

HIGH ORDER RUSH LARSEN SOLVER FOR STIFF ODE_s

YVES COUDIÈRE, CHARLIE DOUANLA LONTSI, AND CHARLES PIERRE

ABSTRACT. In this paper, we introduce a class of high order methods for solving stiff ordinary differential equation systems. The methods extend to high order of accuracy the previous first order method proposed in 1978 by Rush and Larsen [10] and the second order method proposed in 2009 by Perego and Veneziani [9] which are widely used for solving dynamic model of cardiac cells in electro-physiology. These methods belong to the class of exponential integrators but with some flexibilities in the implementation related to choice of the linear part. The convergence, the stability and the accuracy are investigated applying the schemes on the BR [1] and the TNNP [13] ionic models.

Keywords Electro-physiology, ionic models, stiff ordinary differential equation systems, high order Rush Larsen schemes, exponential integrators.

1. INTRODUCTION

A large range of mathematical models used to describe the time evolution of physical phenomena are formulated as a system of ordinary differential equations (ODEs)

$$(1) \quad \frac{dy}{dt} = f(t, y), \quad y(0) = y_0 \in \mathbb{R}^N.$$

There are several classical numerical methods designed to solve (1). These methods are either explicit (forward Euler, explicit Runge Kutta, Adams Bashforth) or implicit (backward Euler, backward differentiation method, Crank Nicholson). However, in the case where the problem considered exhibit a stiff behavior, the numerical method has to be efficient to deal effectively with the stiffness. Many authors interested by the numerical resolution of stiff problems are particularly motivated by exponential integrators these last years (see [2, 4, 7, 14, 8]). Probably because these methods are explicit and have good stability properties unlike the classical explicit methods. But even if a method has good stability properties, it is always advantageous in practice to have a method which is easy to implement and with a less computational cost. All the exponential integrators use a transformation of (1) written in the general form,

$$(2) \quad \frac{dy}{dt} = a(t, y)y + b(t, y), \quad y(0) = y_0 \in \mathbb{R}^N.$$

In cardiac electro-physiology, the models describing the dynamic response of the cardiac cells to a stimulus are consist of a set of reaction-diffusion equations coupled to a system of ordinary differential equations called *ionic models*. Some of *ionic models* as innovated one exhibit a stiffness behavior on some variables. This stiffness induce a considerable computational challenge for realistic simulations based on these models.

Date: July 4, 2016.

Rush and Larsen proposed in 1978 (see [10]) to approximate at every intervals $[t_n, t_n + h]$, from the value $y(t_n) = y_n$, $a(t, y)$ and $b(t, y)$ by the constants $a_n = a(t_n, y_n)$ and $b_n = b(t_n, y_n)$ respectively, then solve exactly the approximated problem obtain by the variation of constant formula. The method is still widely used in cardiac electro-physiology where it is called Rush-Larsen scheme. But this is nothing other than the exponential Euler method implemented in a specific way. The method is popular in this field because in addition to the fact that it doesn't require a big supplementary implementation difficulty compared to forward euler method, it is an explicit method, with good stability properties and no high CPU cost.

Since the Rush Larsen (shortly denoted RL) method were limited at order one only of accuracy the question on how to increase the order of RL eventually with a small additional cost and a small additional implementation difficulty have been the topic of many papers. Sundnes proposed in 2009 (see [8]) a second order method to extend the RL idea. In the same year Perego and Venziani proposed in [9] a second order two-step method close to the original RL that will be called in this work RL_2 . But all these methods are limited at order two of accuracy and then require small time-steps for realistic simulations. This work will be concern to high order Rush Larsen schemes for solving stiff ODEs.

The first contribution of this work is the introduction of the general method to build high order Rush Larsen schemes, from which is derived the order two, three and four of the Rush Larsen method. Our second contribution is the proof of the convergence in the sens of perturbations of RL_k methods $k = 2, 3$ and 4. The third contribution is the numerical analysis of the stability domain of RL_k method dependently on a parameter θ .

The paper is organized as follows. In section 2 are presented the principle used to build the method and the statement of RL_k , $k = 2, 3$ and 4. The properties of the scheme are presented in the section 3 where the consistence, the convergence and the stability in the Dalquist sens are studied. Numerical results are presented in the section 4 and followed by a conclusion final section 5.

2. SCHEME DEFINITION

2.1. Principle of the method. We consider the initial value problem (2), where the two functions a and b have C^k regularity, with the solution $y(t)$ defined on some time interval $[0, T]$, $T > 0$.

We set a time step $h > 0$. An intermediate time instant $t_n \in [0, T]$ being given, so that $t_n + h < T$, the exact solution of (2) satisfies the variation of the constant formula,

$$(3) \quad y(t_n + h) = e^{g(t_n+h)} \left(y(t_n) + \int_{t_n}^{t_n+h} e^{-g(\tau)} b(y(\tau), \tau) d\tau \right), \quad g(t) = \int_{t_n}^t a(\tau, y(\tau)) d\tau,$$

If in the time interval $(t_n, t_n + h]$ we perform the approximations $a(t, y(t)) \simeq \alpha_n \in \mathbb{R}^N \times \mathbb{R}^N$ (a constant matrix) and $b(t, y(t)) = p(t)$ a polynomial in (3), we get,

$$y(t_n + h) \simeq \varphi_0(\alpha_n h) y(t_n) + \sum_{j=0}^n h^{j+1} \varphi_{j+1}(\alpha_n h) \frac{d^j p}{dt^j}(t_n),$$

with n the polynomial $p(t)$ degree and with φ_j the functions introduced in [12] and recursively given by,

$$(4) \quad \varphi_0(z) = e^z, \quad \varphi_{j+1}(z) = \frac{\varphi_j(z) - 1/j!}{z}.$$

In this paper we study approximations built by truncating the series in the previous equation at the first term only, *i.e.*,

$$(5) \quad y(t_n + h) \simeq y_{n+1} = \varphi_0(\alpha_n h)y(t_n) + h\varphi_1(\alpha_n h)\beta_n, \quad \beta_n \in \mathbb{R}^N,$$

which means that both $a(t, y(t))$ and $b(t, y(t))$ are approximated by two constants α_n and β_n on the time interval $(t_n, t_n + h]$ in (3). Note that y_{n+1} in (5) can be simply written as,

$$(6) \quad y_{n+1} = y(t_n) + h\varphi_1(\alpha_n h)(\alpha_n y(t_n) + \beta_n), \quad \varphi_1(z) = \frac{e^z - 1}{z}.$$

