A New Eikonal Solver for Cardiac Electrophysiology in LS-DYNA

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1 Abstract

Heart disease is among the leading causes of death in the western countries; hence, a deeper understanding of cardiac functioning will provide important insights for engineers and clinicians in treating cardiac pathologies. In this paper we will concentrate on electrophysiology (EP), which describes the propagation of the cell transmembrane potential in the heart. In LS-DYNA, EP can be coupled with solid and fluid mechanics for a multiphysics simulation of the heart, but pure EP is also often used to investigate complex phenomena such as cardiac arrhythmia or fibrillations.
The gold standard model for EP is the "bi-domain" model, along with the slightly simplified "mono-domain". These were introduced in LS-DYNA a few years ago [1]. They give very accurate predictions, but the associated computational expenses are significant, which can be an issue for patient-specific predictions, for example, cardiac activation patterns for complex procedures such as cardiac resynchronization therapy (CRT).
In this paper we introduce new computationally efficient eikonal and reaction-eikonal solvers. The eikonal method is very general and describes the propagation of a wavefront in a medium with given propagation velocities. The solution is the arrival time of the wave at each node, which corresponds to the activation time in the case of EP. This activation time can be used to trigger an action potential at each node, either independently from each other, or with an additional spatial diffusion term between nodes so that each node influences its neighbors.
The eikonal solver works on the 3D elements of the myocardium, but also on the beams (or truss elements) composing the rest of the conduction system of the ventricles, i.e. the bundle of His, the left and right bundle branches, and the Purkinje network. Also, the eikonal solver can handle several waves by tracking more than one activation time per node. This allows for example to simulate reentry phenomena.
The eikonal solver will be presented and different examples will be shown, as well as a result and performance comparison between eikonal and monodomain models.

2 Introduction

A cardiac computational model can give biomedical researchers an additional source of information to understand how the heart works. Simulation can be the base of theoretical studies into the mechanisms of cardiac pathologies, provide diagnostic value or can be used to assist in therapy planning. The goal of Ansys is to be able to simulate the pumping heart in LS-DYNA, with a coupling scheme between the Electrophysiology (EP) equations describing the propagation of the electrical wave, the mechanical deformations triggered by the electrical potential, and the blood flow in the pumping heart. This paper will deal with the EP part of the scheme.

The propagation of the cardiac electric impulse in the myocardium can be described by the bidomain or monodomain equations [1], which describe the evolution of the transmembrane potential $\mathrm{Vm}(\mathrm{x},\mathrm{t})$ with a parabolic reaction-diffusion equation, coupled with a system of ODEs which represent either the fluxes of the ion species across the cell membrane or that tries to phenologically reproduce the shape of the action potential. In LS-DYNA, the bidomain and monodomain are solved using the Finite Element Method (FEM) in the mesh representing the myocardium, coupled with ODE solvers for the ionic models at each node of the mesh [1]. The myocardium can be coupled with a network of beams representing the His-Purkinje, through Purkinje-ventricular junctions.
These solvers give very accurate results, but can take a long time to run on large meshes. In some studies very detailed meshes might be needed to capture the front of the transmembrane potential wave, which leads to very large linear systems. The systems of ODEs can also take a significant cpu time, depending on their level of description.

For some of the studies though, where only the activation profile is of interest, the accuracy of the mono/bi-domains may not be required, as the uncertainty introduced by the lack of knowledge of patient-specific tissue properties is far greater than the imprecision that would be introduced by a simpler model choice. The Eikonal family of EP models [4,5] are well recognized for such contexts and have demonstrated a high potential in several clinical applications [4,6].

3 Presentation of the Eikonal model

The Eikonal equation is a very general equation used to solve wave propagations in media with given local propagation velocity tensors. In EP, the solution of the eikonal equation is the arrival time, or activation time $\varphi(x)$ of the electric wave at the different positions x of the myocardium.

The eikonal equation reads [2]:

$$\sqrt{(\nabla\varphi)^T V(\nabla\varphi)} = 1 \; on \; \Omega$$
$$\varphi = \varphi_0 \; on \; \Gamma \tag{1}$$

Where $V(x)$ is a „velocity“ tensor with the squared velocities at position x. Ω is the domain where the wave propages, and Γ the starting boundary for the wave (i.e., where the stimulus is applied).

