High-order finite volume scheme for cardiac electrophysiology

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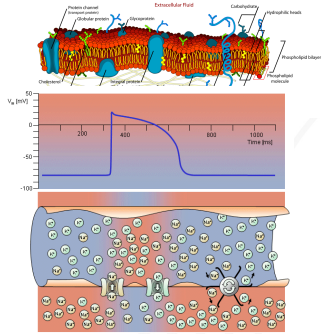
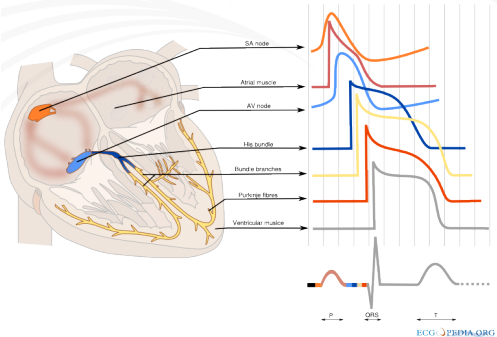
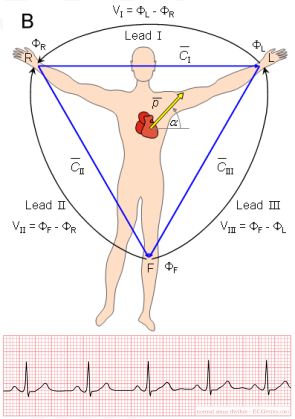
Introduction do electrocardiology





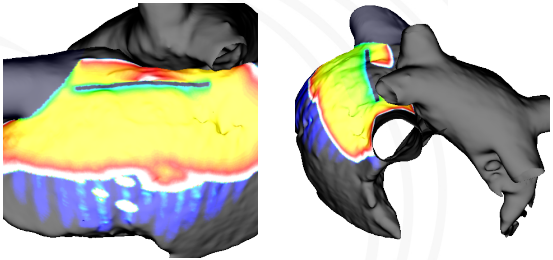


The propagation of a *fast and sharp* wavefront synchronizes the heart, rhythmically

→ reaction-diffusion equations

The monodomain model

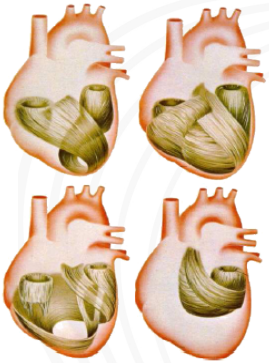
$$\partial_t V + I_{ion}(V, w) = \text{div}\,(D\nabla V),$$
$$\partial_t w = G(V, w),$$

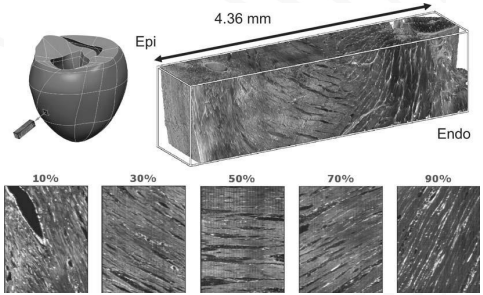


where (time in *ms* and space in *cm*):

- V $[mV]$ is the transmembrane voltage,
- $I_{ion} = I_{ion}(V, w)$ $[A.F^{-1}]$ is the normalized ioinc current per unit surface,
- $D = \frac{G}{A_m C_m}$ $[cm^2.ms^{-1}]$ is the normalized diffusion tensor,
- w contains all auxiliary variables

Anisotropy

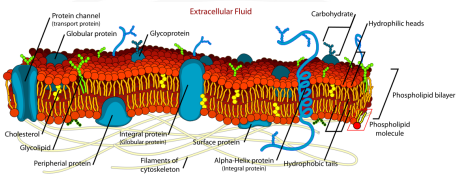


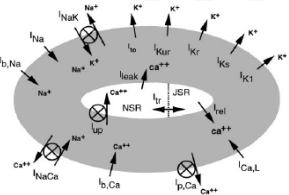


$$D = \sum_{k=1}^{3} d_k u_k(x) u_k(x)^T$$

- (u_1, u_2, u_3) is a Freinet basis associated to the fiber, and the laminae.
- $0 < d_1 \leq d_2 \leq d_3$ are normalized electrical conductivity coefficients

Ionic models





The ionic current I_{ion}, and the function G are given by a so-called *ionic model* which approximates all ionic processes in the cardiac cells:

- *Phenomenological models* (Fitzugh-Nagumo, Aliev-Panfilov, Mitchell-Schaeffer,...) are simple,
- *Hodgkin-Huxley type models* (Beeler-Reuter, Ten Tusscher et al, Luo-Rudy,..) are more complex. Markov chains variants (Iyer et al...) are nowadays widely used by biologists.

Aliev-Panfilov

The Aliev-Panfilov model is a simple 2-equations model:

$$I_{ion} = -\kappa V(V-a)(V-1) - wV,$$
$$g(V,w) = \left(\epsilon + \mu_1 \frac{w}{\mu_2 + V}\right)\left(-w - \kappa V(V-b-1)\right).$$

- Homogeneous monodomain + Aliev-Panfilov
  $\rightarrow$ bistable system which preserves $V \in (V_{min}, V_{max})$
- Its simplicity allows to obtain theoretical results; *e.g.* estimation of propagation velocity

Hodgkin-Huxley formalism

Mimics the behavior of molecular actors in the cell membrane:

$$I_{ion}(V, w) = \sum_j I_j \text{ where the } I_j\text{s are expressed as functions of } \textit{gating variables}$$

Example: $I_{Na} = g_{Na} m^3 hj(V - E_{Na})$, where

- $E_{Na} = \frac{RT}{F} \ln\left(\frac{[Na^+]_e}{[Na^+]_i}\right)$ is Nernst's potential,
- m, h, j are gating variables given by $\frac{d}{dt} m = \frac{m_\infty(V,w) - m}{\tau_m(V,w)}$

$w \in \mathbb{R}^N$, where N ranges from 8 to 100+, contains

- all *gating variables* like m, $0 \leq m \leq 1$
- other variables, and notably ion concentrations, $[Na]_{i,e} > 0$

Complete exemple: CRN [CRN98]

$$\frac{dV}{dt} = \frac{-(I_{ion} + I_{st})}{C_m} \tag{18}$$

$$\begin{aligned} I_{ion} = {} & I_{Na} + I_{K1} + I_{to} + I_{Kur} + I_{Kr} + I_{Ks} + I_{CaL} \\ & + I_{bCa} + I_{NaK} + I_{NaCa} + I_{bNa} + I_{bCa} \end{aligned} \tag{19}$$

$$\frac{dy}{dt} = \frac{y_\infty - y}{\tau_y} \text{ (where } y \text{ is any gating variable)} \tag{20}$$

$$\frac{d[Na^+]_i}{dt} = \frac{-3I_{NaK} - 3I_{NaCa} - I_{bNa} - I_{Na}}{F V_i} \tag{21}$$

$$\frac{d[K^+]_i}{dt} = \frac{2I_{NaK} - I_{K1} - I_{to} - I_{Kur} - I_{Kr} - I_{Ks} - I_{bK}}{F V_i} \tag{22}$$

$$\frac{d[Ca^{2+}]_i}{dt} = \frac{B1}{B2} \tag{23}$$

$$B1 = \frac{2I_{NaCa} - I_{pCa} - I_{CaL} - I_{bCa}}{2F V_i} + \frac{V_{up}(I_{up,leak} - I_{up}) + I_{rel} V_{rel}}{V_i} \tag{24}$$

$$B2 = 1 + \frac{[Trpn]_{max} K_{m,Trpn}}{([Ca^{2+}]_i + K_{m,Trpn})^2} + \frac{[Cmdn]_{max} K_{m,Cmdn}}{([Ca^{2+}]_i + K_{m,Cmdn})^2} \tag{25}$$

$$\frac{d[Ca^{2+}]_{up}}{dt} = I_{up} - I_{up,leak} - \frac{I_{tr} V_{rel}}{V_{up}} \tag{26}$$

$$\frac{d[Ca^{2+}]_{rel}}{dt} = (I_{tr} - I_{rel}) \left(1 + \frac{[Csqn]_{max} K_{m,Csqn}}{([Ca^{2+}]_{rel} + K_{m,Csqn})^2}\right)^{-1} \tag{27}$$