2.2. Parameters α_n and β_n definition. We will derive conditions on α_n and β_n so that the truncation error is at order k , *i.e.*,

$$(7) \quad y(t_n + h) - y_{n+1} = O(h^{k+1}).$$

For this we develop α_n and β_n at order k ,

$$(8) \quad \begin{cases} \alpha_n &= \alpha_{n,0} + \alpha_{n,1}h + \cdots + \alpha_{n,k-1}h^{k-1} + O(h^k), \\ \beta_n &= \beta_{n,0} + \beta_{n,1}h + \cdots + \beta_{n,k-1}h^{k-1} + O(h^k), \end{cases}$$

in order to perform the Taylor expansion of y_{n+1} ,

$$(9) \quad y_{n+1} = y(t_n) + \sum_{j=1}^k \frac{r_j}{j!} h^j + O(h^{k+1}).$$

Introducing the exact solution $y(t_n + h)$ Taylor expansion,

$$(10) \quad y(t_n + h) = y(t_n) + \sum_{j=1}^k \frac{s_j}{j!} h^j + O(h^{k+1}),$$

order k consistency is achieved *iff*,

$$r_1 = s_1, \dots, r_k = s_k.$$

Proposition 2.1. *The consistency is at order k if,*

- $k = 2$,

$$(11) \quad \alpha_n = a_n + \frac{1}{2}a'_n h + O(h^2), \quad \beta_n = b_n + \frac{1}{2}b'_n h + O(h^2),$$

- $k = 3$,

$$(12) \quad \begin{cases} \alpha_n &= a_n + \frac{1}{2}a'_n h + \frac{1}{6}a''_n h^2 + O(h^3), \\ \beta_n &= b_n + \frac{1}{2}b'_n h + \frac{1}{12}(a'_n b_n - a_n b'_n)h^2 + O(h^3), \end{cases}$$

- $k = 4$,

$$(13) \quad \begin{cases} \alpha &= a_n + \frac{1}{2}a'_n h + \frac{1}{6}a''_n h^2 + \frac{1}{24}a'''_n h^3 + O(h^4), \\ \beta &= b_n + \frac{1}{2}b'_n h + \frac{1}{12}(a'_n b_n - a_n b'_n)h^2 + \left(\frac{1}{24}b'''_n + \frac{1}{24}(a''_n b_n - a_n b''_n)\right)h^3 + O(h^4), \end{cases}$$

where $y_n = y(t_n)$, $a_n = a(t_n, y(t_n))$, $b_n = b(t_n, y(t_n))$, $a'_n = \frac{d}{dt}a(t, y(t))|_{t=t_n}$, $b'_n = \frac{d}{dt}b(t, y(t))|_{t=t_n}$, $a''_n = \frac{d^2}{dt^2}a(t, y(t))|_{t=t_n}$, $b''_n = \frac{d^2}{dt^2}b(t, y(t))|_{t=t_n}$, \dots

Proof. Using relation (1) to develop the successive derivatives of $y(t)$ at point t_n , the Taylor expansion for the exact solution $y(t_n + h)$ in (10) is given by,

$$\begin{aligned}
 (14) \quad s_1 &= a_n y_n + b_n, \\
 s_2 &= (a'_n + a_n^2) y_n + a_n b_n + b'_n, \\
 s_3 &= (a''_n + 3a_n a'_n + a_n^3) y_n + b''_n + a_n b'_n + 2a'_n b_n + a_n^2 b_n, \\
 s_4 &= (a'''_n + 4a''_n a_n + 3a_n'^2 + 6a'_n a_n^2 + a_n^4) y_n \\
 &\quad + b'''_n + b''_n a_n + 3a''_n b_n + 5a'_n a_n b_n + 3a'_n b'_n + a_n^3 b_n + a_n^2 b'_n.
 \end{aligned}$$

Otherwise, using the formula (6), the coefficients r_k , $k = 1 \dots 4$ in the Taylor expansion formula (9) of the numerical solution y_{n+1} are given by,

$$\begin{aligned}
 (15) \quad r_1 &= \alpha_{n,0} y_n + \beta_{n,0}, \\
 r_2 &= (2\alpha_{n,1} + \alpha_{n,0}^2) y_n + 2\beta_{n,1} + \alpha_{n,0} \beta_{n,0}, \\
 r_3 &= (6\alpha_{n,2} + \alpha_{n,0}^3 + 6\alpha_{n,0} \alpha_{n,1}) y_n + 3\alpha_{n,1} \beta_{n,0} + 6\beta_{n,2} + \alpha_{n,0}^2 \beta_{n,0} + 3\alpha_{n,0} \beta_{n,1}, \\
 r_4 &= (24\alpha_{n,0} \alpha_{n,2} + 24\alpha_{n,3} + 12\alpha_{n,1} \alpha_{n,0}^2 + 12\alpha_{n,1}^2 + \alpha_{n,0}^4) y_n \\
 &\quad + 12\alpha_{n,2} \beta_{n,0} + 24\beta_{n,3} + 12\alpha_{n,0} \beta_{n,2} + 12\alpha_{n,1} \beta_{n,1} + 4\alpha_{n,0}^2 \beta_{n,1} + 8\alpha_{n,0} \alpha_{n,1} \beta_{n,0} + \alpha_{n,0}^3 \beta_{n,0}.
 \end{aligned}$$

By identifying in $r_l = s_l$ the coefficients in y_n and the coefficients without y_n , we obtain the coefficients $\alpha_{n,l-1}$ and $\beta_{n,l-1}$ successively for $l = 1 \dots k$, with $k = 2, 3, 4$. The coefficients obtained and replaced in (8) give the proposition 2.1. \square

2.3. Rush Larsen scheme statement. Let us denote $t_{n-j} = t_n - jh$, $j = 0, \dots, k-1$, and:

$$y_{n-j} = y(t_{n-j}), \quad a_{n-j} = a(t_{n-j}, y_{n-j}), \quad b_{n-j} = b(t_{n-j}, y_{n-j}).$$

Coefficients α_n and β_n can be defined as functions of y_n and of the a_{n-j} , b_{n-j} for $j = 0, \dots, k-1$ by replacing the derivatives of $a(t, y(t))$ and of $b(t, y(t))$ in the definition of α_n and β_n in proposition 2.1 by forwards finite difference approximations.