In the case of the myocardium, if $(\mathrm{l}(\mathrm{x}), \mathrm{t}(\mathrm{x}), \mathrm{n}(\mathrm{x}))$ are the local longitudinal, transverse and normal directions associated with the fibers, with associated velocities (v_l(x), v_t(x), v_n(x)), then the velocity tensor in (1) reads:

$$V(x) = v_l^2(x) l(x) l^T(x) + v_t^2(x) t(x) t^T(x) + v_n^2(x) n(x) n^T(x) \tag{2}$$

This velocity tensor is based on the same fibers as the electrical conductivity tensors in the mono and bi-domain models. This velocity tensor usually has very different values along the fibers than across the fibers. It is somehow proportional to the conductivity tensor used in the mono and bi domain models, where the proportionality coefficient can be set up by known activation times at different locations, although fitting conductivity to a desired conduction velocity at a given spatial discretization may not be a trivial task and has been discussed in detail in [3].

The basic brick of the numerical method is to compute the activation time φ_4 at the 4th node of a tetrahedron, given activation times (φ_1, φ_2, φ_3) at the 3 other ones, and the velocity tensor V in the tetrahedron, as shown in fig (1). The idea is to find a point (x_5) in the plane (x_1, x_2, x_3), i.e.

$$x_5 = \lambda_1 x_1 + \lambda_2 x_2 + (1 - \lambda_1 - \lambda_2) x_3 \; , \tag{3}$$

that minimizes

$$\varphi_4 = \varphi_5 + \sqrt{e_{5,4}{}^T V e_{5,4}} \; , \tag{4}$$

Where $e_{5,4}$ is the edge vector going from x_5 to x_4, and where

$$\varphi_5 = \lambda_1 \varphi_1 + \lambda_2 \varphi_2 + (1 - \lambda_1 - \lambda_2) \varphi_3, \tag{5}$$

hence a minimization problem on (λ_1, λ_2) for a given set of (φ_1, φ_2, φ_3), and V.

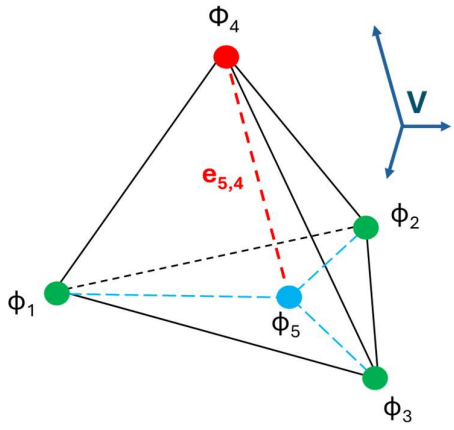

Fig.1: Schematics of the essential brick of the eikonal solver: finding φ_4 given (φ_1, φ_2, φ_3) and V in a tethahedron.

The eikonal solver thus requires a tetrahedral mesh for the myocardium part, which can be coupled with a beam network representing the conduction system.

4 Simple eikonal vs time-stepping multifront (TSMF) eikonal

4.1 Simple eikonal

The simple eikonal model propagates the wave front independently of the local velocity tensor amplitude. So at a given eikonal iteration, activation times in an area with slow velocity may be much larger than in other areas with a larger velocity. This can create some inaccurate activation times in non-convex geometries with different propagation velocities, as illustrated in figures (2) and (3) which show a simple example of wave propagation on a thin slab of tissue with several channels and different propagation velocities.