Equilibrium Potential

$$E_x = \frac{RT}{zF} \log \frac{[X]_o}{[X]_i} \quad \text{for } X = Na^+, K^+, Ca^{2+} \tag{28}$$

Fast Na^+ Current

$$I_{Na} = g_{Na} m^3 h j (V - E_{Na}) \tag{29}$$

$$\alpha_m = \begin{cases} \dfrac{V + 47.13}{1 - \exp\left[-0.1(V + 47.13)\right]} \\ 3.2, \text{ if } V = -47.13 \end{cases} \tag{30}$$

$$\beta_m = 0.08 \exp\left(-\frac{V}{11}\right)$$

$$\alpha_h = \begin{cases} 0.135 \exp\left[-\dfrac{V + 80}{6.8}\right] \\ 0, \text{ if } V \geq -40 \end{cases} \tag{31}$$

$$\beta_h = \begin{cases} 3.56 \exp(0.079V) + 3.1 \times 10^5 \exp(0.35V) \\ 0.13\left[1 + \exp\left(-\dfrac{V + 10.66}{11.1}\right)^{-1}\right], \quad \text{if } V \geq -40 \end{cases}$$

$$\alpha_j = \begin{cases} (-127{,}140 \exp(0.2444V) - 3.474 \times 10^{-5} \exp(-0.04391V)) \dfrac{V + 37.78}{1 + \exp(0.311(V + 79.23))} \\ 0, \quad \text{if } V = -40 \end{cases} \tag{32}$$

$$\beta_j = \begin{cases} \exp(-0.01052V) \\ \dfrac{0.1212}{1 + \exp(-0.1378(V + 40.14))} \\ 0.3\dfrac{\exp(-2.535 \times 10^{-7} V)}{1 + \exp(-0.1(V + 32))}, \quad \text{if } V \geq -40 \end{cases} \tag{33}$$

$$\tau_x = k\tau_x + \beta_{\tau_x}{}^{-1}, \quad \phi_\infty = \alpha_\phi \tau_\phi, \quad \text{for } \phi = m, h, j$$

Time-Independent K^+ Current

$$I_{K1} = \frac{g_{K1}(V - E_K)}{1 + \exp\left[0.07(V + 80)\right]} \tag{35}$$

Transient Outward K^+ Current

$$I_{to} = g_{to}\, a_\infty^3 i_\infty^3 (V - E_K) \tag{36}$$

$$\alpha_{a\infty} = 0.65\left\{\exp\left[-\frac{V + 10}{8.5}\right] + \exp\left[-\frac{V - 30}{59.0}\right]\right\}^{-1} \tag{37}$$

$$\beta_{a\infty} = 0.65\left\{2.5 + \exp\left[\frac{V + 82}{17.0}\right]\right\}^{-1}$$

$$\tau_{a\infty} = [\alpha_{a\infty} + \beta_{a\infty}]^{-1} K_{\tau_{a\infty}}$$

$$\alpha_{i\infty} = \left\{1 + \exp\left[-\frac{V + 20.47}{17.54}\right]\right\}^{-1}$$

$$\beta_{i\infty} = \left\{18.53 + \exp\left[\frac{V + 113.7}{10.95}\right]\right\}^{-1}$$

$$\tau_{i\infty} = [\alpha_{i\infty} + \beta_{i\infty}]^{-1} K_{\tau_{i\infty}}$$

Ultrarapid Delayed Rectifier K^+ Current

$$I_{Kur} = g_{Kur} u_\infty^3 v_\infty (V - E_K) \tag{41}$$

$$g_{Kur} = 0.005 + \frac{0.05}{1 + \exp\left[-\dfrac{V - 15}{13}\right]} \tag{42}$$

$$\alpha_{u\infty} = 0.65\left\{\exp\left[-\frac{V + 10}{8.5}\right] + \exp\left[-\frac{V - 30}{59.0}\right]\right\}^{-1}$$

$$\beta_{u\infty} = 0.65\left\{2.5 + \exp\left[\frac{V + 82}{17.0}\right]\right\}^{-1} \tag{43}$$

$$\tau_{u\infty} = [\alpha_{u\infty} + \beta_{u\infty}]^{-1} K_{\tau_{u\infty}}$$

$$\alpha_{v\infty} = \left\{21 + \exp\left[-\frac{V - 185}{28}\right]\right\}^{-1} \tag{45}$$

$$\beta_{v\infty} = \exp\left[\frac{V - 158}{16}\right]$$

$$\tau_{v\infty} = [\alpha_{v\infty} + \beta_{v\infty}]^{-1} K_{\tau_{v\infty}}$$

$$u_{\infty} = \left\{1 + \exp\left[\frac{V - 99.45}{27.48}\right]\right\}^{-1} \tag{46}$$

Rapid Delayed Outward Rectifier K^+ Current

$$I_{Kr} = g_{Kr} x_r (V - E_K) \tag{47}$$

$$x_{r\infty} = \left\{1 + \exp\left[\frac{V + 15}{22.4}\right]\right\}^{-1}$$

$$\alpha_{x r\infty} = 0.0003\,\frac{V + 14.1}{1 - \exp\left[-\dfrac{V + 14.1}{5}\right]}$$

$$\beta_{x r\infty} = 7.3898 \times 10^{-5}\,\frac{V - 3.3328}{\exp\left[\dfrac{V - 3.3328}{5.1237}\right] - 1} \tag{48}$$

$$\tau_{x r\infty} = [\alpha_{x r\infty} + \beta_{x r\infty}]^{-1}$$

$$x_{r\tau\infty} = \left\{1 + \exp\left[-\frac{V + 14.1}{6.5}\right]\right\}^{-1} \tag{49}$$

Slow Delayed Outward Rectifier K^+ Current

$$I_{Ks} = g_{Ks} x_s^2 (V - E_K) \tag{50}$$

$$\alpha_{x s\infty} = 4 \times 10^{-5}\,\frac{V - 19.9}{1 - \exp\left[-\dfrac{V - 19.9}{17}\right]} \tag{51}$$

$$\beta_{x s\infty} = 3.5 \times 10^{-5}\,\frac{V - 19.9}{\exp\left[\dfrac{V - 19.9}{9}\right] - 1}$$

$$\tau_{x s\infty} = \frac{1}{2}[\alpha_{x s\infty} + \beta_{x s\infty}]^{-1} \tag{52}$$

$$x_{s\infty} = \left[1 + \exp\left(-\frac{V - 19.9}{12.7}\right)^{-1/2}\right.$$