Finite difference formula need to be chosen carefully in order for equations (7) to remain valid (*i.e.* to remain in $O(h^{k+1})$). Depending on the scheme order k , finite difference formula have to provide,

- $k = 2$: an approximation of order 1 of $\alpha_{n,1}$ and $\beta_{n,1}$.
- $k = 3$: an approximation of order 2 of $\alpha_{n,1}$, $\beta_{n,1}$, and of order 1 of $\alpha_{n,2}$ and $\beta_{n,2}$.
- $k = 4$: an approximation of order 3 on $\alpha_{n,1}$, $\beta_{n,1}$, of order 2 of $\alpha_{n,2}$, $\beta_{n,2}$, and of order 1 of $\alpha_{n,3}$ and $\beta_{n,3}$.

Doing so, through the following forward finite difference formula (with obvious notations):

$$\begin{aligned} f'_n &= \frac{f_n - f_{n-1}}{h} + O(h), \quad f'_n = \frac{1}{2h} (3f_n - 4f_{n-1} + f_{n-2}) + O(h^2), \\ f'_n &= \frac{1}{6h} (11f_n - 18f_{n-1} + 9f_{n-2} - 2f_{n-3}) + O(h^3); \\ f''_n &= \frac{1}{h^2} (f_n - 2f_{n-1} + f_{n-2}) + O(h), \quad f''_n = \frac{1}{h^2} (2f_n - 5f_{n-1} + 4f_{n-2} - f_{n-3}) + O(h^2); \\ f'''_n &= \frac{1}{h^3} (f_n - 3f_{n-1} + 3f_{n-2} - f_{n-3}) + O(h), \end{aligned}$$

one gets the following scheme definition.

Definition 2.1. The Rush Larsen scheme general formulation is,

$$(16) \quad y_{n+1} = y_n + h\varphi_1(\alpha_n h)(\alpha_n y_n + \beta_n),$$

where the coefficients α_n and β_n are given relatively to the scheme order k as follows.

- $k = 2$: *Rush Larsen 2 (RL₂)*,

$$\alpha_n = \frac{3}{2}a_n - \frac{1}{2}a_{n-1}, \quad \beta = \frac{3}{2}b_n - \frac{1}{2}b_{n-1}.$$

- $k = 3$: *Rush Larsen 3 (RL₃)*,

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

- $k = 4$: *Rush Larsen 4 (RL₄)*,

$$\begin{aligned} \alpha_n &= \frac{1}{24}(55a_n - 59a_{n-1} + 37a_{n-2} - 9a_{n-3}), \\ \beta_n &= \frac{1}{24}(55b_n - 59b_{n-1} + 37b_{n-2} - 9b_{n-3}) + \frac{h}{12}(a_n(3b_{n-1} - b_{n-2}) - (3a_{n-1} - a_{n-2})b_n). \end{aligned}$$

Remark 2.1. In the case $k = 2$ we precisely recover the scheme originally named *Rush Larsen of order 2* in [9].

When $a = 0$ we retrieve the *Adams Bashforth schemes*.

3. SCHEME PROPERTIES

In the sequel $y(t)$ is the solution of (1) on some time interval $[0, T]$.

3.1. Convergence, stability under perturbation. Let us set k the order of the considered Rush Larsen scheme in definition 2.1. Clearly, the scheme can be formulated as a general k -step non-linear method,

$$(17) \quad \begin{bmatrix} y_{k+1} = s(Y, n, h) \\ y_k \\ \vdots \\ y_2 \end{bmatrix} := S(Y, n, h), \quad \text{for } Y = \begin{bmatrix} y_k \\ \vdots \\ y_1 \end{bmatrix},$$

with,

$$s(Y, n, h) = y_k + \varphi(\alpha(Y, n, h)h) (\alpha(Y, n, h)y_k + \beta(Y, n, h)),$$

where the parameters $\alpha(Y, n, h)$ and $\beta(Y, n, h)$ are the one given in definition 2.1 in a more general framework where $a_{n-i} = a(t_{n-i}, y_{k-i})$ and $b_{n-i} = b(t_{n-i}, y_{k-i})$, $i = 0, \dots, k-1$. With this definition, if we set for $n \geq k$, $Y_n = (y_{n-k}, \dots, y_{n-k+1})$, the vector consisting of the k previous steps data points $y_{n-k}, \dots, y_{n-k+1}$ approximating the exact solution $y(t)$ at the time instants t_n, \dots, t_{n-k+1} respectively, the RL_k method is defined by $Y_{n+1} = S(Y_n, n, h)$ or $y_{n+1} = s(Y_n, n, h)$.

Such a general formulation has been analyzed in [3], where the following two stability criteria have been considered: there exists $h_0 > 0$ so that for $h < h_0$,

$$(18) \quad |S(Y, n, h) - S(Z, n, h)|_\infty \leq |Y - Z|_\infty (1 + Ch(|Y|_\infty + 1)),$$

$$(19) \quad |S(Y, n, h)|_\infty \leq |Y|_\infty (1 + Ch) + Ch$$

where C is a positive constant only depending on the problem data $a(t, y)$, $b(t, y)$ and y_0 in (1).

It has been shown in [3] that in case the scheme generator $S(Y, n, h)$ satisfies (18) (19) then the scheme is stable under perturbation. If moreover it is constant at order k then it is also converging at order k . Assumption for this is that $a(t, y)$ and $b(t, y)$ are C^k functions. It has eventually also been proven in [3] that it is sufficient to prove convergence in case $a(t, y)$ and $b(t, y)$ have compact support to ensure convergence in general.

Theorem 3.1. *Let $a(t, y)$ and $b(t, y)$ in equation (1) be C^k functions. Then the Rush Larsen schemes of order $k = 2, 3$ or 4 in definition (16) are stable under perturbation and convergent at order k .*

Proof. Since consistency at order k has already been proven in proposition 2.1, to prove convergence at order k is sufficient to show that the two stability criteria (18) (19) hold for the RL_k scheme generator $S(Y, n, h)$ in the case where $a(t, y)$ and $b(t, y)$ are C^k with compact support.

