Explicit expression for solution in closed form

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  $\Rightarrow$ Faster production of ethanol
- Under certain additional conditions,
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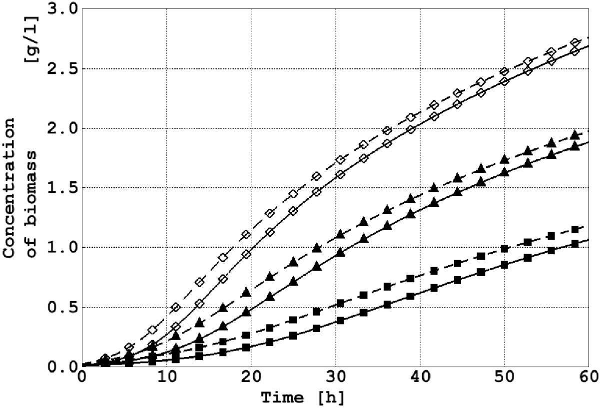
Method of proof:

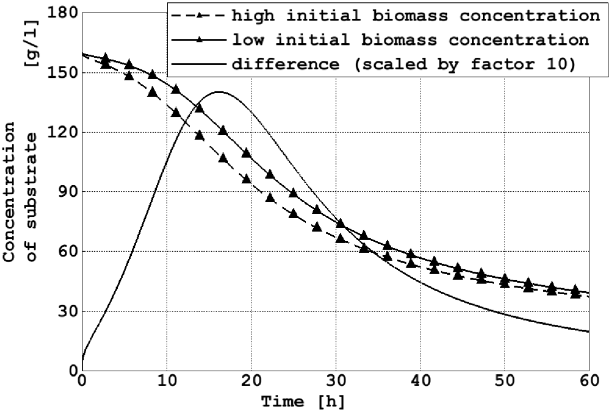
- Explicit expression for solution in closed form **?**

Behaviour of Solutions as Initial Value b_0 Varies



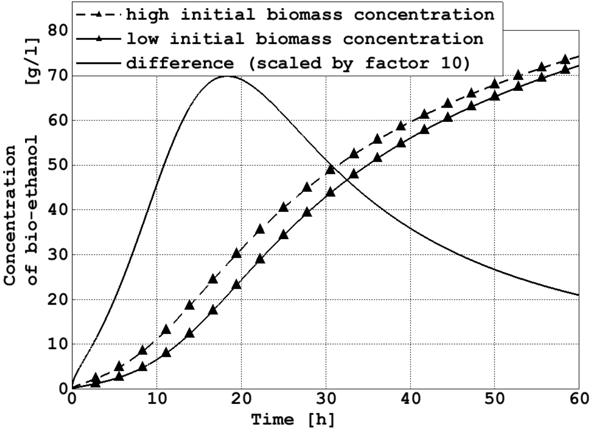
Evolution of biomass concentration for fractional order model with small b_0 (continuous line) and large b_0 (dashed)

Behaviour of Solutions as Initial Value b_0 Varies



Evolution of substrate concentration for fractional order model with different initial values for b_0 and fixed s_0

Behaviour of Solutions as Initial Value b_0 Varies



Evolution of ethanol concentration for fractional order model with different initial values for b_0 and fixed s_0

Behaviour of Solutions as Initial Value s_0 Varies

Integer order case ($m = 0$):

For $s_0 < \tilde{s}_0$ (higher initial concentration of substrate),

- $b(b_0, s_0; t) < b(b_0, \tilde{s}_0; t)$ for all $t > 0$
  $\Rightarrow$ Persistently higher number of bacteria during process
- $e(b_0, s_0; t) < e(b_0, \tilde{s}_0; t)$ for all $t > 0$
  $\Rightarrow$ Faster production of ethanol
- Under certain additional conditions,
  $s(b_0, s_0; t) < s(b_0, \tilde{s}_0; t)$ if and only if t sufficiently small
  $\Rightarrow$ Higher substrate amount not persistent during process

Method of proof:

- Explicit expression for solution in closed form

Behaviour of Solutions as Initial Value s_0 Varies

Fractional order case ($m = 0$):