L-TypeCa^{2+} Current

$$I_{CaL} = g_{CaL}\, d\, f\, f_{Ca}(V - 65) \tag{53}$$

$$\tau_d = \frac{1 - \exp\left[\dfrac{V + 10}{6.24}\right]}{0.035(V + 10)\left(1 + \exp\left[-\dfrac{V + 10}{6.24}\right]\right)} \tag{54}$$

$$d_\infty = \left[1 + \exp\left(-\frac{V + 10}{8}\right)\right]^{-1}$$

$$\tau_f = 9(0.0197 \exp\left(-0.0337^2 (V + 10)^2\right) + 0.02)^{-1} \tag{55}$$

$$f_\infty = \left[1 + \exp\left(\frac{V + 28}{6.9}\right)\right]^{-1}$$

$$\tau_{f Ca} = 2, \quad f_{Ca\infty} = \left[1 + \frac{[Ca^{2+}]_i}{0.00035}\right]^{-1} \tag{56}$$

Na^+-K^+ Pump Current

$$I_{NaK} = I_{NaK(max)} f_{NaK} \frac{1}{1 + \left[K_{m,NaK}/[Na^+]_i\right]^{3.5}} \frac{[K^+]_o}{[K^+]_o + K_{m,K10}} \tag{57}$$

$$f_{NaK} = \left[1 + 0.1245 \exp\left(-0.1\frac{FV}{RT}\right) + 0.0365\sigma \exp\left(-\frac{FV}{RT}\right)\right]^{-1} \tag{58}$$

$$\sigma = \frac{1}{7}\left[\exp\left(\frac{[Na^+]_o}{67.3}\right) - 1\right] \tag{59}$$

Na^+/Ca^{2+} Exchanger Current

$$I_{NaCa} = \frac{I_{NaCa(max)} \exp\left[\gamma FV/RT\right][Na^+]_i^3 [Ca^{2+}]_o - \exp\left[(\gamma - 1)FV/RT\right][Na^+]_o^3 [Ca^{2+}]_i}{(K_{m,Na}^3 + [Na^+]_o^3)(K_{m,Ca} + [Ca^{2+}]_o)(1 + k_{sat} \exp\left[(\gamma - 1)FV/RT\right])} \tag{60}$$

Background Currents

$$I_{bCa} = g_{bCa}(V - E_{Ca}) \tag{61}$$

$$I_{bNa} = g_{bNa}(V - E_{Na}) \tag{62}$$

Ca^{2+} Pump Current

$$I_{pCa} = I_{pCa(max)} \frac{[Ca^{2+}]_i}{0.0005 + [Ca^{2+}]_i} \tag{63}$$

Ca^{2+} Release Current From JSR

$$I_{rel} = k_{rel} u^2 v w ([Ca^{2+}]_{rel} - [Ca^{2+}]_i) \tag{64}$$

$$\tau_v = 8.0, \quad w_\infty = \left[1 + \exp\left[\frac{F_w - 3.4175 \times 10^{-13}}{13.67 \times 10^{-16}}\right]\right]^{-1} \tag{65}$$

$$\tau_v = 1.91 + 2.09\left[1 + \exp\left[-\frac{F_w - 3.4175 \times 10^{-13}}{13.67 \times 10^{-16}}\right]\right]^{-1}$$

$$w_\infty = 1 - \left[1 + \exp\left[-\frac{F_w - 6.835 \times 10^{-14}}{13.67 \times 10^{-16}}\right]\right]^{-1} \tag{66}$$

$$\tau_w = 6.0\frac{1 - \exp\left[\dfrac{V - 7.9}{5}\right]}{\left[1 + 0.3\exp\left[-\dfrac{V - 7.9}{5}\right]\right](V - 7.9)} \tag{67}$$

$$w_\infty = 1 - \left[1 + \exp\left[-\frac{V - 40}{17}\right]\right]^{-1}$$

$$F_w = 10^{-13} V_{up} l_{rel} - \frac{5 \times 10^{-13}}{F}\left(\frac{1}{2} i_{CaL} - \frac{1}{5} i_{NaCa}\right) \tag{68}$$

Transfer Current From NSR to JSR

$$I_{tr} = \frac{[Ca^{2+}]_{up} - [Ca^{2+}]_{rel}}{\tau_{tr}} \tag{69}$$

$$\tau_{tr} = 180 \tag{70}$$

Ca^{2+} Uptake Current by the NSR

$$I_{up} = \frac{I_{up(max)}}{1 + ([K_{m,up}]/[Ca^{2+}]_i)} \tag{71}$$

Ca^{2+} Leak Current by the NSR

$$I_{up,leak} = \frac{[Ca^{2+}]_{up}}{[Ca^{2+}]_{up(max)}} I_{up(max)} \tag{72}$$

Ca^{2+} Buffers

$$[Ca^{2+}]_{i,buffc} = [Cmdn]_{max} \frac{[Ca^{2+}]_i}{[Ca^{2+}]_i + K_{m,Cmdn}} \tag{73}$$

$$[Ca^{2+}]_{i,buffsr} = [Trpn]_{max} \frac{[Ca^{2+}]_i}{[Ca^{2+}]_i + K_{m,Trpn}} \tag{74}$$

$$[Ca^{2+}]_{rel,buffsr} = [Csqn]_{max} \frac{[Ca^{2+}]_{rel}}{[Ca^{2+}]_{rel} + K_{m,Csqn}} \tag{75}$$

Main numerical difficulties

Most codes use for practical computional studies are based on P_1 or equivalent methods with a *mesh length* $\simeq 100\mu m$ (which is too coarse!), and *time step* $\simeq 10\mu s$... And adapt A_m.

- Admissibility of unknowns
  - voltage $V_{\min} \leq V(t,x) \leq V_{\max}$, OK for TPFA, cf [CP06]
  - gating variables $0 \leq m_k(t,x) \leq 1$ (HH models), or specific bound (simple models)
  - ion concentrations $[X] > 0$ (Nernst equilibrium)
- Stiffness
  - in time due to physiological processes (*e.g.* fast Na^+ channels) – ODEs,
  - in space due to depolarization fronts
- Propagation failure (PF)
  - no propagation when the mesh is too coarse
  - wrong propagation velocity
- Complex propagation patterns (spiral waves)

Questions

1. Construction, analysis, numerical experiments of a high-order FV method [CT17]
   - How does high-order methods behave in this context ?
   - Coarser meshes may allow for larger time steps ? Explicit ?
   - FV techniques may be used to control the ionic concentration ($[Na]_{i,e} > 0$) or gating variables ($0 \leq m \leq 1$) for increased stability ?
2. Construction of a parallel (OpenMP) implementation [CT19]
   - What strategy for a scalable scheme, and implementation, order up to 6.
   - How efficient is it for HOFVM ?
3. On-going work: *extension to MPI techniques, and to 3D problems*
   - Accuracy and scalability tests on up to 1024 subdomains
   - Order increased to 8