The compact support assumption imply that, there exists two constants C_1 and δ only depending on $a(t, y)$, $b(t, y)$ and the initial condition y_0 so that for $nh \leq T$,

$$(20) \quad |\alpha(Y, n, h)| \leq C_1, \quad |\beta(Y, n, h)| \leq C_1,$$

$$(21) \quad |\varphi_1(\alpha(Y, n, h)h)\alpha(Y, n, h)| \leq C_1, \quad |\varphi_1(\beta(Y, n, h)h)\beta(Y, n, h)| \leq C_1,$$

and

$$(22) \quad |\varphi_1(\alpha(Y, n, h)h)\alpha(Y, n, h) - \varphi_1(\alpha(Z, n, h)h)\alpha(Z, n, h)| \leq \delta|Y - Z|_\infty,$$

$$|\varphi_1(\alpha(Y, n, h)h)\beta(Y, n, h) - \varphi_1(\alpha(Z, n, h)h)\beta(Z, n, h)| \leq \delta|Y - Z|_\infty.$$

Indeed a and b are globally bounded and Lipschitz by hypothesis. Hence the functions $\alpha : Y \in \mathbb{R}^N \mapsto \alpha(Y, n, h) \in \mathbb{R}^N \times \mathbb{R}^N$ and $\beta : Y \in \mathbb{R}^N \mapsto \beta(Y, n, h) \in \mathbb{R}^N$ are also globally bounded and (20) is then verified. More over, these functions are also globally Lipschitz. Indeed, α and β are both linear combination of Lipschitz functions ($a(t, y)$ and $b(t, y)$) with the difference that in β there is a linear combination of the products $a(t, y)b(t, y)$. But since a and b are globally bounded and Lipschitz, their product remains globally bounded and Lipschitz.

Argument à ajouter : φ_1 est analytique sur \mathbb{C} On the other hand, the function $\varphi_1 : z \in \mathbb{R}^N \times \mathbb{R}^N \mapsto \varphi_1(z) \in \mathbb{R}^N \times \mathbb{R}^N$ is C^k in all bounded domain of $\mathbb{R}^N \times \mathbb{R}^N$. So φ_1 is globally bounded and Lipschitz in all bounded domain of $\mathbb{R}^N \times \mathbb{R}^N$. Otherwise, since for $h < h_0 < T$, the function $h\alpha : Y \in \mathbb{R}^N \mapsto \alpha(Y, n, h)h \in \mathbb{R}^N \times \mathbb{R}^N$ is globally bounded and Lipschitz, the function $Y \in \mathbb{R}^N \mapsto \varphi_1(\alpha(Y, n, h)h) \in$

$\mathbb{R}^N \times \mathbb{R}^N$ is globally bounded and Lipschitz as composition of two globally bounded and Lipschitz functions. It follows that the functions $Y \mapsto \varphi_1(\alpha(Y, n, h)h)\alpha(Y, n, h)$ and $Y \mapsto \varphi_1(\alpha(Y, n, h)h)\beta(Y, n, h)$ are globally bounded and Lipschitz as product of globally bounded and Lipschitz functions, therefore (21) and (22) are verified.

For the sake of simplicity, we use the notations $S_Y = S(Y, n, h)$, $S_Z = S(Z, n, h)$, $\alpha_Y = \alpha_{[Y, n, h]}$ and $\beta_Y = \beta_{[Y, n, h]}$ in the following.

$$|S_Y - S_Z| = |y_k - z_k + h(\varphi_1(\alpha_Y h)\alpha_Y y_k - \varphi_1(\alpha_Z h)\alpha_Z z_k + \varphi_1(\alpha_Y h)\beta_Y - \varphi_1(\alpha_Z h)\beta_Z)|$$

Introducing the term $\varphi_1(\alpha_Z h)\alpha_Z y_k$ we obtain,

$$\begin{aligned} |S_Y - S_Z| \leq & |y_k - z_k| + h|\varphi_1(\alpha_Y h)\alpha_Y - \varphi_1(\alpha_Z h)\alpha_Z| |y_k| \\ & + h|\varphi_1(\alpha_Z h)\alpha_Z| |y_k - z_k| + h|\varphi_1(\alpha_Y h)\beta_Y - \varphi_1(\alpha_Z h)\beta_Z| \end{aligned}$$

From (21) and (22) we obtain,

$$|S_Y - S_Z| \leq |Y - Z|_\infty + h\delta|Y - Z|_\infty |Y|_\infty + hC_1|Y - Z| + h\delta|Y - Z|$$

The condition (18) follows with $\gamma = \delta + C_1$. It remain to prove (19).

$$|S_Y| = |y_k + h\varphi_1(\alpha_Y h)(\alpha_Y y_k + \beta_Y)| \leq |Y|_\infty + hC_1|Y|_\infty + hC_1 \text{ (from (21))}.$$

The condition (19) then follows with $C = C_1$. \square

3.2. Stability in the sense of Dalquist. When considering problem (1) together with the *Dahquist test function*,

$$f(t, y) = \lambda y, \quad \lambda \in \mathbb{C},$$

the exact solution satisfies $|y(t_n + h)/y(t_n)| \leq 1$ as soon as $\text{Re}(\lambda) \leq 0$. The stability domain for a given numerical scheme is made of the $z \in \mathbb{C}$ so that for $\lambda h = z$, the numerical solution associated to the Dahquist test function $f(t, y) = \lambda y$ satisfies $|y_{n+1}/y_n| \leq 1$. Let us recall that a scheme is said to be,

- *A* stable (or absolutely stable) if $\mathbb{C}^- \subset D$,
- *A*(α) stable if D contains the cone with axis \mathbb{R}^- and with half angle α ,
- stiff stable if D contains a half plane $\text{Re } z < x \in \mathbb{R}^-$,
- *A*(0) stable if $\mathbb{R}^- \subset D$.

For the computational determination of the stability domain for multistep methods we refer to [5].

For the Rush Larsen scheme, the determination of the stability domain depends on the definition of the linear and non linear parts $a(t, y)$ and $b(t, y)$ relatively to the Dahquist test function $f(t, y) = \lambda y = a(t, y)y + b(t, y)$. In case $\lambda = a(t, y)$ the method is exact and the method is *A* stable. We want to know more generally what happens in case the stabilizer does not match the exact problem linear part. For this, as in [3], we consider the splitting,

$$a(t, y) = \theta\lambda, \quad b(t, y) = (1 - \theta)\lambda y,$$

for a scalar θ , so that the stability domain depends on θ and will therefore be denoted D_θ .

