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STABILITY OF TWO TIME-INTEGRATORS FOR THE ALIEV-PANFILOV SYSTEM

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Abstract. We propose a second-order accurate method for computing the solutions to the Aliev-Panfilov model of cardiac excitation. This two-variable reaction-diffusion system is due to its simplicity a popular choice for modeling important problems in electrocardiology; e.g. cardiac arrhythmias. The solutions might be very complicated in structure, and hence highly resolved numerical simulations are called for to capture the fine details. Usually the forward Euler time-integrator is applied in these computations; it is very simple to implement and can be effective for coarse grids. For fine-scale simulations, however, the forward Euler method suffers from a severe time-step restriction, rendering it less efficient for simulations where high resolution and accuracy are important.

We analyze the stability of the proposed second-order method and the forward Euler scheme when applied to the Aliev-Panfilov model. Compared to the Euler method the suggested scheme has a much weaker time-step restriction, and promises to be more efficient for computations on finer meshes.

Key Words. reaction-diffusion system, implict Runge-Kutta, electrocardiology

1. Introduction

Pulse propagation in cardiac tissue can adequately be simulated by the use of modern ionic models with diffusive coupling between myocytes. Today's detailed ionic models, however, consist of dozens of ODEs that represent a great numerical challenge to solve at every mesh point for large spatial domains. Such large spatial regions are relevant for the study of for example re-entrant cardiac arrhythmias. If in addition a high spatial resolution is required, it may not be feasible to solve these models on present day computers. The Aliev-Panfilov model [1] was constructed to ameliorate this problem and capture the qualitative behavior of the cardiac tissue in a mathematically and computationally tractable model. It builds upon the FitzHugh-Nagumo model [8, 15] and retains its simplicity while more accurately describing the pulse propagation in collections of heart cells. The Aliev-Panfilov model has been applied in many computationally demanding problems; e.g. spiral wave breakup in coupled cells [17, 23], scroll waves in excitable medium [20].

The bidomain and monodomain models [10, 11, 22] are commonly used to describe the electrical activity in the heart at tissue level. Mathematically, these models are partial differential equations of reaction-diffusion type. Two electrical potentials, the transmembrane and the extracellular, are accounted for in the

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bidomain model. A simplifying assumption reduces the bidomain description to the monodomain model, which only models the transmembrane potential. We will consider the monodomain model description of cardiac tissue with Aliev-Panfilov cell dynamics: On the space-time domain $\Omega_T := \Omega \times (0, T]$ the Aliev-Panfilov model reads

$$\frac{\partial e}{\partial t} = \delta \nabla^2 e - ke(e-a)(e-1) - er, \qquad \text{on } \Omega_T, \tag{1}$$

$$\frac{\partial r}{\partial t} = -\left[\varepsilon + \frac{\mu_1 r}{\mu_2 + e}\right][r + ke(e-b-1)], \qquad \text{on } \Omega_T, \tag{2}$$

and

$$\vec{n} \cdot \delta \nabla e = 0 \text{ on } \partial\Omega, \quad \text{and} \quad (e, r)_{t=0} = (e(0, \cdot), r(0, \cdot)), \tag{3}$$

where $\vec{n}$ is the outer normal vector of the boundary $\partial\Omega$. Here e represents the scaled transmembrane potential, r is the variable responsible for recovery of the tissue and Ω is a two-dimensional domain in the present paper. For the stability analysis of the time-integrators in this paper we will assume that the Aliev-Panfilov parameters μ_1, μ_2, k, ε, b, a and δ are positive. Numerical experiments will be performed in order to investigate the sharpness of the obtained time step restrictions. For these computations we will fix the parameters to the physiological values $\mu_1 = 0.07$, $\mu_2 = 0.3$, $k = 8$, $\varepsilon = 0.01$, $b = 0.1$, $a = 0.1$ and $\delta = 5 \times 10^{-5}$.

A variety of schemes has been applied in numerical electrophysiology. In [4] a finite volume scheme, with explicit Euler time-stepping, for the monodomain model in connection with Aliev-Panfilov or FitzHugh-Nagumo cell kinetics was proven to be first order convergent. Stability properties of several first and second order accurate time-integrators, and even a third order scheme, for the bidomain model with FitzHugh-Nagumo dynamics were studied in [7]. Implicit Euler was used in e.g. [9], where finite element discretization was employed in space. An adaptive method for the Aliev-Panfilov model was recently presented in [2].

The forward Euler method has, however, emerged as the standard approach to solve the Aliev-Panfilov system in time; see e.g [23, 19, 14, 13, 20]. Without doubt this is due to its big advantage of simplicity. Unfortunately, the method becomes less efficient as the spatial resolution is increased because of its very severe time step restriction. Numerical computations on highly resolved meshes are relevant in many important applications; e.g. in fibrillation where a spiral wave pattern needs to be resolved and we want to capture the fine details. These considerations motivate us to consider an alternative scheme for fine-scale computations.

We will present a second-order method for the system (1)-(3) and compare it to the standard forward Euler scheme in terms of stability. The second-order accurate time integration we consider is the Singly Diagonally Implicit Runge-Kutta (SDIRK) method in [3]. To our knowledge the stability of this method when applied to the Aliev-Panfilov system has not been analyzed previously and no time step restriction has been given. We analyze both the forward Euler scheme and the second-order scheme by giving a maximum principle revealing the time step condition needed to keep the solution within the physiologically relevant bounds. The second-order method hinges on a decomposition of the Aliev-Panfilov model into a PDE and two coupled ODEs by an operator-splitting technique in time. The second-order accurate SDIRK method is applied to integrate the ODE system in time. Compared to the forward Euler scheme, we will show that the second-order method has considerably improved stability properties. Although the proposed scheme is more computationally costly than the forward Euler method for coarse grids, the weaker time step restriction makes it competitive for fine-scale computations. The actual break-even point in terms of computational cost and accuracy is problem dependent and might be determined by numerical experiments for the given application.