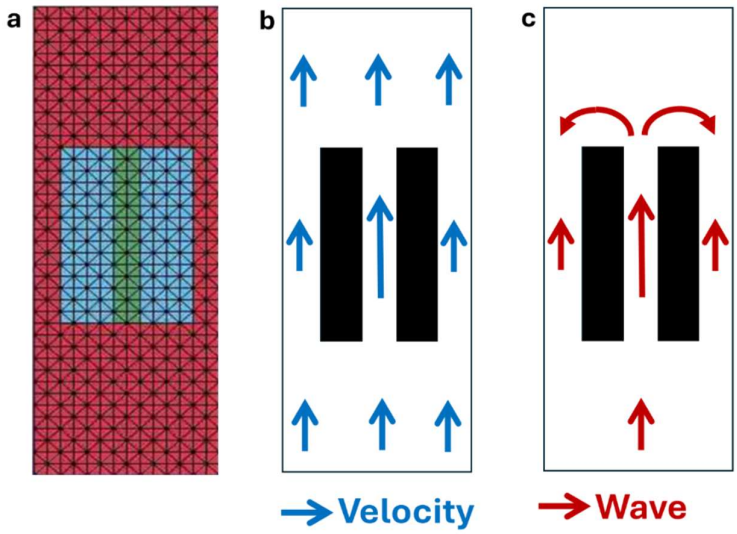

Fig.2: Example of a slab geometry with different propagation velocities. a- shows the mesh and b- the corresponding propagation velocities. The red part has a small velocity, the green part a large one, and there is no propagation in theblue part. c- shows how the waves should look like.

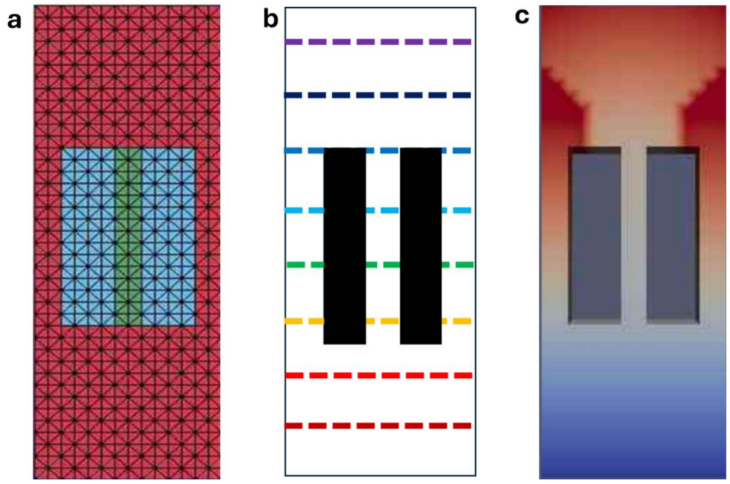

Fig.3: Results of the simple eikonal model on the example presented in figure 2. b- isocontour of the eikonal iteration number. c- fringes of the activation time where the return of the central wave through the lateral channels is missed.

4.2 Time stepping multi-front (TSMF) eikonal

4.2.1 *Time-stepping*

In this solver, an additional global time t_{eik} and time step time dt_{eik} are added to the iterations of the eikonal solver. During the eikonal iterations, only the elements having nodal activation times smaller than the current global time t_{eik} are allowed to propagate the front. The other ones stay idle until t_{eik} becomes large enough. When all the elements are above t_{eik}, it is advanced by the time step, $t_{eik} \coloneqq t_{eik} + dt_{eik}$. This method allows the eikonal iterations to follow accurately the wavefront, which depends on the local velocities.
Figure (4) shows the result of the TSMF eikonal solver on the small test case presented in figure (2).

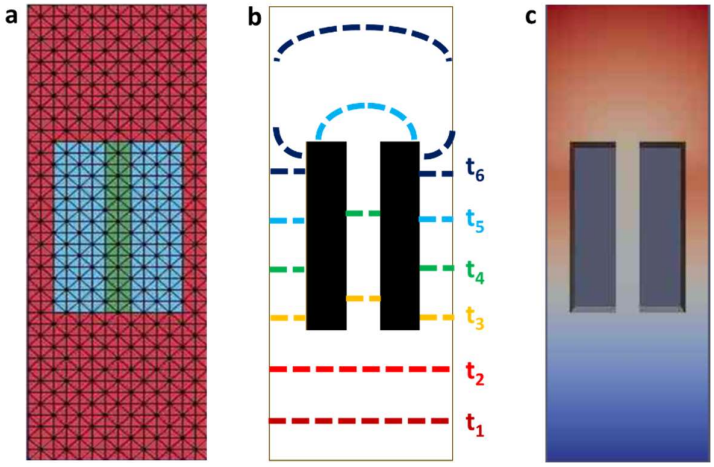

Fig.4: Result of the time-stepping eikonal solver on the small case presented in figure 2. The eikonal iso-iteration contours (b) now follow the wave front. c- shows the fringes of the activation time which corresponds to what was expected in figure (2-c)