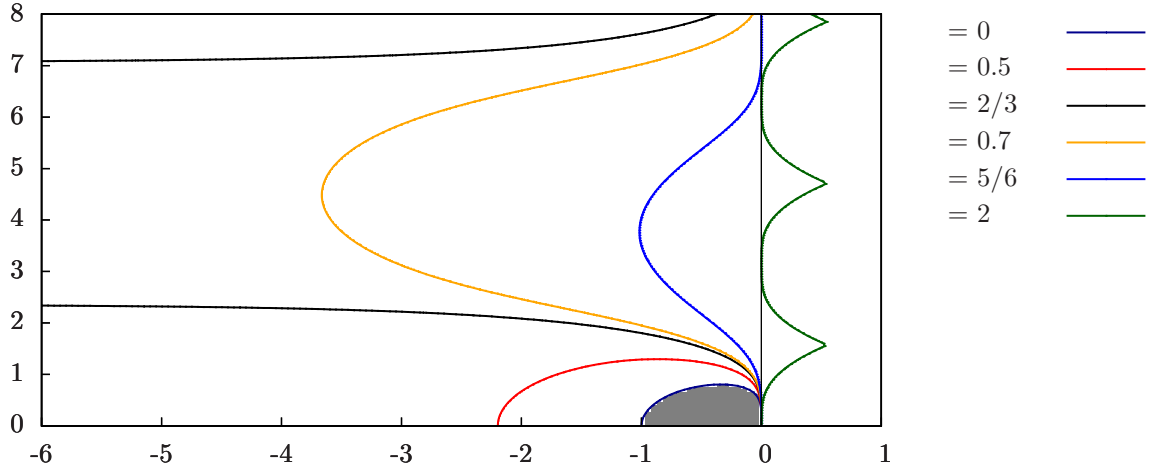


FIGURE 1. Stability domain D_θ for the RL_2 scheme for various values of θ . The stability domain for the particular case $\theta = 0$ (no stabilization) is in grey, corresponding to the classical Adams Bashforth multistep scheme of order 2.

3.2.1. *Order 2 Rush Larsen.* The stability domain for the RL_2 scheme had already been studied in [9]. The situation for this scheme is quite interesting and we reproduced [9] numerical results that are depicted on figure 1.

In case $0 \leq \theta < 2/3$ the stability domain D_θ is bounded and the method has no absolute stability property, however the stability domain has an increasing size with θ , starting from $\theta = 0$ with no stabilization, corresponding to the multistep Adams Bashforth scheme of order 2.

The threshold case $\theta = 2/3$ is quite interesting: D_θ contains the negative real axis and the method then is $A(0)$ stable, the domain boundary is asymptotically parallel to the real axis so that the method is not $A(\alpha)$ -stable.

When $\theta > 2/3$, the stability domain now remains located around the y -axis so that the method now becomes $A(\alpha)$ -stable with an angle α increasing with θ and going to $\pi/2$ as $\theta \rightarrow 1^-$.

Finally it is observed that the method is A stable when $\theta \geq 1$.

3.2.2. *Order 3, 4 Rush Larsen.* The situation is quite different for the Rush Larsen methods of order 3 and 4. The stability domains D_θ for various values of θ have been numerically computed and depicted on figures 2 and 3.

Excepted for the case $\theta = 1$, the schemes do not exhibit absolutely stable behaviors. The stability domains are always bounded. However, this stability domain, for values of $\theta \simeq 1$ are much larger than the $D_{\theta|_{\theta=0}}$ stability domain when no stabilisation occurs and corresponding to the Adams Bashforth scheme of order 3 or 4. This is particularly true for the order 3 case, where the stability domain $D_{\theta|_{\theta=0.85}}$ already is by 25 times wider on the left than $D_{\theta|_{\theta=0}}$, and more than 400 times wider on the left for $\theta = 1.05$.

For the order 4 Rush Larsen scheme stability domains are smaller but still $D_{\theta|_{\theta=1.05}}$ is almost 300 times wider on the left than $D_{\theta|_{\theta=0}}$.

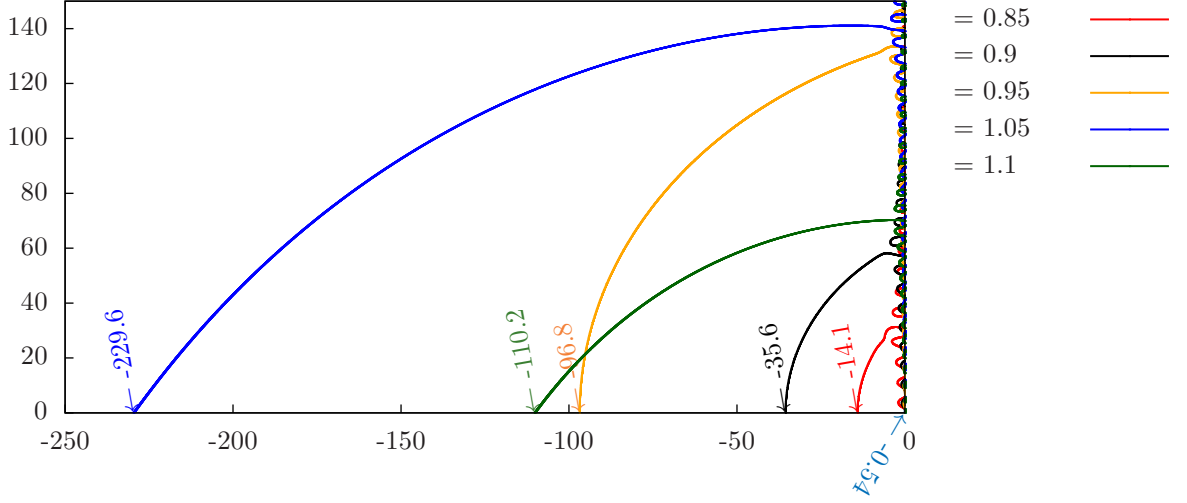


FIGURE 2. Stability domain D_θ for the RL_3 scheme. In the particular case $\theta = 0$ (no stabilisation, corresponding to the Adams Bashforth scheme of order 3), the stability domain crosses the x -axis at $x \simeq -0.54$ (dark blue arrow).