2. Numerical methods

The system defined by (1)-(3) only involves two variables, and yet it is quite complicated to treat as a coupled system. A widely used way to handle problems of this type is therefore to split the equations into a PDE and a set of two ODEs, to be solved alternately. It is possible to choose an operator splitting technique which gives second-order accuracy in time, namely the Strang splitting, thoroughly described in [21, 18]. We shall use this splitting approach together with a Crank-Nicolson method for the PDE. Moreover we use the two-stage SDIRK method from [3], resulting in an overall second-order accurate solver in both time and space. In addition, we shall approximate the equations under consideration by a standard forward Euler scheme, which admits first-order accuracy in time. Both these methods will be discussed regarding stability and efficiency. We introduce a uniform mesh $(x_i, y_j) = (i\Delta x, j\Delta y) \in \Omega$ at all times $t_n = n\Delta t$, $n = 1, \ldots, M$.

The overall second-order numerical scheme is summarized in the following three-step procedure, where in each step a second-order accurate algorithm should be used.

Procedure 2.1. *(Strang splitting)*

Step 1. With e^n, r^n as initial conditions, solve

$$\frac{\partial e}{\partial t} = -ke(e-a)(e-1) - er, \tag{4}$$

$$\frac{\partial r}{\partial t} = -\left[\varepsilon + \frac{\mu_1 r}{\mu_2 + e}\right][r + ke(e-b-1)], \tag{5}$$

from time t_n to $t_{n+\frac{1}{2}}$, to obtain $e^{n+1/2}$ and $r^{n+1/2}$.

Step 2. Solve the PDE

$$\frac{\partial e_*}{\partial t} = \delta\nabla^2 e_*\,, \tag{6}$$

from t_n to t_{n+1}, using $e^{n+1/2}$ as initial condition and the no-flow boundary condition $\vec{n}\cdot\delta\nabla e_* = 0$. Here a Crank-Nicolson method is used to obtain the intermediate solution e_*^{n+1}. The semi-discrete scheme writes

$$\frac{e_*^{n+1} - e_*^n}{\Delta t} = \frac{1}{2}\delta\nabla^2(e_*^{n+1} + e_*^n)\,, \tag{7}$$

with $e_*^n = e^{n+1/2}$.

Step 3. Solve the ODE system (4)-(5) from $t_{n+1/2}$ to t_{n+1} with e_*^{n+1} and $r^{n+1/2}$ as initial conditions, to get e^{n+1} and r^{n+1}.

In Step 2 above, we use a Crank-Nicolson method to obtain second-order accuracy in time; the spatial discretization of the Laplacian operator ∇^2 is typically done using finite differences or finite elements. For efficiency an order optimal linear system solver [12] should be applied in this step.

In Step 1 and Step 3 we need to apply an ODE solver which preserves the second-order of accuracy achievable by the Strang splitting. There are several choices available, but one option that admits particularly good stability properties is the second-order SDIRK method. Note that the SDIRK method for the ODEs in Procedure 2.1 is applied in half steps, $\Delta t/2$. For convenience we therefore define $\overline{\Delta t} = \Delta t/2$. In what follows we will describe the application of the SDIRK method on the Aliev-Panfilov system in Step 1 above, that is the step $t_n \to t_{n+1/2}$.

Denote by F and G the right hand sides of (4) and (5) respectively,

$$F(e,r) = -ke(e-a)(e-1) - er, \tag{8}$$

$$G(e,r) = -\left[\varepsilon + \frac{\mu_1 r}{\mu_2 + e}\right][r + ke(e-b-1)]. \tag{9}$$

First we take half a step to calculate

$$e^{n+1/4} = e^n + \frac{\overline{\Delta t}}{2} F(e^{n+1/4}, r^n), \tag{10}$$

$$r^{n+1/4} = r^n + \frac{\overline{\Delta t}}{2} G(e^n, r^{n+1/4}). \tag{11}$$

Next $e^{n+1/4}$ is used to find $r^{n+1/2}$

$$r_1 = r^n + \gamma\overline{\Delta t} G(e^{n+1/4}, r_1), \tag{12}$$

$$r^{n+1/2} = r^n + (1-\gamma)\overline{\Delta t} G(e^{n+1/4}, r_1) + \gamma\overline{\Delta t} G(e^{n+1/4}, r^{n+1/2}), \tag{13}$$

and finally we obtain $e^{n+1/2}$ by

$$e_1 = e^n + \gamma\overline{\Delta t} F(e_1, r^{n+1/4}), \tag{14}$$

$$e^{n+1/2} = e^n + (1-\gamma)\overline{\Delta t} F(e_1, r^{n+1/4}) + \gamma\overline{\Delta t} F(e^{n+1/2}, r^{n+1/4}). \tag{15}$$

Here $\gamma = \frac{2-\sqrt{2}}{2}$ gives a second-order accurate scheme. Note that we need to employ a non-linear solver, e.g. Newton's method, to solve these equations.

The forward Euler method, approximating (1)-(2) can be written as

$$\frac{e_{i,j}^{n+1} - e_{i,j}^n}{\Delta t} = \delta \frac{e_{i+1,j}^n - 2e_{i,j}^n + e_{i-1,j}^n}{\Delta x^2} + \delta \frac{e_{i,j+1}^n - 2e_{i,j}^n + e_{i,j-1}^n}{\Delta y^2} - ke_{i,j}^n(e_{i,j}^n - a)(e_{i,j}^n - 1) - e_{i,j}^n r_{i,j}^n, \tag{16}$$

$$\frac{r_{i,j}^{n+1} - r_{i,j}^n}{\Delta t} = -\left[\varepsilon + \frac{\mu_1 r_{i,j}^n}{\mu_2 + e_{i,j}^n}\right]\left[r_{i,j}^n + ke_{i,j}^n(e_{i,j}^n - b - 1)\right], \tag{17}$$

and similarly for the boundary nodes.