4.2.2 Multifront

The global time t_{eik} can be compared to the local activation time at each node, and allows to check whether the node is in an active (or refractory) state, or if it is in a passive (or resting) state.
More precisely, given a ionic model (which can depend on the node), one can compute the refractory time t_{ref} associated to the cell model (see figure 5), and use it during the eikonal iterations:

$$\begin{cases} if\ t_{eik} - \varphi_{node} < t_{ref},\ then\ the\ node\ is\ active \\ if\ t_{eik} - \varphi_{node} > t_{ref},\ then\ the\ node\ is\ passive \end{cases} \quad (6)$$

We then keep track of the active/passive state of the nodes, and when a wave reaches a given node, it will only propagate if the node is in a passive state. If the node is active, the wave will stop there.

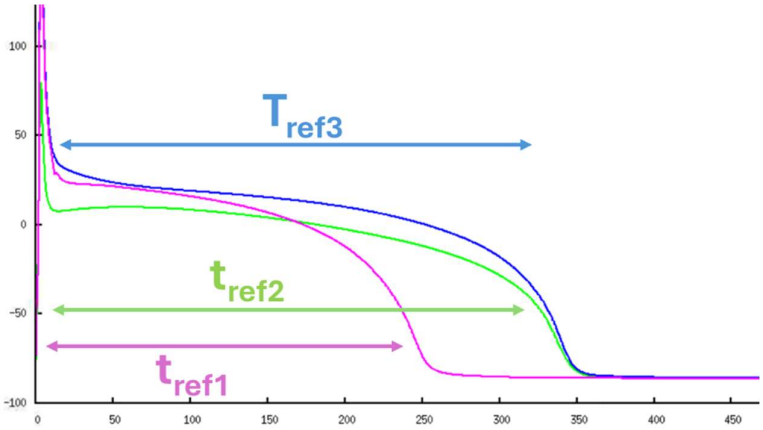

Fig.5: Action potentials and refractory times for 3 different ionic models

Several waves can thus propagate through the same medium, as long as the time between 2 waves is larger than the refractory time. One can then monitor the successive activation times $(\varphi_1, \varphi_2, \varphi_3, \varphi_4, \dots, \varphi_n)$ at a given node as the different waves pass through it.

5 Reaction eikonal

As mentioned before, the eikonal model just gives the nodal activation time φ (or a series of activation times $(\varphi_1, \varphi_2, \varphi_3, \varphi_4, \dots, \varphi_n)$ in the case of the TSMF eikonal). This is what we call the eikonal solver, and it is set up with **EMSOL=14** in ***EM_CONTROL**. The run will stop at the end of the eikonal step and the activation map is output in vtk format in a „vtk“ directory.

One can extend the eikonal model in order to get a fuller EP model with Transmembrane Potential and possibly other ion model variables like Calcium Concentration, that allows coupling with cardiac mechanics. In these runs, an eikonal solve is done first to compute the activation times (we call this part the eikonal solve), which then, are used in a standard explicit or implicit LS-DYNA run, possibly coupled with the mechanics and the CFD solvers (we call that second part the EP part of the run).

5.1 RE- solver

The simplest way to do so is to locally depolarize the ionic ODE model by adding an artificial foot current $I_{foot}(t)$ of duration T_{foot}, at activation time, i.e such that:

$$\begin{cases} I_{foot}(x,t) = I_{foot}(t)\ if\ \varphi(x) < t < \varphi(x) + T_{foot} \\ I_{foot}(x,t) = 0\ if\ not \end{cases} \quad (7)$$

For simple eikonal, and:

$$\begin{cases} I_{foot}(x,t) = I_{foot}(t) \; if \; \exists \; i \; such \; that \; \varphi_i(x) < t < \varphi_i(x) + T_{foot} \\ I_{foot}(x,t) = 0 \; if \; not \end{cases} \quad (8)$$

For the time stepping multifront eikonal model.