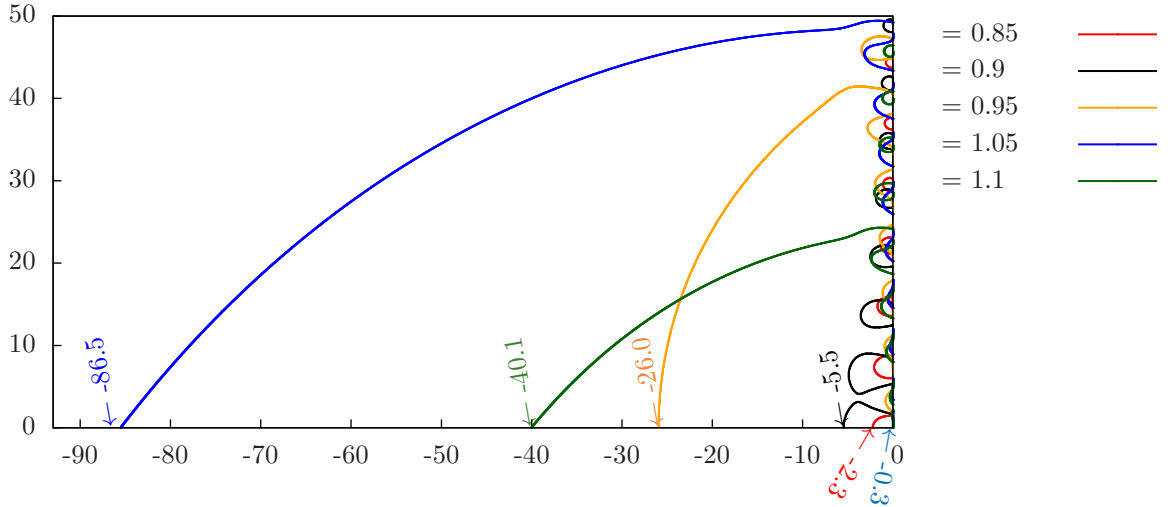


FIGURE 3. Stability domain D_θ for the RL_4 scheme. In the particular case $\theta = 0$ (no stabilisation, corresponding to the Adams Bashforth scheme of order 3), the stability domain crosses the x -axis at $x \simeq -0.3$ (dark blue arrow).

Although RL_3 and RL_4 methods are not $A(0)$ stable, the increase in size of the stability domain is significant when $\theta \simeq 1$ and sufficient for the method to be competitive in term of stability with $A(\alpha)$ stable methods, such as the exponential Adams Bashforth method studied in term of Dahiquist stability in [3], as detailed in section 4.

4. NUMERICAL RESULTS

Comme dans le papier EAB, on peut justifier le choix de l'application numérique par rapport à la méthode : taideur, $a(t,y)$ donné par le modèle ...

De plus par rapport au choix des modèles, on peut développer que TNNP est 15 fois plus raide que BR avec référence, que cela permet d'étudier le comportement du schéma par rapport à la raideur.

En plus on peut dire que l'on se servira de EAB comme d'un étalon avec lequel on compare notre méthode, et que EAB a par ailleurs déjà été comparé avec d'autres méthodes sur le même cas test.

In this section, we present numerical experiments whose purpose is to investigate the convergence, accuracy and stability of the RL_k schemes. As an applica-

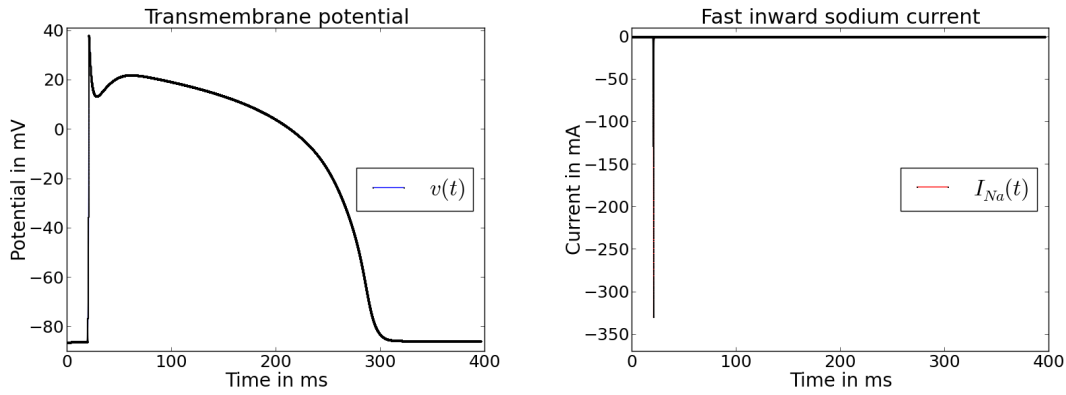


FIGURE 4. TNNP Model illustration. Left, cellular action potential : starting at a (negative) rest value, the membrane potential $v(t)$ has a stiff depolarization followed by a plateau and repolarizing to the rest value. Right : depolarization is induced by an ionic sodium current I_{Na} , the stiffness of which is illustrated here at action potential duration time scale.

tive context, cellular electro physiology has been considered, more precisely the *BeelerReuter* model (BR) [1] or the TNNP model [13] for human cardiac cells. These models describe cell membrane potential v time evolution. The choice of the two models is motivated by the fact that some variables of the model display stiff behaviors as depicted on figure 4, due to the presence of different time scales : from 1 ms to 100 ms roughly speaking. More precisely, it is shown in [11] that the largest negative real parts of eigenvalues of the Jacobian during one simulation are of -1170 and -82 for the TNNP and BR models respectively. This makes these models both stiff but with TNNP model about 15 times stiffer than the BR model and so will help us to study the robustness of RL_k method to the stiffness.

The BR model mathematically is expressed as an ODE system,

$$(23) \quad \begin{cases} \frac{dw_i}{dt} = \frac{w_{\infty,i}(v) - w_i}{\tau_i(v)} \\ \frac{dc}{dt} = g(w, c, v) \\ \frac{dv}{dt} = -I_{ion}(w, c, v) + I_{st}(t) \end{cases} \quad w_i \in \mathbb{R}, \quad i = 1, \dots, p \quad c \in \mathbb{R}^q, \quad v \in \mathbb{R},$$

where $w = (w_1, \dots, w_p) \in \mathbb{R}^p$ is the vector of gating variables, $c \in \mathbb{R}^q$ is a vector of ionic concentrations and $v \in \mathbb{R}$ is the cell membrane potential. The 4 functions $w_{\infty,i}(v)$, $\tau_i(v)$, $g(w, c, v)$ and $I_{ion}(w, c, v)$ are the reaction terms and $I_{st}(t)$ is the source term.