Semi-discrete scheme

- cell-centered FV scheme: unknowns are mean values of V and w in each cell K:

$$\frac{d}{dt}V_K + I_K = \frac{1}{|K|}\sum_{e_i \in \mathcal{E}_K} F_{Ke} \cdot n_{Ke},$$

$$\frac{d}{dt}w_K = G_K,$$

- The scheme is determined by the choices of
  - the numerical flux of diffusion $F_{Ke} \cdot n_{ke}$
  - the numerical reaction terms I_K, and G_K
- Idea: polynomial approximations of V and w [CM14], and quadrature rules [Dun85]

Approximation on cell edges – Diffusion

Given a degree $m > 0$

1. we define *a polynomial reconstruction of degree m* on each interface $e \in \mathcal{E}$:

$$V_e(x, y) = \sum_{i+j \leq m} \gamma_{i,j,e} (x - x_e)^i (y - y_e)^j$$

2. the $\frac{1}{2}(m+1)(m+2)$ coeffs $\Gamma_e = (\gamma_{i,j,e})_{i,j}$ are obtained by computing the minimum of

$$J(\Gamma_e) = \frac{1}{2} \sum_{C \in S_e} \omega_{C,e} \left(V_e(x_C, y_C) - V_C \right)^2,$$

3. where S_e *is a neighborhood of e, with* $\#S_e \geq \frac{1}{2}(m+1)(m+2)$

Approximation on cell edges – Diffusion

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$$V_e(x,y) = \mathbb{X}_e(x,y)\Gamma_e, \qquad \mathbb{X}_e(x,y) = \left[(x-x_e)^i (y-y_e)^j\right]^T_{i+j\leq m}$$

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3. where S_e *is a neighborhood of e, with* $\#S_e \geq \frac{1}{2}(m+1)(m+2)$

Solving the local quadratic optimisation problems

Therefore, Γ_e is the solution of the system:

$$\left(X_e^T \Omega_e X_e\right) \Gamma_e = X_e^T \Omega_e \mathbb{V},$$

where

- matrix of the basis functions evaluated at cell centers in S_e :

$$X_e = \left(\mathbb{X}_e(x_C, y_C)\right)_{C \in S_e} = \left[(x_C - x_e)^i (y_C - y_e)^j\right]_{\substack{C \in S_e \\ i+j \leq m}}$$

- diagonal matrix of the weights $\Omega_e = \text{diag}\left(\omega_{C,e}\right)_{C \in S_e}$
- vector of the unknowns on the stencil: $\mathbb{V} = (V_C)_{C \in S_e}$.
- In practice, $X_e^T \Omega_e X_e$ is a matrix of size $\frac{1}{2}(m+1)(m+2)$
- invertible as soon as $\#S_e$ is large enough

Computing the diffusion flux

$$D(x,y)n_{Ke} \cdot \nabla V_e(x,y) = D(x,y)n_{Ke} \cdot \nabla \mathbb{X}_e(x,y)\Gamma_e$$

- we compute once (*offline*) the matrix

$$Y_e = \left(X_e^T \Omega_e X_e\right)^{-1} X_e^T \Omega_e, \quad \text{such that } \Gamma_e = Y_e \mathbb{V}$$

- we use *a quadrature formula* to obtain the flux $F_{Ke} \cdot n_{Ke}$

$$F_{Ke} \cdot n_{Ke} = |e| \sum_q \omega_q \left[D(x_q, y_q)n_{Ke} \cdot \nabla \mathbb{X}_e(x_q, y_q) Y_e\right] \mathbb{V}$$

- we precompute (offline) the $[D(x_q, y_q)n_{Ke} \cdot \nabla \mathbb{X}_e(x_q, y_q) Y_e]$

Approximation on cells – Reaction

Given a degree $p > 0$

1. we define *a polynomial reconstruction of degree p* on each cell K:

$$\tilde{V}_K(x,y) = V_K + \sum_{1 \le i+j \le p} \lambda_{i,j,K} \left[(x - x_K)^i (y - y_K)^j - \frac{1}{|K|} \int_K (x - x_K)^i (y - y_K)^j dxdy \right]$$

   which is such that $\frac{1}{|K|} \int_K \tilde{V}_K(x,y) = V_K$

2. the $\frac{1}{2}(p+1)(p+2)$ coeffs $\Lambda_K = (\lambda_{i,j,K})_{i,j}$ are obtained from the minimization of

$$J(\Lambda_K) = \frac{1}{2} \sum_{C \in S_K} \omega_{C,K} \left(\langle \tilde{V}_K \rangle_C - V_C \right)^2,$$

3. where S_K *is a neighborhood of* K, with $\#S_K \ge \frac{1}{2}(p+1)(p+1)$

Approximation on cells – Reaction

Given a degree $p > 0$

1. we define *a polynomial reconstruction of degree p* on each cell K:

$$\tilde{V}_K(x,y) = V_K + (\mathbb{X}_K(x,y) - \langle \mathbb{X}_K \rangle_K)\,\Lambda_K, \quad \text{where } \langle\cdot\rangle_K = \frac{1}{|K|}\int_K \cdot$$

   which is such that $\frac{1}{|K|}\int_K \tilde{V}_K(x,y) = V_K$

2. the $\frac{1}{2}(p+1)(p+2)$ coeffs $\Lambda_K = (\lambda_{i,j,K})_{i,j}$ are obtained from the minimization of

$$J(\Lambda_K) = \frac{1}{2}\sum_{C \in S_K} \omega_{C,K}\left(\langle \tilde{V}_K \rangle_C - V_C\right)^2,$$

3. where S_K *is a neighborhood of* K, with $\#S_K \geq \frac{1}{2}(p+1)(p+1)$

The local quadratic optimisation problems

Again, the vector Λ_K is solution to

$$\left(X_K^T \Omega_K X_K\right) \Lambda_K = X_K^T \Omega_K \left(\mathbb{V} - V_K\right),$$

where

- matrix of the *basis functions with* 0 *mean value on* K:

$$X_K = \left(\langle \mathbb{X}_K \rangle_C - \langle \mathbb{X}_K \rangle_K\right)_{C \in S_K}$$

- diagonal matrix of the weights $\Omega_K = \mathrm{diag}\left(\omega_{C,K}\right)_{C \in S_K}$
- vector of the unknown on the stencil : $\mathbb{V} = \left(V_C\right)_{C \in S_K}$.
- In practice, $X_K^T \Omega_K X_K$ is a matrix of size $\frac{1}{2}(p+1)(p+1) - 1$
- invertible as soon as $\# S_K$ is large enough
- We use the same polynomial approximation for V and all variables $w = (w_1, \dots w_N)$

Computing the reaction terms

- we compute once (*offline*) the matrix

$$Y_K = \left(X_K^T \Omega_K X_K\right)^{-1} X_K^T \Omega_K, \quad \text{such that } \Lambda_K = Y_K \left(\mathbb{V} - V_K\right)$$

- we use *a quadrature formula* to obtain the reaction terms

$$I_K = \sum_q \omega_q J_{\text{ion}} \left(\tilde{V}_K(x_q, y_q), \tilde{w}_K(x_q, y_q)\right), \quad D_K = \sum_q \omega_q D \left(\tilde{V}_K(x_i, y_i), \tilde{w}_K(x_i, y_i)\right)$$

  where $\tilde{V}_K(x, y) = V_K + \left(\mathbb{X}_K(x, y) - \langle \mathbb{X}_K \rangle_K\right) Y_K \left(\mathbb{V} - V_K\right)$
- we precompute (offline) the $\left(\mathbb{X}_K(x_q, y_q) - \langle \mathbb{X}_K \rangle_K\right) Y_K$