In [4] the existence of an *invariant region* for the Aliev-Panfilov model (1)-(3) is established. Such an invariant region is a closed subset $\Sigma \subset \mathbb{R}^2$. Now, if the initial data $(e,r)_{t=0}$ are inside Σ, then the solution (e,r) will remain in Σ. Therefore, it is reasonable to attempt to bound the numerical solution in an adequate state space. The discretization parameters will be chosen such that both methods under consideration produce numerical solutions in the physiologic state space $(e_{i,j}^n, r_{i,j}^n) \in (0,1) \times (0, r_+)$, where r_+ is the upper bound of r given below.

3. Stability analysis

In this section we will prove that, with suitable choices of discretization parameters, the numerical solutions computed by the two schemes under consideration stay within the desired state space throughout the computational domain. The model parameters are as specified in Section 1. We want

$$0 \le e_{i,j}^n \le 1, \tag{18}$$

$$0 \le r_{i,j}^n \le r_+, \tag{19}$$

for all relevant i, j and n, where the upper bound of r is defined by

$$r_+ = k\left(\frac{b+1}{2}\right)^2, \quad k > 0, b > 0. \tag{20}$$

For convenience we define a function q,

$$q(e) = e(e - b - 1), \tag{21}$$

which has the properties

$$-\frac{r_+}{k} = -\left(\frac{b+1}{2}\right)^2 \leq q(e) \leq 0, \quad \text{for } e \in [0,1], b > 0. \tag{22}$$

Our aim is to derive proper conditions on the mesh parameters in order to guarantee that the numerical solution remains in a fixed physiologically relevant range; i.e., satisfying (18)-(19).

3.1. Time step restriction for forward Euler. We will investigate the forward Euler scheme in terms of numerical stability. Introduce variables e_W, e_N, e_E, e_S, e, r to represent respectively the numerical solution at points $(i-1, j), (i, j+1), (i+1, j), (i, j-1)$,$(i, j)$ and (i, j) at time step n. Moreover set

$$\lambda = \frac{\delta \Delta t}{\Delta x^2}, \tag{23}$$

where a uniform mesh $\Delta x = \Delta y$ is assumed, and define the functions

$$E(e_W, e_N, e_E, e_S, e, r) = \lambda(e_W + e_N + e_E + e_S) + (1 - 4\lambda)e - \Delta t k e(e-a)(e-1) - \Delta t e r,$$

$$R(e, r) = r - \Delta t\left[\varepsilon + \frac{\mu_1 r}{\mu_2 + e}\right]\left[r + ke(e - b - 1)\right],$$

such that the explicit scheme can be written as

$$e_{i,j}^{n+1} = E(e_W, e_N, e_E, e_S, e, r), \tag{24}$$

$$r_{i,j}^{n+1} = R(e, r). \tag{25}$$

Assume in the following that e_W, e_N, e_E, e_S, e, r are within the bounds defined by (18)-(19).

Bounds on $e_{i,j}^{n+1}$.

First observe that

$$\frac{\partial E}{\partial e_x} = \lambda > 0 \tag{26}$$

for $x = W, N, E, S$. Consequently,

$$e_{i,j}^{n+1} = E(e_W, e_N, e_E, e_S, e, r) \leq E(1, 1, 1, 1, e, r) \equiv H(e, r)$$

where we have introduced

$$H(e, r) = 4\lambda + (1 - 4\lambda)e - \Delta t k e(e-a)(e-1) - \Delta t e r.$$

Differentiate H with respect to e and get

$$\begin{aligned}\frac{\partial H}{\partial e} &= (1 - 4\lambda) - \Delta t k\left[e(e-1) + e(e-a) + (e-1)(e-a)\right] - \Delta t r \\ &\equiv p(e, r).\end{aligned}$$

We want to find a condition on Δt such that H is a nondecreasing function in e which implies that $p(e, r) \geq 0$. Since

$$\frac{\partial^2 p}{(\partial e)^2} = -6\Delta t k < 0,$$

the minimum of p is found at the end points. We write

$$p_- = \min(p(0, r), p(1, r)),$$

and calculate

$$p(0, r) = (1 - 4\lambda) - \Delta t k a - \Delta t r \quad \text{and} \quad p(1, r) = (1 - 4\lambda) - \Delta t k(1 - a) - \Delta t r.$$

The worst case is obtained for r_+, so

$$p_- = p(1, r_+) = (1 - 4\lambda) - \Delta t \max(ka, k(1 - a)) - \Delta t r_+. \tag{27}$$

To ensure that p_- is non-negative, it must be required that

$$\Delta t \leq \frac{1}{\frac{4\delta}{\Delta x^2} + \max(ka, k(1 - a)) + r_+}, \tag{28}$$

where we have recalled that $\lambda = \frac{\delta \Delta t}{\Delta x^2}$. Hence H is ensured to be a nondecreasing function in e, so we deduce

$$e_{i,j}^{n+1} \leq H(e, r) \leq H(1, r) = 1 - \Delta t r \leq 1,$$

since r is non-negative.

Similarly, we will show that $e_{i,j}^{n+1} \geq 0$. It follows from (26) that

$$e_{i,j}^{n+1} = E(e_W, e_N, e_E, e_S, e, r) \geq E(0, 0, 0, 0, e, r) = J(e, r),$$

where we have defined

$$e_{i,j}^{n+1} = J(e, r) = (1 - 4\lambda)e - \Delta t k e(e - a)(e - 1) - \Delta t e r. \tag{29}$$

Since the derivative of J with respect to e is identical to that of H, so

$$\frac{\partial J(e, r)}{\partial e} \geq 0,$$

provided that (28) holds. Therefore, from (29), we obtain

$$e_{i,j}^{n+1} \geq J(0, r) = 0,$$

so the lower bound is also satisfied.

Bounds on r^{n+1}.