For $s_0 < \tilde{s}_0$ (higher initial concentration of substrate),

- $b(b_0, s_0; t) < b(b_0, \tilde{s}_0; t)$ for all $t > 0$
  $\Rightarrow$ Persistently higher number of bacteria during process **?**
- $e(b_0, s_0; t) < e(b_0, \tilde{s}_0; t)$ for all $t > 0$ **?**
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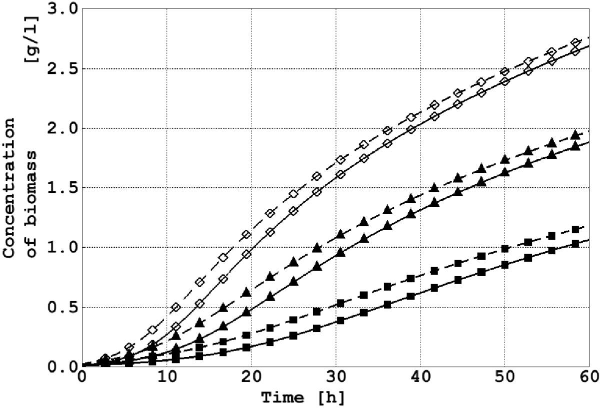
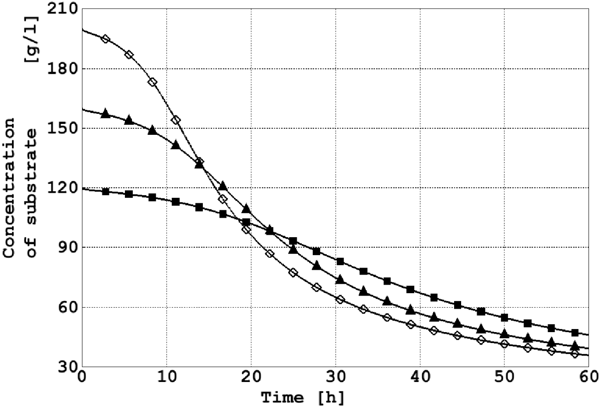
Behaviour of Solutions as Initial Value s_0 Varies



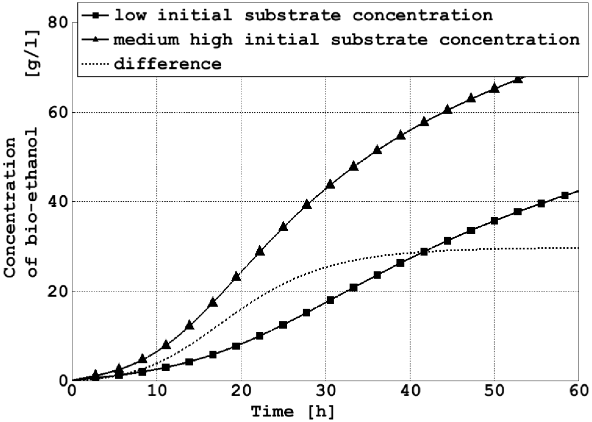
Evolution of biomass concentration for fractional order model with small b_0 (continuous line) and large b_0 (dashed)

Behaviour of Solutions as Initial Value s_0 Varies



Evolution of substrate concentration for fractional order model with different initial values for s_0 and fixed b_0

Behaviour of Solutions as Initial Value s_0 Varies



Evolution of ethanol concentration for fractional order model with different initial values for s_0 and fixed b_0

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Future Work

- Investigate behaviour subject to change of b_0 or s_0 also in case $m > 0$
- Perform exhaustive investigation of numerical examples
  - all possible combinations of orders β, σ, and ϵ
  - significantly varying choices of initial values b_0 and s_0 and parameters c, m, k, and p
  - behaviour of solutions for very large times t
- Develop techniques for analytically proving conjectured properties
  (not only for this special ODE system but in more general case)

Design of Numerical Experiments

Numerical experiments require solution of large number of fractional ODE systems on very long time intervals

- Extremely high computational cost
- Use of High Performance Computing platforms required
- Corresponding software needs to be optimized with respect to performance and energy requirements

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The READEX Toolsuite

READEX toolsuite (currently under development) allows (semi-)automatic tuning of HPC codes for energy without significant loss of performance