The system (23) directly reformulates under problem (1) form,

$$\frac{dy}{dt} = a(t, y)y + b(t, y), t \in (0, T], \quad y(0) = y^0 \in \mathbb{R}^N,$$

with $y = {}^T(w, c, v) \in \mathbb{R}^N$, $N = p + d + 1$ and,

$$(24) \quad a(t, y) = \begin{bmatrix} -1/\tau(v) & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}, \quad b(t, y) = \begin{bmatrix} w_{\infty}(v)/\tau(v) \\ g(y) \\ -I_{ion}(y) + I_{st}(t) \end{bmatrix},$$

where $-1/\tau(v)$ (*resp.* $w_{\infty}(v)/\tau(v)$) is the diagonal matrix with diagonal coefficients $-1/\tau_i(v)$ (*resp.* $w_{\infty,i}(v)/\tau_i(v)$). Therefore, RL_k schemes is directly applied to the BR and TNNP models with definition (24).

For the comparisons between methods, the RL_k will be compared with the EAB scheme that have been compared itself with other schemes for the same application (see [3]).

4.1. Convergence. To study convergence, a numerical solutions $y_h = (y_0, \dots, y_{T/h})$, $y_i \in \mathbb{R}^N$, computed with some time step h is interpolated as piecewise continuous polynomial of degree 3 (using Lagrange interpolation) and projected onto a reference time grid where they can be compared with a reference numerical solution y_{ref} . Since the exact solution is not available, a reference solution y_{ref} has been computed with the Runge Kutta solver of order 4. Note that during the simulation $T = 396 \text{ ms}$.

The numerical and reference solutions are then compared in L^∞ norm on their last component v (the cell membrane potential), which component exhibits the fastest variations. The error is defined as,

$$(25) \quad e(h) = \frac{\max |v_{ref} - v_h|}{\max |v_{ref}|}.$$

The function $h \mapsto e(h)$ has been plotted in Log/Log scale for the RL_k , $k = 2, 3, 4$. All schemes exhibit the same expected asymptotic behavior $e(h) = O(h^k)$ as $h \mapsto 0$ according to the general convergence theorem 3.1.

4.2. Stability. Tu peux revoir la définition de pas de temps critique : on l'a passablement modifiée dans EAB. Il faut parler de robustesse par rapport à la raideur. En commentaire on peut développer : EAB est $A(\alpha)$ stable, pas RL, mais cependant on a la même robustesse par rapport à la raideur, même un peu mieux stable aux ordres 3 et 4 sur ce cas précis.

We investigate in this section the stability properties of the RL_k schemes. We proceed as follows. For a given scheme is defined its *critical time step* as the largest real Δt_0 so that for $h \in (0, \Delta t_0]$ the numerical simulation runs without overflow, nor non converging newton solver (for implicit methods). The critical time steps of the RL_k and EAB_k schemes for the TNNP and the BR models are collected in the table 1. The robustness to stiffness of RL_k schemes is evaluated by comparing the critical time step Δt_0 for the TNNP and the BR models.

The critical time step of RL_k exhibit a good robustness to stiffness: its critical time steps are relatively large despite the stiffness of considered models. Furthermore,

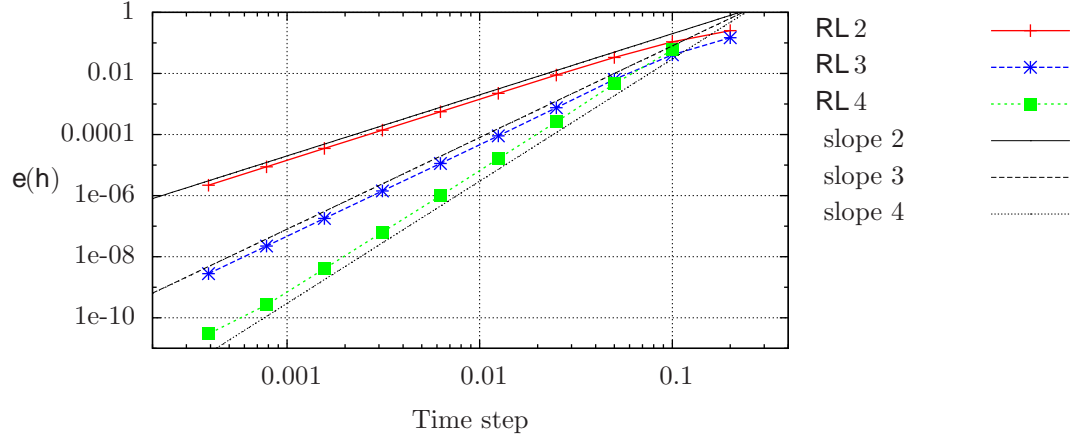


FIGURE 5. Relative error $e(h)$ (definition (25)) as a function of the time step h for the RL_k schemes, for $k = 2$ to 4 and in Log/Log scale.

method	RL_2	RL_3	RL_4	EAB_2	EAB_3	EAB_4
BR	0.323	0.200	0.149	0.424	0.203	0.123
TNNP	0.120	0.148	0.111	0.233	0.108	$7.56 \cdot 10^{-2}$

TABLE 1. Critical time step Δt_0 for the RL_k and EAB_k schemes

when moving from BR model to TNNP model the critical time steps are divided by 2.95, 1.5 and 1.08 for RL_2 , RL_3 and RL_4 respectively. It is not possible to have the same coefficients for classical explicit schemes because they don't resist to the stiffness and for such situation the critical time step will be divided by about 15. More details can be find in [3] where one can observe the big differences between the critical time steps of classical schemes and EAB_k .

Even if the RL_k scheme ($k = 2, 3$) is not $A(0)$ -stable like EAB_k , its stability domain can be large enough for a good choice of the function $a(t, y)$ during the transformation of (1) in (2). In this case its critical time steps are almost the same with the one of EAB_k when the BR model is considered and are even better when moving from the BR to the $TNNP$ model.

4.3. Accuracy. Tu peux aller plus vite à la conclusion : en bref à l'ordre 2 il vaut mieux utiliser EAB, mais aux ordres 3 et 4 il vaut mieux utiliser RL
Ensuite tu peux développer de manière plus générale, notamment en parlant du cout (tu peux t'inspirer de EAB).

Est ce qu'on laisse les 1ères lignes des deux tables ?