First, we find that

$$R(e, r) \leq r - \Delta t \left[\varepsilon + \frac{\mu_1 r}{\mu_2 + e}\right] \left[r - k\left(\frac{b + 1}{2}\right)^2\right] = r + \Delta t \left[\varepsilon + \frac{\mu_1 r}{\mu_2 + e}\right] [r_+ - r],$$

where we have used the lower bound $-r^+/k$ in (22) of $q(e)$. Now, since $e \geq 0$ we find that

$$R(e, r) \leq R(0, r) = r + \Delta t \left[\varepsilon + \frac{\mu_1}{\mu_2} r\right] [r_+ - r] \equiv \psi(r).$$

We want to find a condition on Δt such that ψ is a nondecreasing function in r. Assume that

$$\Delta t \leq \frac{1}{\varepsilon + \frac{\mu_1}{\mu_2} r_+}. \tag{30}$$

Then

$$\psi'(r) = 1 + \Delta t\left(\frac{\mu_1}{\mu_2}(r_+ - 2r) - \varepsilon\right) \geq 1 - \Delta t\left(\frac{\mu_1}{\mu_2}r_+ + \varepsilon\right) \geq 0,$$

and consequently,

$$r_{i,j}^{n+1} = R(e,r) \leq \psi(r) \leq \psi(r_+) = r_+.$$

We conclude that the upper bound is satisfied, i.e.

$$r_{i,j}^{n+1} = R(e_{i,j}^n, r_{i,j}^n) \leq r_+.$$

It remains to prove that also the lower bound of $r_{i,j}^{n+1}$ is fulfilled. Note that

$$r_{i,j}^{n+1} = R(e,r) \geq r - \Delta t\left[\varepsilon + \frac{\mu_1 r}{\mu_2 + e}\right] r \geq r\left(1 - \Delta t\left[\varepsilon + \frac{\mu_1}{\mu_2}r_+\right]\right) \geq 0,$$

for any Δt that satisfies (30). Hence we have proved that the solution set at all inner points at time t_{n+1} are within the desired range. Therefore, since the initial conditions satisfy

$$0 \leq e_{i,j}^0 \leq 1 \quad \text{and} \quad 0 \leq r_{i,j}^0 \leq r_+,$$

it follows by induction on n that $\{e_{i,j}^n, r_{i,j}^n\}$ stays within the desired bounds for all relevant (i,j) and $n > 0$ as long as

$$\Delta t \leq \min\left\{\frac{1}{\frac{4\delta}{\Delta x^2} + \max(ka, k(1-a)) + r_+}, \frac{1}{\varepsilon + \frac{\mu_1}{\mu_2}r_+}\right\}$$

holds.

3.2. Time step restriction for the SDIRK scheme. Our purpose is to determine the time step restriction for the SDIRK scheme applied in Step 1 and Step 3 of Procedure 2.1. These steps are identical except for the initial conditions. In Step 3 the initial condition on the transmembrane potential stems from the solution of the heat equation (6) in the second step of the procedure. As previously mentioned this PDE is solved by the Crank-Nicolson scheme in connection with finite difference discretization in space. For stability of the Crank-Nicolson method applied to the heat equation see e.g. [6]; stability analysis that applies for this method is also available in [5]. We will not theoretically consider stability of the Crank-Nicolson method with finite difference discretization in space here, but assume that it generates data within physiological bounds when applied with time steps smaller than required for the SDIRK method. This is verified in our numerical computations:

Step 2 of Procedure 2.1 requires solving the PDE (6) from t_n to t_{n+1} with the Crank-Nicolson scheme (7) for the temporal discretization. It is well known that the Crank-Nicolson scheme gives second-order accuracy in time, but we also want to ensure stability for reasonable sizes of the time step $\Delta t = t_{n+1} - t_n$. That is, values of e_*^{n+1} remain inside $[0,1]$ if $e_*^n \in [0,1]$.

To this purpose we choose the unit square as the solution domain of (6), and δ is chosen as 5×10^{-5}. Standard central finite differences are used to discretize (7) in the spatial direction. The resulting linear system is then solved by a preconditioned conjugate gradient solver. As initial values we have used the following formula:

$$e_*^n(x_i, y_j) = \frac{1}{4}\left(1 - \cos(i\Delta x\pi)\right)\left(1 - \cos(j\Delta y\pi)\right),$$

where $\Delta x = \Delta y = \frac{1}{3200}$. A series of increasing Δt values has been tested, and we have observed that values of $e_*^{n+1}(x,y)$ only exceed the range of $[0,1]$ for $\Delta t > 6000$ (ms). With a propagation pulse sequence (including resting state) of duration about one second, this means that the practical time step restriction corresponds to six heart beats. Thus, the numerical experiments show that the Crank-Nicolson scheme (7) gives stable solutions even for time step sizes that are much larger than relevant for Procedure 2.1.

Under the assumption that the Crank-Nicolson method generates data within the required bounds it is sufficient to analyze the SDIRK method (10)-(15) applied in Step 1, to obtain results for the complete scheme.

3.2.1. Bounds on the solution. Assume that all parameters and initial conditions are as for the explicit method. For convenience of notation we drop the subscripts i and j, and keep in mind that (e^n, r^n) live throughout $\bar{\Omega}_T$.

For some time step number $n > 0$, we assume that $0 \leq e^n \leq 1$ and $0 \leq r^n \leq r_+$, where r_+ is defined in (20). Under these assumptions we will prove that the SDIRK method (10)-(15) gives

$$\begin{aligned} 0 \leq & e^{n+1/4} \leq 1, \\ 0 \leq & r^{n+1/4} \leq r_+, \\ 0 \leq & r_1 \leq r_+, \\ 0 \leq & r^{n+1/2} \leq r_+, \\ 0 \leq & e_1 \leq 1, \\ 0 \leq & e^{n+1/2} \leq 1, \end{aligned}$$

possibly with a restriction on the time step. To this end we will define functions A_ι, $\iota = 1, \ldots, 6$ directly from (10)-(15), such that $A_\iota(x, \cdot) = 0$. Here, x corresponds to the relevant argument: $A_1(e^{n+1/4}, \cdot) = 0$, $A_2(r^{n+1/4}, \cdot) = 0$, and so on. In order to prove that $A_\iota(x, \cdot) = 0$ has a unique solution satisfying the relevant bound above, it is sufficient to show that

(31)

$$i) \quad A_\iota(0, \cdot) \geq 0, \quad ii) \quad A_\iota(x_+, \cdot) \leq 0, \quad \text{and} \quad iii) \quad \frac{\partial A_\iota(x, \cdot)}{\partial x} < 0, \quad \iota = 1, \ldots, 6.$$

Recall in what follows the definition $\overline{\Delta t} = \Delta t/2$ on half the time step.