Summary

- The scheme definition requires
  - the choice of the polynomial degrees $m > 0$ (edges) and $p > 0$ (cells),
  - rules to build the stencils S_e and S_K: n levels of neighbours (neighbours = shared vertex)
  - weights: $\omega_{C,K} = (X_C - X_K)^{-s}$, with $s > 0$, same for $\omega_{C,e}$
  - quadrature formulas
    - ⋆ on the edges: Gauss-Legendre exact for polynomials of degree $m - 1$
    - ⋆ on the cells: formulas on triangles from [Dun85]
- The local matrices are computed offline
- The implementation is matrix-free

A few remarks

- 1 unknown per quadrature point *vs* cell reconstruction for the variables w:
  - 1 unkwown / quadrature point: no need for interpolation by cell but many more nonlinear unknowns,
  - cell reconstruction: quadrature and evaluation of the polynomial at the quadrature points (expensive), but less memory requirement.
- Preservation of admissibility:

  a posteriori limitation on each quadrature point,
- No preconditionning, though $X^T \Omega X$ are ill-conditionnned matrices (Vandermonde)

Time integration

- Explicit schemes:
  - ionic model *requires small* Δt
  - high order $\rightarrow$ "reasonable" mesh
  - preservation of admissibility is easier
- We want $\Delta t = \mathcal{O}(h^2)$, then time order = (required space order)/2
- Preservation of admissibility: SSP-RK
  - Forward Euler, SSP-RK(2,2), SSP-RK(3,3), SSP-RK(5,4), SSP-RK(10,5)

Convergence result

Theorem

For the equation

$$\partial_t u = \Delta u + f(u), \tag{1}$$

with homogeneous Neumann boundary conditions, L^2 initial data, $f \in C^{p+1}(\mathbb{R})$ and Lipshitz, under the additional coercivity property: $\exists \beta > 0$ such that,

$$\beta \, |\mathrm{e}|_1^2 := \beta \sum_{e \in \mathcal{E}} \left| \frac{\mathrm{e}_L - \mathrm{e}_K}{d_{KL}} \right|^2 |e| \, d_{KL} \leq \sum_{e \in \mathcal{E}} F_{K,e}(\mathrm{e}_h) \frac{\mathrm{e}_L - \mathrm{e}_K}{d_{KL}} \, |e| \, d_{KL},$$

then, the spatial error is

$$\|\mathrm{e}_h(t)\|_2 \leq \mathcal{O}(h^{\min(m,p+1)}) e^{Ct}, \quad |\mathrm{e}_h(t)|_1 \leq \mathcal{O}(h^{\min(m,p+1)}) e^{Ct}.$$

Remarks

- We don't known how to prove the discrete coercivity in general – as usual
- Experimentally, the L^2 error is $\|e_h(t)\|_2 \leq \mathcal{O}(h^{\min(m+1,p+1)})e^{Ct}$

Proof

A key point is an *unusual regularity assumption*, that writes in terms of the matrices

$$Y_e = \left(X_e^T \Omega_e X_e\right)^{-1} X_e^T \Omega_e, \quad Y_K = \left(X_K^T \Omega_K X_K\right)^{-1} X_K^T \Omega_K$$

such that

$$\Gamma_e = Y_e \mathbb{V}, \quad \Lambda_K = Y_K \left(\mathbb{V} - V_K\right)$$

1. Write the error equation
2. Identify the errors of consistency on the diffusion, and reaction terms
3. Diffusion: quadrature error + reconstruction error – everything is linear.
4. Reaction: 3 terms
5. Finalize with coercivity and a Gronwall lemma.

Preliminary estimate

Observation on the coefficients of $Y_e = (Y_{e,\alpha,C})_{|\alpha|\leq m, C\in S_e}$ where $\alpha = (i,j)$

$$\sum_{|\alpha|\leq m} \left(X_e^T \Omega_e X_e\right)_{\beta,\alpha} Y_{e,\alpha,C} = \left(X_e^T \Omega_e\right)_{\beta,C} = (\Omega_e X_e)_{C,\beta}\,,$$

$$\sum_{|\alpha|\leq m} \mathcal{O}\left(h^{|\beta|+|\alpha|}\right) Y_{e,\alpha,C} = \mathcal{O}\left(h^{|\beta|}\right),$$

$$\sum_{|\alpha|\leq m} \mathcal{O}\left(h^{|\alpha|}\right) Y_{e,\alpha,C} = \mathcal{O}(1),$$

Hence, we expect that $Y_{e,\alpha,C} = \mathcal{O}(h^{-|\alpha|})$ (true unless cancelations occur).

Mesh regularity assumption

There exists a constant $M > 0$ uniform with respect to the family of meshes, such that

$$\max_{\substack{x \in K \\ K \in S_e}} |x - x_e| \leq Mh,$$

$$\max_{\substack{x \in C \\ C \in S_K}} |x - x_K| \leq Mh,$$

$$\forall\, |\alpha| \leq m,\ C \in S_e, \quad |Y_{e,\alpha,C}| \leq Mh^{-|\alpha|},$$

$$\forall 1 \leq |\alpha| \leq p,\ C \in S_K, \quad |Y_{K,\alpha,C}| \leq Mh^{-|\alpha|},$$

In practice, extending the stencil allows to recover the property.

Exemple on a Cartesian grid

$p = 2$, $\Omega_K = \mathrm{Id}$, and 9-point stencils are considered, the matrix Y_K is:

$$Y_K = \begin{pmatrix} \frac{-1}{6h} & \frac{-1}{6h} & \frac{-1}{6h} & 0 & 0 & 0 & \frac{1}{6h} & \frac{1}{6h} & \frac{1}{6h} \\ \frac{-1}{6h} & 0 & \frac{1}{6h} & \frac{-1}{6h} & 0 & \frac{1}{6h} & \frac{-1}{6h} & 0 & \frac{1}{6h} \\ \frac{1}{10h^2} & \frac{3}{10h^2} & \frac{1}{10h^2} & \frac{-1}{5h^2} & 0 & \frac{-1}{5h^2} & \frac{1}{10h^2} & \frac{3}{10h^2} & \frac{1}{10h^2} \\ \frac{1}{4h^2} & 0 & \frac{-1}{4h^2} & 0 & 0 & 0 & \frac{-1}{4h^2} & 0 & \frac{1}{4h^2} \\ \frac{1}{10h^2} & \frac{-1}{5h^2} & \frac{1}{10h^2} & \frac{3}{10h^2} & 0 & \frac{3}{10h^2} & \frac{1}{10h^2} & \frac{-1}{5h^2} & \frac{1}{10h^2} \end{pmatrix}$$

Consistency for the diffusion flux I

$$\overline{F_{Ke}}(u) - F_{Ke}(\overline{u}) = \underbrace{\overline{F_{Ke}}(u) - \mathcal{Q}_e(\nabla u \cdot n_{Ke})}_{\text{quadrature error}} + \underbrace{\mathcal{Q}_e(\nabla u \cdot n_{Ke}) - F_{Ke}(\overline{u})}_{\text{Reconstruction error}},$$

- Quadrature error:

$$\overline{F_{K,e}}(u) - \mathcal{Q}_e(\nabla u \cdot n_{K,e}) = \frac{1}{|e|}\int_e \nabla u \cdot n_{K,e} d\sigma - \mathcal{Q}_e(\nabla u \cdot n_{K,e}) = \mathcal{O}(h^m)$$

- Reconstruction error:

$$\mathcal{Q}_e(\nabla u \cdot n_{K,e}) - F_{K,e}(\overline{u}) = \mathcal{Q}_e\left(\nabla(u - \mathcal{R}_e u) \cdot n_{K,e}\right),$$

where $\mathcal{R}_e u := \tilde{V}_e$ is the reconstruction on the edge e made on the mean values of u on the cells $C \in S_e$.

