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High order time-stepping methods for cardiac electrophysiology models

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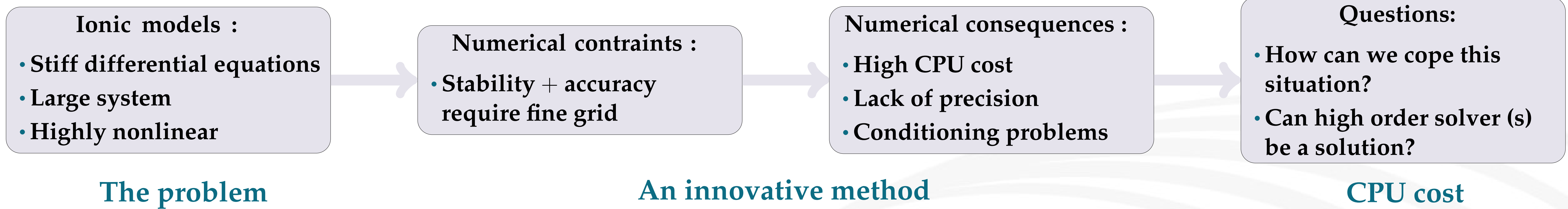
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Problematic of the time numerical integration in cardiac electrophysiology



EXAMPLE IONIC MODEL (TNNP)

Behavior of the physiological parameters :

- Different time and space scales.
- Fast and slow variables.
- Stiff wave fronts.

Numerical consequences :

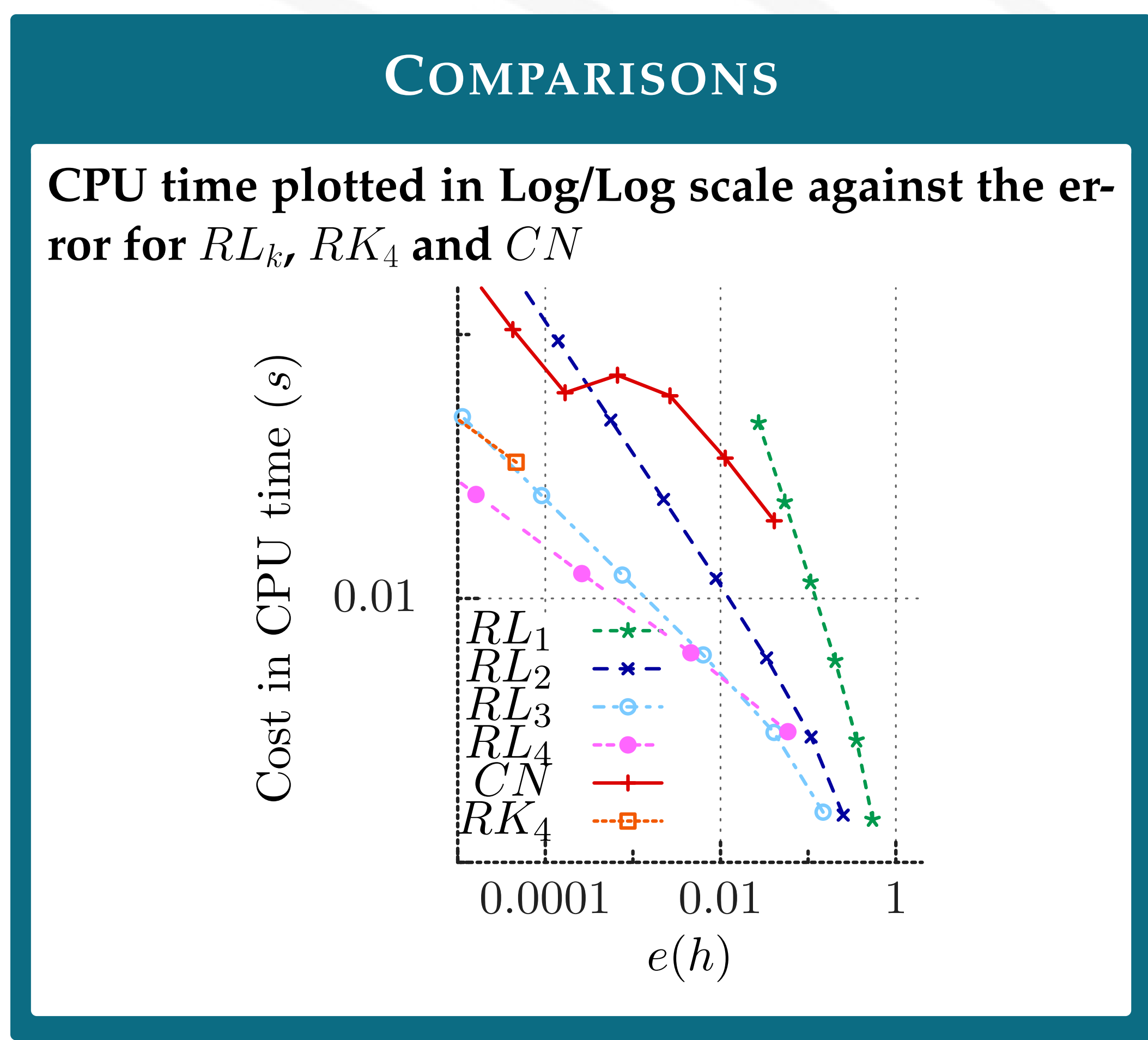
- Numerical instabilities.
- High computational cost.
- Significant loss of accuracy