This foot current will trigger an action potential at the arrival of the transmembrane potential wave, with all the state variables of the ionic model locally available. Again, these can include the calcium concentration which could be used to couple the EP model with mechanical deformations using ***MAT_295**.

The monodomain equation reads [1]:

$$C_m \frac{\partial V_m}{\partial t} + I_{ion} - \frac{1}{\beta} \nabla \cdot (\sigma \nabla V_m) = I_{stim}(x,t) \quad (9)$$

Where V_m is the transmembrane potential, C_m the membrane capacity per unit area, β is the membrane surface to volume ratio, I_{ion} the ionic current generated by the cell membrane, and I_{stim} a stimulus current.

This first EP solve corresponds to neglecting the diffusion term and keeping only:

$$C_m \frac{\partial V_m}{\partial t} = I_{foot}(x,t) - I_{ion} \quad (10)$$

This is what we call the RE- model, keeping the nomenclature of [4]. It is triggered by using **EMSOL=15** in ***EM_CONTROL.**

5.2 Spline ionic model

Since in RE- solver the same ODE's with the same excitations are solved at each node, we might as well solve them once and for all and store the results in a spline format, so that during the EP part of the run, we can get $V_m(x,t)$ just by a lookup, based on $t - \varphi(x)$, as shown on figure (6). At this time, V_m, and the Calcium Concentration are stored in such splines, but other state variables could be added in the future. This is what we call the „spline" way to solve the ionic model. Since a simple lookup takes much less time than a full ODE system solve, the global run is much faster using the spline way for ionic models, and this capability has also been extended to the mono and bi- domain models. This method is triggered by setting **ionSolver to 2** in ***EM_CONTROL_EP to 2**. A second line was added to ***EM_CONTROL_EP** with **spliTend and spliDt** in order to define the end time and time step of the initial spline generation.

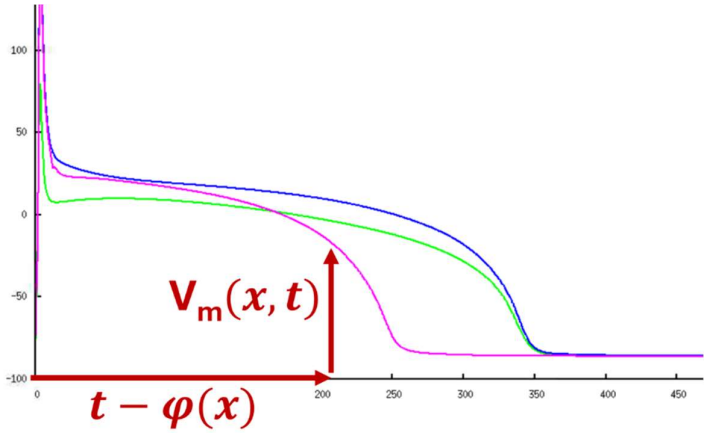

Fig.6: Lookup into a spline instead of solving an ionic model ODE

5.3 RE+ solver

In some cases, it may be interesting to keep the diffusion part of the monodomain equation, since diffusion plays an important role in smoothing out gradients of $V_m(x,t)$ during repolarization and avoid distortions in electrograms and the ECG. We can thus add the diffusion term by solving:

$$C_m \frac{\partial V_m}{\partial t} = \frac{1}{\beta}\nabla \cdot (\sigma \nabla V_m) + I_{foot}(x,t) - I_{ion} \quad (11)$$

This is called the RE+ model according to **[4]** and is triggered by using **EMSOL=16** in ***EM_CONTROL.** The diffusion part of equation (11) is solved using FEM, while the ionic model can be solved using either standart ODE's resolution methods at each node, or the „spline ionic model" of section 5.2.

6 Example of a reentry with the TSMF eikonal solver

Cardiac arrhythmias are generally produced by one of three mechanisms: enhanced automaticity, triggered activity, or reentry [7]. Reentries are due to a closed circuit within the myocardium and can prevent the propagating EP wave from dying out after a normal activation. It is the EP mechanism responsible for the majority of clinically important arrhythmias.