Consistency for the diffusion flux II

The reconstruction $\mathcal{R}_e u$ is exact for polynomials of degree $\leq m$. Hence, after the Taylor expansion of u:

$$\mathcal{R}_e u(\mathrm{x}) = u(\mathrm{x}_e) + Du(\mathrm{x})(\mathrm{x}-\mathrm{x}_e) + \ldots + D^m u(\mathrm{x})(\mathrm{x}-\mathrm{x}_e)^m + \mathcal{R}_e\left(|\mathrm{x}-\mathrm{x}_e|^{m+1} R_0(\mathrm{x})\right),$$

Use the assumption of the reconstruction matrix Y_e:

$$\mathcal{R}_e\left(|\mathrm{x}-\mathrm{x}_e|^{m+1} R_0(\mathrm{x})\right) = X^T Y^e \left(\begin{array}{c} \vdots \\ \langle |\mathrm{x}-\mathrm{x}_e|^{m+1} R_0(\mathrm{x}) \rangle_C \\ \vdots \end{array} \right)_{C \in S_e} = \mathcal{O}\left(|\mathrm{x}-\mathrm{x}_e|^{m+1}\right)$$

$$\rightarrow \mathcal{O}(h^m) \quad \text{for the flux (gradient)}$$

Consistency for the reaction source term

The total error of consistency is

$$\frac{1}{|K|}\int_K f(u)dx - \mathcal{Q}_K f(\tilde{u}_K) = \underbrace{\frac{1}{|K|}\int_K f(u)dx - \mathcal{Q}_K(f(u))}_{\mathcal{O}(h^{p+1})\text{(quadrature error)}} + \underbrace{\mathcal{Q}_K\big(f(u) - f(\mathcal{R}^K u)\big)}_{:=A_K} + \underbrace{\mathcal{Q}_K\left(f(\mathcal{R}^K u) - f(\tilde{u}_K)\right)}_{:=B_K}$$

The term A_K is bounded like before + Lipschitz condition on f.
The term B_K is more difficult to estimate. We find that

$$\sum_K B_K\, \mathrm{e}_K\, |K| = \mathcal{O}(1)\, \|\mathrm{e}_h\|_2^2$$

Finally, the total error of consistency on the reaction term is

$$\sum_{K\in\mathcal{M}} e_K \left(\int_K f(u)dx - |K|\, \mathcal{Q}_K f(\tilde{u}_K)\right) = \mathcal{O}(h^{2p+2}) + \mathcal{O}(1)\, \|\mathrm{e}_h\|_2^2 .$$

Order of convergence – sequential

- Forward Euler, SSPRK(2,2), SSPRK(3,3)
- Ad hoc choice of I_{ion} in order to have *an analytical solution*

$$e^2 := \sum_{K \in \mathcal{M}} |K| \left| u_K - \langle u \rangle_K \right|^2 = \sum_{K \in \mathcal{M}} |K| \left| u_K - \sum_q \omega_q u(x_q) \right|^2 .$$

h	p=2	ord.	p=3	ord.	p=4	ord.	p=5	ord.
1.2E-2	2.4E-5	n/a	6.8E-6	n/a	2.9E-6	n/a	9.5E-7	n/a
6.1E-3	5.6E-6	2.09	5.1E-7	3.75	1.3E-7	4.51	2.1E-8	5.52
3.1E-3	1.3E-6	2.09	3.2E-8	3.97	5.2E-9	4.60	3.7E-10	5.80
1.5E-3	3.2E-7	2.03	2.0E-9	4.04	2.4E-10	4.46	6.3E-11	2.57

Table: L^2 errors for the analytical test case

Planar waves – AP, $D = 1.e-1$ – sequential

$$\Delta t = \min\left(\Delta t_{\max}, \frac{C}{D}h^2\right), \quad \Delta t_{\max} = 0.1ms$$

Mesh	h	Δt	order 2	order 4	order 6
1	9.87E-002	1.00E-001	3.25E-001	3.97E-001	4.40E-001
2	4.80E-002	4.61E-002	3.79E-001	4.22E-001	4.43E-001
3	2.24E-002	1.00E-002	4.09E-001	4.37E-001	
4	1.05E-002	2.21E-003	4.21E-001	4.43E-001	
5	5.34E-003	5.70E-004	4.22E-001		

Table: Velocity – Aliev-Panfilov: $D = 1.0 \times 10^{-1}$, $c = 4.43 \times 10^{-1}$cm/ms.

Planar waves – AP, $D = 1.e-2$ – sequential

Mesh	h	Δt	order 2	order 4	order 6
1	9.87E-002	1.00E-001	PF	1.63E-001	1.71E-001
2	4.80E-002	1.00E-001	PF	1.30E-001	1.40E-001
3	2.24E-002	1.00E-001	1.05E-001	1.40E-001	1.40E-001
4	1.05E-002	2.21E-002	1.37E-001		
5	5.34E-003	5.70E-003	1.40E-001		

Table: Velocity – Aliev-Panfilov: $D = 1.0 \times 10^{-2}$, $c = 1.40 \times 10^{-1}$cm/ms.

Planar waves – AP, $D = 1.e-3$ – sequential

Mesh	h	Δt	order 2	order 4	order 6
1	9.87E-002	1.00E-001	PF	PF	PF
2	4.80E-002	1.00E-001	PF	PF	4.25E-002
3	2.24E-002	1.00E-001	PF	4.27E-002	4.68E-002
4	1.05E-002	1.00E-001	3.01E-002	4.18E-002	4.43E-002
5	5.34E-003	5.70E-002	3.49E-002		

Table: Velocity – Aliev-Panfilov: $D = 1.0 \times 10^{-3}$, $c = 4.43 \times 10^{-2}$cm/ms.

Spiral waves — 100 ms – sequential

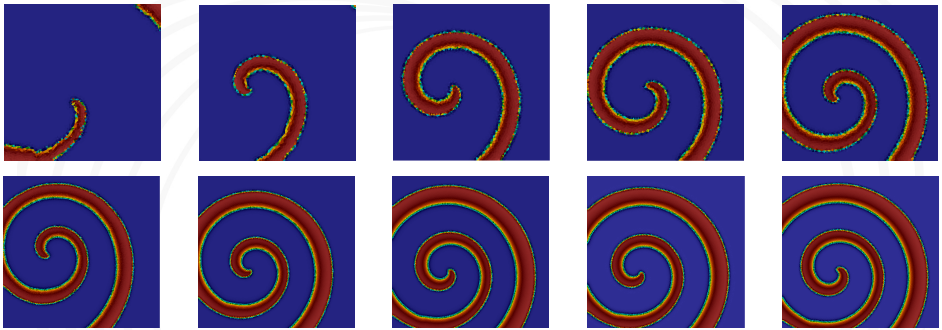


Figure: Spiral wave (AP model) obtained on a moderately coarse mesh (top – 224µm) and a fine mesh (bottom – 105µm) with the schemes from order 2 (left) to 6 (right), $t = 100$ms.