Bounds on $e^{n+1/4}$.

Define a function

$$A_1(e, e^n, r^n) = -e + e^n + \frac{\overline{\Delta t}}{2} F(e, r^n),$$

such that $e^{n+1/4}$ solves $A_1(e^{n+1/4}, e^n, r^n) = 0$. Property i) and ii) are satisfied since

$$A_1(0, e^n, r^n) = e^n + \frac{\overline{\Delta t}}{2} F(0, r^n) = e^n \geq 0$$

and

$$A_1(1, e^n, r^n) = -1 + e^n + \frac{\overline{\Delta t}}{2} F(1, r^n) = -1 + e^n - \frac{\overline{\Delta t}}{2} r^n \leq 0.$$

The derivative of A_1 with respect to e is

$$\frac{\partial A_1}{\partial e} = -1 + \frac{\overline{\Delta t}}{2} \frac{\partial F}{\partial e},$$

where F is as defined in (8). In order to find a condition on $\overline{\Delta t}$ such that $\frac{\partial A_1}{\partial e}$ is a decreasing function, set

$$\zeta = \max_{e,r} \frac{\partial F}{\partial e} > 0. \tag{32}$$

If the time step is chosen according to

$$\overline{\Delta t} < \frac{2}{\zeta}, \tag{33}$$

then property iii) holds and there is a unique $e^{n+1/4}$ within the unit interval, i.e.,

$$0 \leq e^{n+1/4} \leq 1. \tag{34}$$

Bounds on $r^{n+1/4}$.

As above, we define a function

$$A_2(r, e^n, r^n) = -r + r^n + \frac{\overline{\Delta t}}{2} G(e^n, r), \tag{35}$$

where G is defined by (9), so that $r^{n+1/4}$ solves the equation $A_2(r^{n+1/4}, e^n, r^n) = 0$. We observe that properties i) and ii) hold since

$$A_2(0, e^n, r^n) = r^n + \frac{\overline{\Delta t}}{2} G(e^n, 0) = r^n - \frac{\overline{\Delta t}}{2} \left(\varepsilon q(e^n)\right) \geq 0,$$

and

$$A_2(r_+, e^n, r^n) = -r_+ + r^n + \frac{\overline{\Delta t}}{2} G(e^n, r_+) \leq -\frac{\overline{\Delta t}}{2} \left(\varepsilon + \frac{\mu_1 r_+}{\mu_2 + e^n}\right) \big(r_+ + kq(e^n)\big) \leq 0.$$

Moreover, we find a restriction on the time step, such that property iii) holds and define

$$\eta = \max_{e,r} \frac{\partial G}{\partial r}. \tag{36}$$

Since

$$\frac{\partial A_2}{\partial r} = -1 + \frac{\overline{\Delta t}}{2} \frac{\partial G}{\partial r} \leq -1 + \frac{\overline{\Delta t}}{2} \eta,$$

we must choose

$$\overline{\Delta t} < \frac{2}{\eta}, \tag{37}$$

such that the derivative of A_2 with respect to r is negative.

Bounds on $r^{n+1/2}$.

In order to prove bounds on $r^{n+1/2}$, we first investigate the scheme for r_1 which reads

$$r_1 = r^n - \gamma \overline{\Delta t} \left(\varepsilon + \frac{\mu_1 r_1}{\mu_2 + e^{n+1/4}}\right) \big(r_1 + k e^{n+1/4}(e^{n+1/4} - b - 1)\big).$$

Define a function

$$A_3(r, e^{n+1/4}, r^n) = -r + r^n - \gamma \overline{\Delta t} \left(\varepsilon + \frac{\mu_1 r}{\mu_2 + e^{n+1/4}}\right) \big(r + k e^{n+1/4}(e^{n+1/4} - b - 1)\big),$$

such that r_1 is the solution of $A_3(r_1, e^{n+1/4}, r^n) = 0$. First check property i) and calculate

$$A_3(0, e^{n+1/4}, r^n) = r^n - \gamma\overline{\Delta t}\varepsilon(ke^{n+1/4}(e^{n+1/4} - b - 1)) \geq \gamma\overline{\Delta t}\varepsilon(ke^{n+1/4}(1 + b - e^{n+1/4})) \geq 0,$$

since $e^{n+1/4}$ is in the unit interval and $b > 0$. Moreover,

$$A_3(r_+, e^{n+1/4}, r^n) \leq -\gamma\overline{\Delta t}\left(q\varepsilon + \frac{\mu_1 r_+}{\mu_2 + e^{n+1/4}}\right)\left(r_+ + kq(e^{n+1/4})\right),$$

where we have used q in (21) and replaced r^n by its upper bound. Now due to (22), $r_+ + q(e^{n+1/4}) \geq 0$ so $A_3(r_+, e^{n+1/4}, r^n) \leq 0$ and hence property ii) holds. The derivative of A_3 with respect to r is given by

$$\frac{\partial A_3}{\partial r} = -1 + \gamma\overline{\Delta t}\frac{\partial G}{\partial r},$$

where G is as defined in (9). In order to find a condition on $\overline{\Delta t}$ such that property iii) holds, calculate

$$\frac{\partial A_3}{\partial r} \leq -1 + \gamma\overline{\Delta t}\eta.$$

Here we must choose

$$\overline{\Delta t} < \frac{1}{\gamma\eta}, \tag{38}$$

such that the derivative of A_3 with respect to r is negative. Hence there is a unique $r_1 \in [0, r_+]$ for any $e^{n+1/4}, r^n$ within the desired interval.