A small test case was setup to illustrate how such a reentry can be generated and studied using the RE-solver. It consists of a thin slab with 2 parts representing tissue with the same ten-Tusscher ionic model, but very different propagation velocities, and a third part representing scar tissue with no propagation (see figure 7). 2 stimuli are applied at the bottom of the slab with a precise interval between them, so that the conditions for creation of a reentry wave are satisfied.

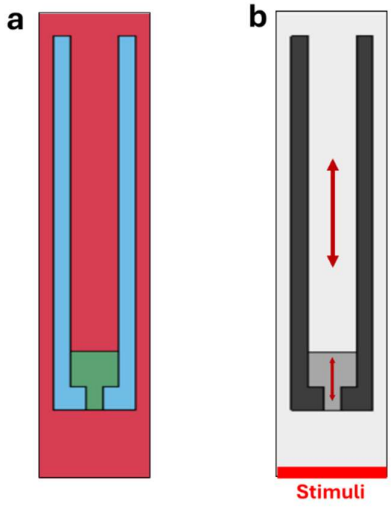

Fig.7: Setup of the reentry test case. a): setup of the case, a thin slab of tissue with 3 different parts, red: healthy tissue with high wave velocity, green „bottleneck": unhealthy tissue with a small velocity, blue: scar tissue with no propagation. b) velocities in the different parts, as well as the area where the 2 stimuli are done.

Figure (8) shows the evolution of the EP wave.

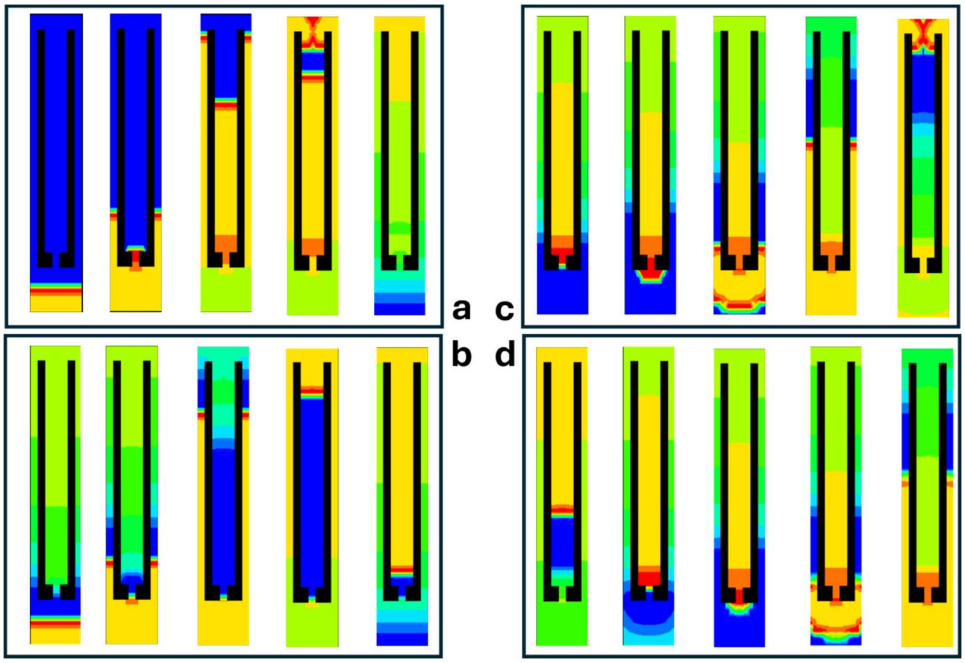

Fig.8: Evolution of the EP wave, with the fringes of V_m at increasing times a): the first stimulus at the bottom triggers a wave going up. The wave is ahead on the external areas because of the slow velocity in the „bottleneck" part in the center. The 2 waves meet at the top of the center channel. b): just as the bottom part becomes passive, a second stimulus is triggered at the bottom. The wave can propagate on the external parts which become refractory just ahead of it, but not through the center bottleneck part which is still active because of the small velocity there. c): the wave coming down in the center part exits the bottleneck just after the bottom area has become passive and can thus propagate there by going up on the external parts. d): the self sustaining loop is created with a wave going up through the outside parts and coming back down through the inside part.