- at software design time:
  - run program with typical input data sets
  - identify regions of code with significant influence on performance and energy
  - for each region, test different environment settings (# of MPI taks, # of OpenMP threads, CPU frequency, . . .) and determine optimal choice for possible scenarios
- at runtime:
  - READEX runtime library switches environment parameters to optimal values for each part of the program execution

Further information: `http://www.readex.eu`

Current Tools Landscape

Unified measurement infrastructure

Score-P (`http://www.score-p.org`)

Current Tools Landscape

Analysis tools for performance

- CUBE: Profiling
- Scalasca: Automatic trace analysis
- Vampir: Interactive trace analysis
- TAU: Profiling and tracing
- Periscope Tuning Framework:
  On-line analysis and tuning

Unified measurement infrastructure

Score-P (`http://www.score-p.org`)

Current Tools Landscape

Analysis tools for performance and energy requirements

- CUBE: Profiling
- Scalasca: Automatic trace analysis
- Vampir: Interactive trace analysis
- TAU: Profiling and tracing

new: visualization & analysis capabilities for energy related metrics

- Periscope Tuning Framework: On-line analysis and tuning

new: energy tuning plugins (PCAP, DVFS, MPIProcs, ...)

Unified measurement infrastructure

Score-P (`http://www.score-p.org`)

new: interface to energy measurement hardware

Extensions (Work in Progress in READEX Project)

(Semi)-automatic energy tuning I: At design time

Extensions (Work in Progress in READEX Project)

(Semi)-automatic energy tuning I: At design time

- Select parameters to be used for tuning, e.g.
  - # of OpenMP threads
  - # of MPI processes
  - CPU frequency
  - different code paths
  - . . .

Extensions (Work in Progress in READEX Project)

(Semi)-automatic energy tuning I: At design time

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- Identify points in code where change of tuning parameters is reasonable

Extensions (Work in Progress in READEX Project)

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Extensions (Work in Progress in READEX Project)

(Semi)-automatic energy tuning I: At design time

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  - ...
- Identify points in code where change of tuning parameters is reasonable
- Identify certain scenarios at design time
- Find energy-optimal configuration for continuation of program run

Extensions (Work in Progress in READEX Project)

(Semi)-automatic energy tuning II: At run time

Extensions (Work in Progress in READEX Project)

(Semi)-automatic energy tuning II: At run time

- Automatic switching between configurations at run time according to current scenario (via READEX runtime library)

Extensions (Work in Progress in READEX Project)

(Semi)-automatic energy tuning II: At run time

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Advantages:

- Platform-independent software development process
- User friendliness

Extensions (Work in Progress in READEX Project)

(Semi)-automatic energy tuning II: At run time

- Automatic switching between configurations at run time according to current scenario (via READEX runtime library)

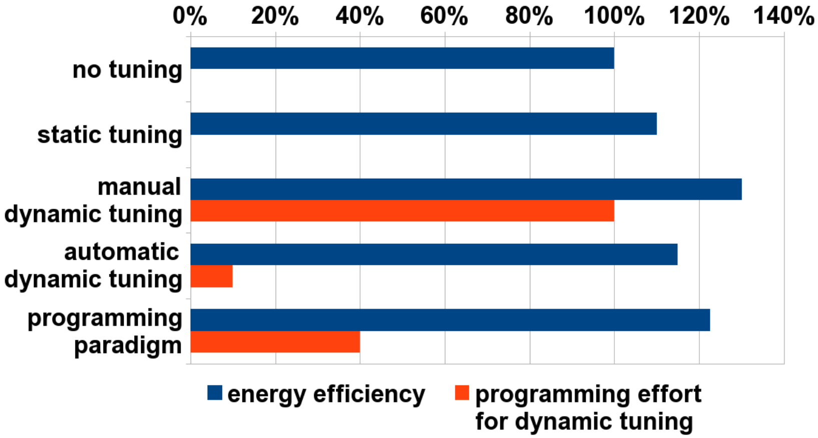
Advantages:

- Platform-independent software development process
- User friendliness

Future work:

- Development of programming paradigm for expressing dynamism
  Goal: further improvement of automatic dynamic tuning

Typical Outcome



Thank you for your attention!

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Further information:
http://www.vi-hps.org/projects/score-e
http://www.readex.eu

Further discussion on my blog:
http://fractionalworld.wordpress.com