Now, examine the update scheme for $r^{n+1/2}$ and define a function A_4 from (13) by placing all terms on one hand side and use (12) to eliminate r^n, i.e.

$$A_4(r, r_1, e^{n+1/4}) = -r + r_1 + (1 - 2\gamma)\overline{\Delta t}G(e^{n+1/4}, r_1) + \gamma\overline{\Delta t}G(e^{n+1/4}, r) \tag{39}$$

so that $r^{n+1/2}$ solves $A_4(r^{n+1/2}, r_1, e^{n+1/4}) = 0$. First, note that $\frac{\partial A_4}{\partial r}$ is identical to $\frac{\partial A_3}{\partial r}$, and hence property iii) holds as long as (38) is satisfied. We turn to property i); compute

$$A_4(0, r_1, e^{n+1/4}) = r_1 + (1 - 2\gamma)\overline{\Delta t}G(e^{n+1/4}, r_1) + \gamma\overline{\Delta t}G(e^{n+1/4}, 0). \tag{40}$$

For convenience we design a function

$$\Phi(e, r) = r + (1 - 2\gamma)\overline{\Delta t}G(e, r), \tag{41}$$

so that

$$A_4(r, r_1, e^{n+1/4}) = -r + \Phi(e^{n+1/4}, r_1) + \gamma\overline{\Delta t}G(e^{n+1/4}, r).$$

We want $\Phi(e, r)$ to be a nondecreasing function in r for all values of $e \in [0, 1]$. So, differentiate with respect to r and obtain

$$\frac{\partial \Phi}{\partial r} = 1 + (1 - 2\gamma)\overline{\Delta t}\frac{\partial G}{\partial r} \geq 1 - (1 - 2\gamma)\overline{\Delta t}\vartheta.$$

where we have set

$$\vartheta = -\min_{e,r}\frac{\partial G}{\partial r},$$

such that ϑ is a positive number. If we require

$$\overline{\Delta t} \leq \frac{1}{(1 - 2\gamma)\vartheta}, \tag{42}$$

we are guaranteed that the derivative of Φ with respect to r is always non-negative. Now, inserting for the lower bound of Φ gives

$$A_4(0,0,e^{n+1/4}) \geq (1-2\gamma)\overline{\Delta t}G(e^{n+1/4},0)+\gamma\overline{\Delta t}G(e^{n+1/4},0) \geq 0,$$

which is always greater or equal to zero since

$$G(e^{n+1/4},0) = -\varepsilon kq(e^{n+1/4}) \geq 0, \quad \text{for all} \quad e^{n+1/4} \in [0,1].$$

Then property i) holds. It remains to check property ii). Calculate

$$A_4(r_+,r_1,e^{n+1/4}) = -r_+ + r_1 + (1-2\gamma)\overline{\Delta t}G(e^{n+1/4},r_1)+\gamma\overline{\Delta t}G(e^{n+1/4},r_+). \tag{43}$$

We recognize the two mid terms as $\Phi(e^{n+1/4}, r_1)$, so insert for the upper bound of this function to obtain

$$A_4(r_+,r_1,e^{n+1/4}) \leq A_4(r_+,r_+,e^{n+1/4}) = (1-2\gamma)\overline{\Delta t}G(e^{n+1/4},r_+)+\gamma\overline{\Delta t}G(e^{n+1/4},r_+) \leq 0,$$

which is always non-positive for $\gamma = (2-\sqrt{2})/2$ and any $e^{n+1/4}$ within the unit interval. Thus all the properties in (31) are fulfilled and we conclude that there is a unique $r^{n+1/2}$ within the desired interval, i.e.

$$0 \leq r^{n+1/2} \leq r_+. \tag{44}$$

Bounds on $e^{n+1/2}$.

Consider first the update scheme for e_1 and define a function

$$A_5(e,e^n,r^{n+1/4}) = -e+e^n+\gamma\overline{\Delta t}F(e,r^{n+1/4}),$$

so that $A_5(e_1,e^n,r^{n+1/4}) = 0$ solves the scheme

$$e_1 = e^n + \gamma\overline{\Delta t}\big(-ke_1(e_1-a)(e_1-1)-e_1r^{n+1/4}\big),$$

obtained from (14). Properties i) and ii) hold since

$$A_5(0,e^n,r^{n+1/4}) = -0+e^n+\gamma\overline{\Delta t}F(0,r^{n+1/4}) = e^n \geq 0,$$

and

$$A_5(1,e^n,r^{n+1/4}) = -1+e^n+\gamma\overline{\Delta t}F(1,r^{n+1/4}) = -1+e^n-\gamma\overline{\Delta t}r^{n+1/4} \leq 0.$$

As for property iii) we need

$$\frac{\partial A_5}{\partial e} = -1+\gamma\overline{\Delta t}\frac{\partial F}{\partial e}(e,r^{n+1/4}) < 0. \tag{45}$$

Suppose that $\overline{\Delta t}$ is chosen according to

$$\overline{\Delta t} < \frac{1}{\gamma\zeta}, \tag{46}$$

where ζ is as defined in (32). Then (45) is satisfied for any $r^{n+1/4}$ within the desired bounds, and there is hence a unique root $e_1 \in [0,1]$. This time step restriction is fulfilled for $\gamma = (2-\sqrt{2})/2$, if condition (33) holds.