7 Comparison of RE- to monodomain model

To evaluate the precision of the RE- model, we compared it to the standard monodomain model. The comparison was done on a rectangular slab of orthotropic tissue, stimulated on one corner. The chosen ionic model for both simulations was the ten-Tusscher model [8]. A qualitative analysis was done on the full activation time fields (figure 9) and on the transmembrane potential at three specific points (figure 10). A brief quantitative comparison is shown in table 2. The simulation time for the RE- model was approximately half the simulation time for the monodomain model, with the same mesh and time stepping. However, as mentioned above, the RE- model allows for much coarser meshing and time stepping, and thus much faster simulation. To illustrate this, we added a RE- model with a coarse mesh and time grid to the comparison. This third model will be referred to as Coarse RE-. A monodomain model using the same coarse mesh will not be shown as it is numerically unstable. Model specifications are summarized in table 1.

The presented results were obtained after manual adjustment of the RE- model wave velocities in the fiber and cross-fiber directions in order to match the monodomain results. In short, activation times were measured on points B and C (see figure 9) after simulating the monodomain and RE- models with default parameters. The velocities of the RE- models were then corrected with the corresponding activation time ratios. The wave velocity parameters are identical between RE- and Coarse RE- models.

		Monodomain	RE-	Coarse RE-
Number of elements		520 500	520 500	2800
Time step (ms)		0.01	0.01	1
Spline time step (ms)		--	0.01	0.01
Simulation time	28 CPUs	60 min	32 min	10 s
	1 CPU	25 h	13 h	9 s

Table 1: Specifications for the Monodomain, RE- and Coarse RE- models. Note: the ionic model spline time step is kept at 0.01ms in Coarse RE- to ensure numerical stability.

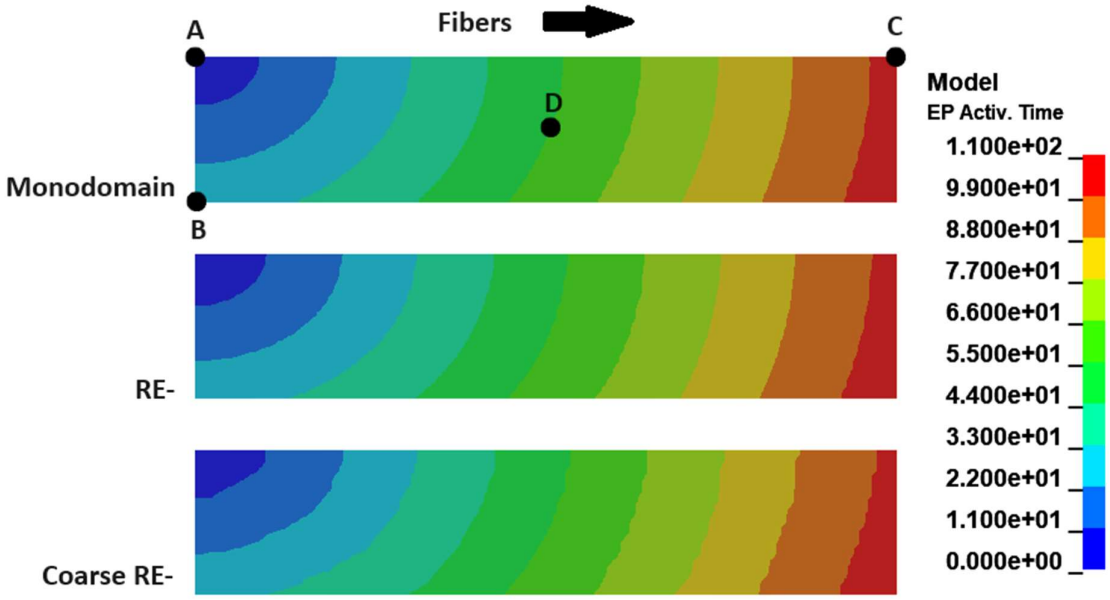

Fig.9: Activation time fields for the monodomain, RE- and Coarse RE- models. The stimulation is done on point A. Visually, the 10 isochrones have the same shape and positions on all three models. The distortion visible on Coarse RE- isochrones is due to the large element size. The fiber direction is horizontal and the cross-fiber direction is vertical.