Spiral waves – 150 ms – sequential

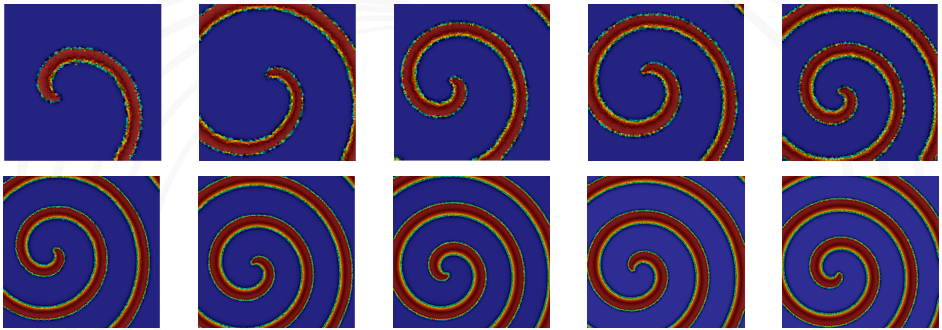


Figure: Spiral wave (AP model) obtained on a moderately coarse mesh (top – 224µm) and a fine mesh (bottom – 105µm) with the schemes from order 2 (left) to 6 (right), $t = 150$ms.

Spiral waves – 200 ms – sequential

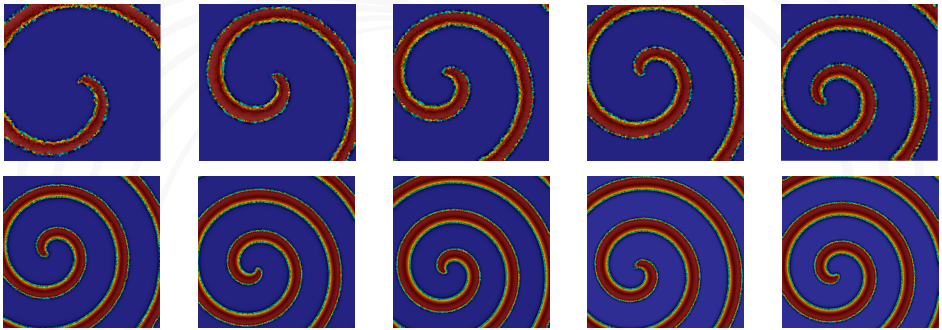


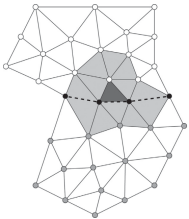
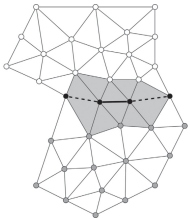
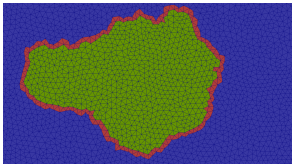
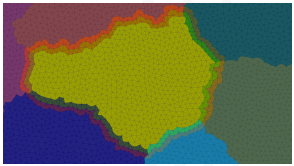
Figure: Spiral wave (AP model) obtained on a moderately coarse mesh (top – 224µm) and a fine mesh (bottom – 105µm) with the schemes from order 2 (left) to 6 (right), $t = 200$ms.

Summary, sequential computations

- 2nd vs 4th order: 6 to 8 times more expensive,
- dividing h by 2: 3 to 20 times more expensive,
- 4th order is more efficient than 2nd order, better than implicit Euler + P1
- AP: the higher order, the better,
- Realistic models: efficiency of high order is reduced (stiffness $\rightarrow$ limitation).
- Needs be faster for long-duration / realistic simulations

Principle of parallel implementation

No numerical issue with the boundary condition
$\rightarrow$ constrain the stencil for parallel implementation may be a good idea

- Stencil S_e or S_K is inside the *extended subdomain* = subdomain + halo
- Halo : 1 layer of neighbors (sharing 1 node), add more cells if really needed

OMP, and then MPI Parallel implementation

Using `scotch` to split the domain $\rightarrow$ balances the # cells / # interfaces

OMP each thread computes 1 subdomain

- renumbering *cells and edges* for contiguous data / subdomain
- reaction is fine because only reading memory, and writing into subdomain
- diffusion need to take care of interfaces shared by 2 subdomains (treated separately)

MPI each process computes 1 subdomain

- reaction and diffusion computed within each subdomain, using values from the extended subdomain
- shared interfaces are computed twice (once per subdomain)
- data to communicate = unknowns u_K^n in the halo

Order of convergence and accuracy of the parallel version

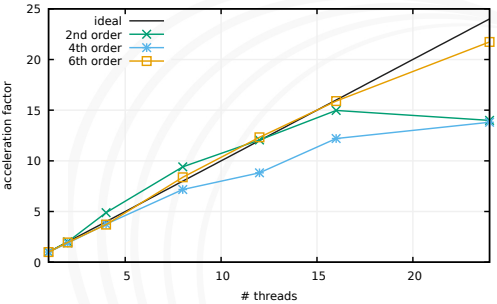
h	p=1	order	p=3	order	p=5	order
6.2E-3	5.93E-1	n/a	1.47E-1	n/a	5.95E-2	n/a
3.0E-3	1.06E-1	2.37	1.20E-2	3.45	1.42E-3	5.14
1.5E-3	1.86E-2	2.51	6.78E-4	4.14	3.08E-5	5.52

Table: L^2 errors for the analytical test case – 24 subdmoains

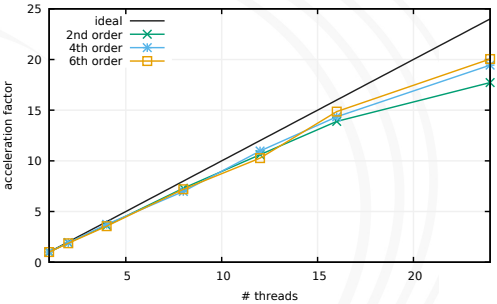
h	p=1	p=3	p=5
6.2E-3	7.61E-4	1.05E-2	1.38E-2
3.0E-3	8.27E-6	2.58E-4	3.61E-4
1.5E-3	6.34E-7	2.78E-5	7.25E-6