In this part, the accuracy of RL_k is evaluated and compared with Exponential Adams Bashforth scheme (EAB_k) studied in [3], where it is compared with several classical schemes and shown to be better for stiff ODEs. This evaluation is done by computing the relative error $e(h)$ for a scheme given and for various time steps h . The results are collected in the tables 2 and 3 for BR model and TNNP model respectively.

RL_2 vs. EAB_2 : Applied on BR (resp: TNNP) model, EAB_2 is usually more accurate than RL_2 excepted the case where the time step considered is $h = 0.2$ (resp: $h = 0.1$ and $h = 0.05$). So if we need only the order two of accuracy it is

better to use EAB_2 scheme than the RL_2 scheme.

RL_3 vs. EAB_3 : Applied on BR model RL_3 , is always more accurate with a ratio 3.5 on the largest time step $h = 0.2$ and with an accuracy ratio going to 1.5 on the finest time steps. When the TNNP model is considered, RL_3 and EAB_3 are very close in terms of accuracy excepted the case the time-step considered is $h = 0.1$ where RL_3 is more accurate than EAB_3 with a ratio of about 1.7.

RL_4 vs. EAB_4 : For the BR (resp: TNNP) model, RL_4 is always more accurate, with a ratio going from 1.9 to 1.6 (resp: 1.9 to 1.4) from the largest to the finest time steps.

If we take in account the CPU cost, the RL_k schemes are always better than the EAB_k schemes.

h	RL_2	RL_3	RL_4	EAB_2	EAB_3	EAB_4
0.2	0.251	0.147	-	0.284	0.516	-
0.1	0.107	$4.07 \cdot 10^{-2}$	$5.86 \cdot 10^{-2}$	$9.26 \cdot 10^{-2}$	$9.17 \cdot 10^{-2}$	0.119
0.05	$3.35 \cdot 10^{-2}$	$6.34 \cdot 10^{-3}$	$4.58 \cdot 10^{-3}$	$2.31 \cdot 10^{-2}$	$1.09 \cdot 10^{-2}$	$8.96 \cdot 10^{-3}$
0.025	$8.88 \cdot 10^{-3}$	$7.57 \cdot 10^{-4}$	$2.61 \cdot 10^{-4}$	$5.39 \cdot 10^{-3}$	$1.17 \cdot 10^{-3}$	$4.33 \cdot 10^{-4}$

TABLE 2. RL_k and EAB_k schemes : relative error $e(h)$ (definition (25)) for various time steps h (BR model).

h	RL_2	RL_3	RL_4	EAB_2	EAB_3	EAB_4
0.1	0.177	0.305	0.421	0.351	0.530	-
0.05	$7.39 \cdot 10^{-2}$	$4.54 \cdot 10^{-2}$	$4.61 \cdot 10^{-2}$	$9.01 \cdot 10^{-2}$	$5.59 \cdot 10^{-2}$	$8.93 \cdot 10^{-2}$
0.025	$2.21 \cdot 10^{-2}$	$6.53 \cdot 10^{-3}$	$5.96 \cdot 10^{-3}$	$2.14 \cdot 10^{-2}$	$7.34 \cdot 10^{-3}$	$8.34 \cdot 10^{-3}$
0.0125	$5.75 \cdot 10^{-3}$	$8.05 \cdot 10^{-4}$	$3.21 \cdot 10^{-4}$	$5.11 \cdot 10^{-3}$	$7.62 \cdot 10^{-4}$	$3.70 \cdot 10^{-4}$

TABLE 3. RL_k and EAB_k schemes : relative error $e(h)$ (definition (25)) for various time steps h (TNNP model).

REFERENCES

- [1] G.W. Beeler and H. Reuter. Reconstruction of the Action Potential of Ventricular Myocardial Fibres. *J. Physiol.*, 268:177–210, 1977.
- [2] M. P. Calvo and C. Palencia. *A class of explicit multistep exponential integrators for semilinear problems*, volume 102, pages 367–381. Springer-Verlag, December 2005.
- [3] Y. Coudière, C. Douanla Lontsi, and C. Pierre. *Exponential Adams Bashforth ODE solver for stiff problems*. PhD thesis, 2005.
- [4] S. M. Cox and P. C. Matthews. *Exponential Time Differencing for Stiff System*, volume 176, pages 430–455. Elsevier Science, August 2002.
- [5] E. Hairer, S. P. Norsett, and G. Wanner. *Solving ordinary differential equations. I*, volume 8 of *Springer Series in Computational Mathematics*. Springer-Verlag, Berlin, second edition, 1993. Nonstiff problems.
- [6] E. Hairer and G. Wanner. *Solving ordinary differential equations. II*, volume 14 of *Springer Series in Computational Mathematics*. Springer-Verlag, Berlin, 2010. Stiff and differential-algebraic problems, Second revised edition, paperback.
- [7] M. Hochbruck and A. Ostermann. Exponential integrators. *Acta Numer.*, 19:209–286, 2010.

- [8] Sundnes J. Artebrant R. Skavhaug O and Tveito A. A second-order Algorithm for solving Dynamic cell Membrane Equations. *IEEE Transactions On Biomedical Engineering*, 26:2546–2548, oct 2009.
- [9] M. Perego and A. Veneziani. An efficient generalization of the Rush-Larsen method for solving electro-physiology membrane equations. *ETNA*, 35:234–256, 2009.
- [10] S Rush and H Larsen. A practical algorithm for solving dynamic membrane equations. *IEEE Trans Biomed Eng*, 25(4):389–92, July 1978.
- [11] Raymond J. Spiteri and Ryan C. Deam. Stiffness Analysis of Cardiac Electrophysiological Models. *Annals of Biomedical Engineering*, 38:3592–3604, Dec 2010.
- [12] P Syvert and Nørsett. An A-stable modification of the Adams-Bashforth methods. In *Conference on the Numerical Solution of Differential Equations*, volume 109 of *Lecture Notes in Mathematics*, pages 214–219. Springer, Berlin, 1969.
- [13] K.H. Ten Tusscher, D. Noble, P.J. Noble, and A.V. Panfilov. A Model for Human Ventricular Tissue. *Am J Physiol Heart Circ Physiol*, 286, 2004.
- [14] L. Vu Thai and A. Ostermann. Explicit exponential Runge-Kutta methods of high order for parabolic problems. *J. Comput. Appl. Math.*, 256:168–179, 2014.