Finally, we investigate the update scheme for $e^{n+1/2}$ in the same manner. Use (14) to eliminate e^n from (15) and define a function A_6 by

$$A_6(e,e_1,r^{n+1/4}) = -e+e_1+(1-2\gamma)\overline{\Delta t}F(e_1,r^{n+1/4})+\gamma\overline{\Delta t}F(e,r^{n+1/4}),$$

such that $e^{n+1/2}$ is the solution of $A_6(e^{n+1/2}, e_1, r^{n+1/4}) = 0$. Note that

$$\frac{\partial A_6}{\partial e} = -1 + \gamma\overline{\Delta t}\frac{\partial F(e, r^{n+1/4})}{\partial e}$$

which is the exact same expression as that for $\frac{\partial A_5}{\partial e}$. Thus, $\frac{\partial A_6}{\partial e}$ is negative as long as (46) is satisfied, and then property iii) holds. Next, check property i) and calculate

$$\begin{aligned} A_6(0, e_1, r^{n+1/4}) &= 0 + e_1 + (1-2\gamma)F(e_1, r^{n+1/4}) + \gamma\overline{\Delta t}F(0, r^{n+1/4}) \\ &= e_1 + (1-2\gamma)\overline{\Delta t}F(e_1, r^{n+1/4}). \end{aligned}$$

In order for this to be a non-negative number for any relevant $e_1, r^{n+1/4}$, we must have

$$e_1 + (1-2\gamma)\overline{\Delta t}F(e_1, r^{n+1/4}) \geq 0.$$

Since F takes on both positive and negative numbers, we need to ensure that the inequality is satisfied for the worst case, i.e. when F reaches minimum. Define $\min F(e_1, r^{n+1/4}) = -\kappa$, where κ is a positive number. Then

$$(1-2\gamma)\overline{\Delta t}\kappa \leq e_1 \leq 1,$$

so the time step is restricted to

$$\overline{\Delta t} \leq \frac{1}{(1-2\gamma)\kappa}, \tag{47}$$

in order to guarantee that property i) is satisfied. It remains to check property ii). Calculate

$$A_6(1, e_1, r^{n+1/4}) = -1 + e_1 + (1-2\gamma)\overline{\Delta t}F(e_1, r^{n+1/4}) - \gamma\overline{\Delta t}r^{n+1/4}.$$

First, note that

$$\frac{\partial A_6(1, e_1, r^{n+1/4})}{\partial r^{n+1/4}} = -\gamma\overline{\Delta t} - (1-2\gamma)\overline{\Delta t}e_1 < 0\,,$$

so the maximum is attained at $r^{n+1/4} = 0$ for some e_1. Now, observe that $A_6(1, 0, 0) = -1$, and $A_6(1, 1, 0) = 0$. This means that if we can enforce $A_6(1, e_1, 0)$ to be a nondecreasing function in e_1, we have assured that $A_6(1, e_1, r) \leq A_6(1, e_1, 0) \leq 0$ and thus property ii) will be fulfilled. We therefore want to find a condition on $\overline{\Delta t}$ such that this is the case. Note that

$$\frac{\partial A_6(1, e_1, 0)}{\partial e_1} = 1 + (1-2\gamma)\overline{\Delta t}\frac{\partial F(e_1, 0)}{\partial e_1} \geq 1 + (1-2\gamma)\overline{\Delta t}\min_{e_1}\frac{\partial F(e_1, 0)}{\partial e_1}. \tag{48}$$

Define $s(e_1) = \frac{\partial F(e_1,0)}{\partial e_1}$ and find $\frac{\partial^2 s(e_1)}{\partial e_1^2} = -6k < 0$. Thus, the minimum of s is attained at the end points $e_1 = 0$ or $e_1 = 1$, where we have $s(0) = -ka$ and $s(1) = -k(1-a)$. Therefore, with

$$\nu = -\min_{e_1}\frac{\partial F}{\partial e_1} = \max(ka, k(1-a)), \tag{49}$$

we may choose

$$\overline{\Delta t} \leq \frac{1}{(1-2\gamma)\nu}, \tag{50}$$

so that (48) is always non-negative, and property ii) holds.

In summary, if (18)-(19) hold, then

$$0 \leq e^{n+1/4} \leq 1,$$
$$0 \leq e^{n+1/2} \leq 1,$$
$$0 \leq r^{n+1/4} \leq r_+,$$
$$0 \leq r^{n+1/2} \leq r_+,$$

under the time step restriction found by taking the smallest $\overline{\Delta t}$ from (33), (37), (38), (42), (47) and (50); this will be quantified in the next subsection. Under the assumption that the data from Step 2 of Procedure 2.1 also is within the physiological range, the SDIRK method applied in the third step of the procedure will, under identical condition on the time step, generate physiological data as well.

3.3. Discussion of the time step restrictions. Above it was proven that both our numerical schemes produce solutions within the physiologically relevant range under certain conditions on the time step. We complete this section by comparing these restrictions, to uncover how strict the conditions are in order to ensure numerical stability. In order to find actual values for the stability conditions, we need to calculate the maximum and minimum values of the derivatives of F in (8) and G in (9). With the model parameters as described in Section 1, we find

$$\zeta = \max_{e,r} \frac{\partial F}{\partial e} = 2.43, \quad \text{and} \quad \nu = -\min_{e} \frac{\partial F}{\partial e} = 7.2. \tag{51}$$

Moreover

$$\eta = \max_{e,r} \frac{\partial G}{\partial r} = 0.22, \quad \text{and} \quad \vartheta = -\min_{e,r} \frac{\partial G}{\partial r} = 1.14.$$

In addition we find the minimum of F to be

$$\kappa = -\min_{e,r} F(e,r) = 2.42.$$

We summarize the time step restrictions found in the previous subsection. For $e^{n+1/4}$ to be bounded within the unit interval we required

$$\overline{\Delta t} < \frac{2}{\zeta} = 0.82, \tag{52}$$

whereas $r^{n+1/4}$ is within the desired interval as long as

$$\overline{\Delta t} < \frac{2}{\eta} = 9.1. \tag{53}$$

As for the bounds on $r^{n+1/2}$, we found two restrictions which become

$$\overline{\Delta t} < \frac{1}{\gamma\eta} = 15.80, \quad \text{and} \quad \overline{\Delta t} \leq \frac{1}{(1-2\gamma)\vartheta} = 2.12. \tag{54}$$