Table: Difference between the solution with 1 and 24 subdomains

Scalability – OMP



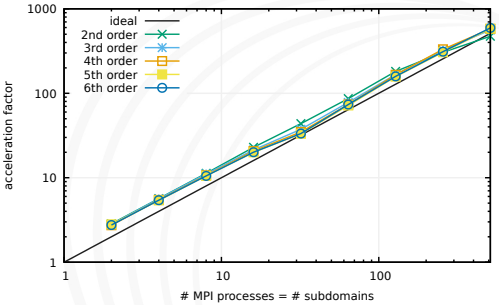
(a) Mesh #4



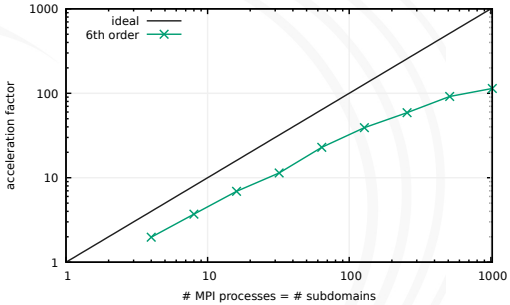
(b) Mesh #5

Figure: Scalability for the AP model

Scalability – MPI



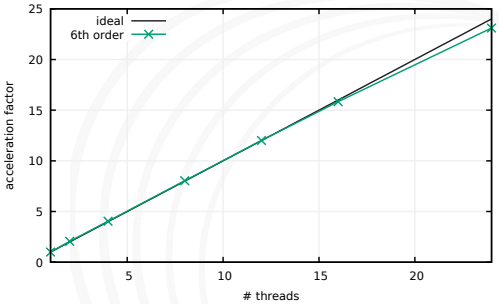
(a) Test case with analytic solution



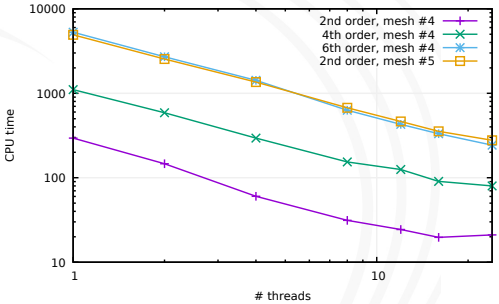
(b) Planar wave for the AP model

Figure: Scalability on mesh #6

Scalability and CPU time – OMP



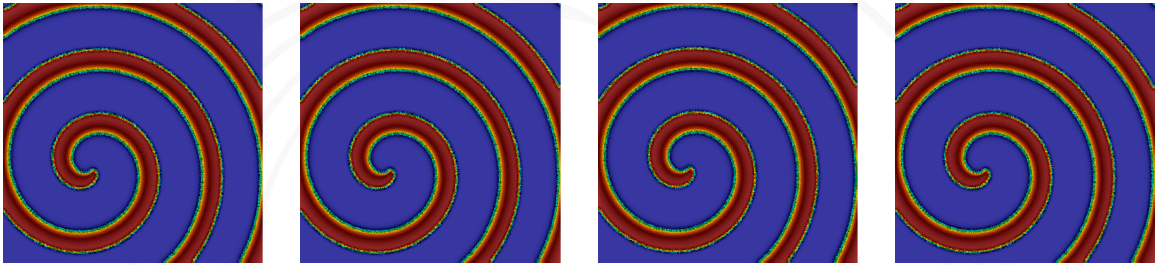
(a) Scalability on mesh #4, order 6



(b) CPU time versus # threads

Figure: Numerical study for the TNNP06 model.

Spiral wave in parallel (OMP)



(a) 1 subdomain (b) 4 subdomains (c) 24 subdomains (d) 128 subdomains

Figure: Spiral wave (AP model), $t = 150$ms, order 6.

Conclusion and perspectives

- High-order is very interesting in this context, notably for complex propagation patterns,
- Scalable as long as the subdomains have enough (depends on the order) cells
- Flexible scheme: change order, or dimension easily
- good properties remain for larger MPI runs
- Currently: implementation of 3D
- more details:

[CT17] Yves Coudière and Rodolphe Turpault. "Very high order finite volume methods for cardiac electrophysiology". In: *Computers & Mathematics with Applications* 74.4 (2017), pp. 684–700. DOI: https://doi.org/10.1016/j.camwa.2017.05.012.

[CT19] Yves Coudière and Rodolphe Turpault. "A domain decomposition strategy for a very high-order finite volumes scheme applied to cardiac electrophysiology". In: *Journal of Computational Science* 37 (2019), p. 101025. DOI: https://doi.org/10.1016/j.jocs.2019.101025.

Thanks for your attention!

Other references

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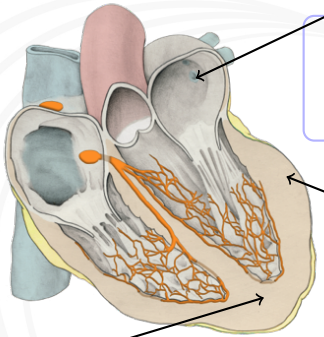
[CP06] Y. Coudière and C. Pierre. "Stability And Convergence Of A Finite Volume Method For Two Systems Of Reaction-Diffusion Equations In Electro-Cardiology". In: *Nonlinear Anal. Real World Appl.* 7.4 (2006), pp. 916–935.

[CRN98] M. Courtemanche, R. J. Ramirez, and S. Nattel. "Ionic mechanisms underlying human atrial action potential properties: insights from a mathematical model.". In: *American Journal of Physiology* 275.1 Pt 2 (July 1998), H301–h321.

[Dun85] D. A. Dunavant. "High degree efficient symmetrical Gaussian quadrature rules for the triangle". In: *International Journal for Numerical Methods in Engineering* 21.6 (1985), pp. 1129–1148.

A specific subject: cardiac arrhythmias



Atrial Fibrillation

- 5 million in Europe (6 – 10 %)
- Major cause of stroke

Ventricular Fibrillation

→ sudden cardiac death (SCD)

- 350 000 death/year in Europe
- 1/10 000 inhab/year

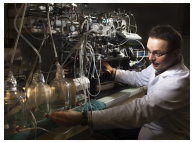
Heart Failure and dyssynchrony

- 9 million in Europe
- 350 000 death/year

IHU Liryc

L'Institut de Rythmologie et *modélisation* Cardiaque

- Combines (same location):
  - clinical cardiology
  - electrophysiology – cell, tissue
  - imaging – 2 MR[, CT], EP lab
  - *Modeling*
  - Signal processing
- training center & industrial partners



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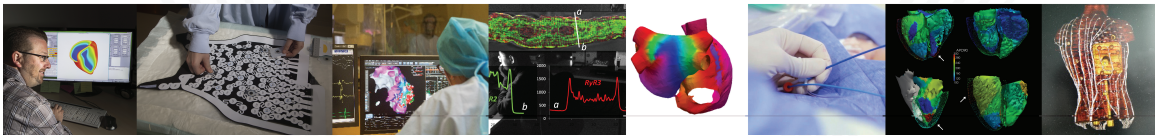
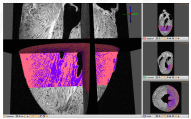
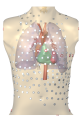


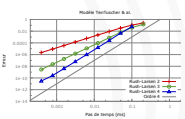
LIRYC | Restoring the rhythm of life

Inria Carmen

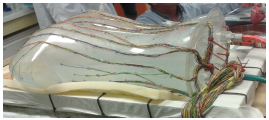
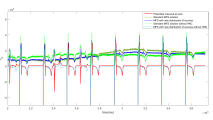
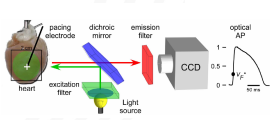
Modeling cardiac electrophysiology

- We develop numerical models, study specific pathologies related to AF or VF (Brugada, ERS...)

- We work on the body surface signals and related inverse problems.

- Develop some softwares...

Spiral waves – initial data