HIGH-ORDER RUSH LARSEN METHODS

Consider the problem,
 $y' = a(t, y)y + b(t, y), y(0) = y_0,$
 transformed in each time discretization interval $(t_n, t_{n+1}]$ into,
 $y' = \alpha_n y + c_n(t, y),$
 with $c_n(t, y) = (a(t, y) - \alpha_n)y + b(t, y)$ and α_n a stabilizer. For $t \in (t_n, t_{n+1}]$, the exact solution of this problem satisfies the *variation of constant* formula
 $y(t) = e^{A(t)}(y_n + \int_{t_n}^t e^{-A(\tau)} c_n(\tau, y) d\tau),$
 with $A(t) = \alpha_n(t - t_n)$. If we set $t = t_{n+1}$ and approximate c_n by a constant β_n , we obtain the following definition of RL_k
 $y_{n+1} = y_n + h\varphi_1(\alpha_n h)(\alpha_n y_n + \beta_n).$
 $\varphi_1(z) = \frac{e^z - 1}{z}, \alpha_n$ and β_n are set so that the convergence order k is ensured.

RUSH LARSEN ORDER 3

$$\alpha_n = \frac{1}{12}(23a_n - 16a_{n-1} + 5a_{n-2}),$$

$$\beta_n = \frac{1}{12}(23b_n - 16b_{n-1} + 5b_{n-2}) + \frac{h}{12}(a_n b_{n-1} - a_{n-1} b_n).$$


Scheme properties

ADVANTAGES AND CONVERGENCE

- Explicit k -multi-step method:
 $y_n, y_{n-1}, \dots, y_{n-k+1} \rightarrow y_{n+1}.$
- Stability: The same critical time-step as the implicit schemes.
- Easy to implement.
- Cost: one evaluation of the model at every time step (minimal).

THEOREM. The RL_k scheme is stable under perturbation and converges with an error of order k , under the assumptions that $a(t, y)$ and $b(t, y)$ in the previous problem are C^k functions and its solution $y(t)$ is defined in $[0, T)$.

NUMERICAL ILLUSTRATION (Relative error for the BR model in Log/Log scale)

Discussion and conclusion

DISCUSSION:

- Ionic models are very stiff \Rightarrow classical explicit numerical solver must use small time-steps for stability \Rightarrow **Large CPU time.**
- **High order RL_k remain stable for large time-steps. Their critical time-steps don't depend on the stiffness but on the stabilizer's choice.**

CONCLUSION:

- We found that high order RL_k is a good alternative to improve the accuracy with negligible additional cost w/r to RL1 scheme.
- High order RL_k allow the use of large time steps unlike classical explicit schemes. They are suitable for solving stiff ODE.
- High order schemes in cardiac electrophysiology may allow more reliable simulations of long lasting events.

State of the art

STABILIZATION PRINCIPLE AND SOME STABILIZED SOLVERS

Equation on gating variables :
 $\frac{dW}{dt} = \frac{W_\infty(V) - W}{\tau(V)}$

Forward Backward scheme :
 $\frac{W^{n+1} - W^n}{\Delta t} = \frac{W_\infty(V^n) - W^{n+1}}{\tau(V^n)}$

This scheme allows large Δt , linear part = $\frac{-1}{\tau(V)}$.
Linear part known at time $t_n \Rightarrow$ Stabilization.

ORDER ONE SOLVERS :

- Forward backward Euler
- RL1: Rush Larsen (1978).

ORDER TWO SOLVER :

- RL2: Perego and Veneziani (2009).

HIGH ORDER METHODS :

- Exponential integrator of Adams type: Norsett (1969).
- Exponential Runge kutta and exponential multi-step (the last ten years).

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