The time step restrictions to ensure $e^{n+1/2}$ within $[0,1]$ were found to be

$$\overline{\Delta t} \leq \frac{1}{(1-2\gamma)\kappa} = 1.00, \quad \text{and} \quad \overline{\Delta t} \leq \frac{1}{(1-2\gamma)\nu} = 0.335. \tag{55}$$

We observe that the sharpest restriction on $\overline{\Delta t}$ is that required to ensure the desired bounds on $e^{n+1/2}$, and conclude that the time step condition $\Delta t_s = 2\overline{\Delta t}$ for the second-order method is

$$\Delta t_s = 2\overline{\Delta t} \leq 2\frac{1}{(1-2\gamma)\nu} = 0.671. \tag{56}$$

Note that, under our assumptions, the above restrictions are sufficient but not necessary for numerical stability and might be too strict in practice.

We turn to the forward Euler scheme. The time step condition was found to be

$$\Delta t_e \le \min\left\{ \frac{1}{\frac{4\delta}{\Delta x^2} + \max(ka, k(1-a)) + r_+}, \frac{1}{\varepsilon + \frac{\mu_1}{\mu_2} r_+} \right\} = \min\left\{ \frac{1}{\frac{2\times 10^{-4}}{\Delta x^2} + 9.62}, 1.74 \right\}$$
$$= \frac{1}{\frac{2\times 10^{-4}}{\Delta x^2} + 9.62},$$

where we have inserted for the parameter values given in Section 1. In contrast to the $\Delta t_s = \mathcal{O}(1)$ condition on the second-order method, the Euler time step restriction $\Delta t_e = \mathcal{O}(\Delta x^2)$ limits the efficiency of the scheme for fine-scale computations.

3.3.1. Numerical experiments on the time step restriction for the forward Euler and SDIRK schemes. We have chosen the following parameter values for the Panfilov model: $\mu_1 = 0.07$, $\mu_2 = 0.3$, $k = 8$, $b = 0.1$, $a = 0.1$, and $\delta = 5 \times 10^{-5}$. These parameters result in that the theoretical restriction on Δt_e has the following specific formula:

$$\Delta t_e \le \frac{1}{\frac{2\times 10^{-4}}{\Delta x^2} + 9.62}.$$

To check the sharpness of the theoretical restriction, the forward Euler scheme is used on a series of refined 2D uniform meshes, for which we have tried $\Delta x = \frac{1}{400}, \frac{1}{800}, \frac{1}{1600}, \frac{1}{3200}, \frac{1}{6400}$. All the simulations are carried out for $0 < t \le 100$, using the same initial conditions as follows:

$$e(x, y, 0) = \frac{1}{2}(1 - \cos(\pi x)),$$
$$r(x, y, 0) = \frac{r_+}{2}(1 - \cos(\pi y)).$$

For each spatial mesh resolution, a series of time step sizes is tried as $\Delta t = 1.00\Delta t_e, 1.01\Delta t_e, 1.02\Delta t_e, \ldots$, and so on. The numerical solutions $e^n_{i,j}$ and $r^n_{i,j}$ from each time step are examined with respect to the requirements:

$$0 \le e^n_{i,j} \le 1 \quad \text{and} \quad 0 \le r^n_{i,j} \le r_+.$$

If any numerical value of a simulation fails the above requirements, the particular choice of Δt is considered to be too large. The numerical experiments are summarized in Table 1. It can be seen from the table that the theoretical restriction on Δt_e is sharp for small values of Δx.

Δx	Theoretical Δt_e	Largest working Δt
$\frac{1}{400}$	2.40269×10^{-2}	$1.19\Delta t_e$
$\frac{1}{800}$	7.26639×10^{-3}	$1.05\Delta t_e$
$\frac{1}{1600}$	1.91710×10^{-3}	$1.01\Delta t_e$
$\frac{1}{3200}$	4.85998×10^{-4}	$1.00\Delta t_e$
$\frac{1}{6400}$	1.21927×10^{-4}	$1.00\Delta t_e$

TABLE 1. The largest working time step in relation to the theoretical restriction on Δt_e.

Regarding the SDIRK scheme, which is used as Step 1 and Step 3 in Procedure 2.1, we have done numerical experiments for a large number of different initial e and r values. The purpose is to check sharpness of the theoretical restriction on

Δt_s given in (56). More specifically, we have tested the following combinations of initial (e_i, r_j) values:

$$\begin{aligned} e_i &= \frac{i}{1000} \quad 0 \le i \le 1000, \\ r_j &= \frac{j}{1000} r_+ \quad 0 \le j \le 1000. \end{aligned}$$

For each combination of initial e and r initial values, the SDIRK scheme is tested with different time step sizes: $0.98\Delta t_s$, $0.99\Delta t_s$, $1.00\Delta t_s$,..., and so on. The numerical experiments show that the largest time step size working for all the (e_i, r_j) initial values is $1.06\Delta t_s$. In other words, the theoretical restriction (56) seems to be slightly too conservative.

4. Concluding remarks

We have proposed a second-order scheme for the Aliev-Panfilov model and compared it to the forward Euler method with respect to stability. The forward Euler method has the huge advantage of simplicity, but the calculated time step restriction shows that it might be less efficient for very resolved spatial meshes. In contrast, the suggested second-order method is more complicated but admits a much larger time step for fine-scale computations. This suggests that the proposed scheme is a good choice when high resolution and accuracy are important.

In a forthcoming paper we will perform extensive numerical computations to compare the schemes of the present paper in terms of computational cost, accuracy and efficiency. We will also study the extremely complex solutions to the Aliev-Panfilov model on very refined grids; e.g. spiral wave creation and spiral wave breakup in the myocardium. For these kinds of problems where great spatial resolution is needed our second-order scheme is a promising candidate. To make this study feasible we will develop parallel codes running on rather large computational clusters.

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