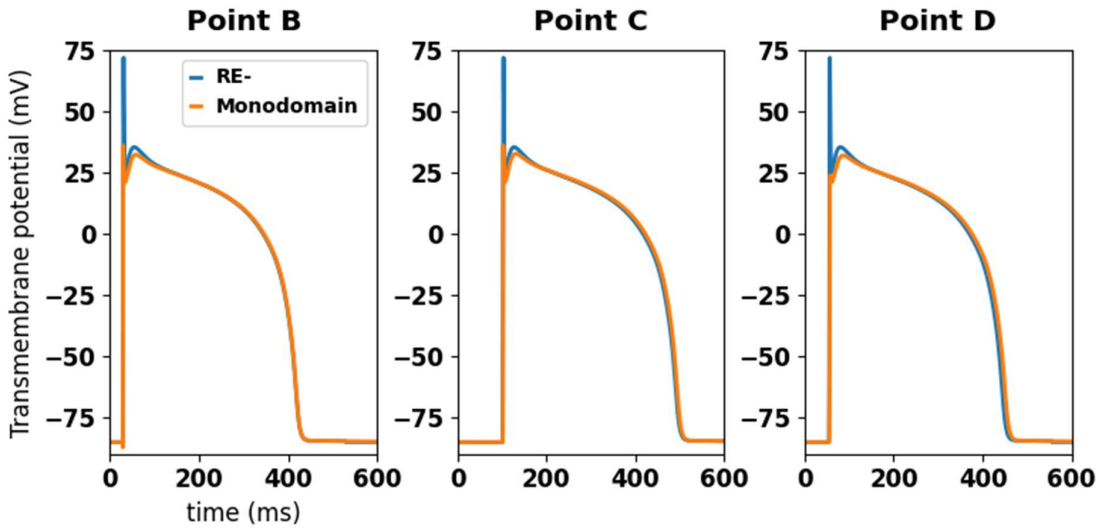

Fig.10: Transmembrane potential curves at points B, C and D (see figure 9). Activation time corresponds to the sharp increase of transmembrane potential. Although their ionic models are identical, the transmembrane potential differs slightly between RE- and monodomain simulations because potential diffusion is present in the latter. Note: the transmembrane potential curves have an identical shape on all points of the RE- model (with a delay corresponding to the activation time, see section 5.2). The Coarse RE- curves are not included as they also have exactly the same shape as the RE- curves.

	Activation Times (ms)		
	Monodomain	**RE-**	**Coarse RE-**
Maximum	106.6	107.3	107.
Average	55.8	55.3	55.8
Point B	29.7	29.8	30.
Point C	103.1	102.9	102.
Point D	56.3	55.6	56.

Table 2: Comparison of the activation times between RE-, Coarse RE- and Monodomain models.

8 Keywords and variables used to setup the models

8.1 *EM_CONTROL

Card 1	1	2	3	4	5	6	7	8
Variable	EMSOL							
Type								

EMSOL=14 : simple eikonal where the LS-DYNA run stops at the end of the eikonal iterations with the activation time in VTK format (see section 5).

EMSOL=15: RE- solver (see section 5.1).

EMSOL=16: RE+ model (see section 5.3).

8.2 *EM_CONTROL_EP

Card 1	1	2	3	4	5	6	7	8
Variable				IONSOLVER				
Type	I	I	I	I				

IONSOLVER=2: spline ionic model (see section 5.2).

Card 2	1	2	3	4	5	6	7	8
Variable	SPLITEND	SPLIDT						
Type	F	F						

SPLITEND: end time used when generating the spline ionic model. The user needs to make sure it is larger than the action potentials (see section 5.2).
SPLIDT: time step used when generating the spline ionic model (see section 5.2).

8.3 *EM_EP_EIKONAL

Card 1	1	2	3	4	5	6	7	8
Variable	EIKID	EIKPST	EIKSNS	EIKSDF				
Type	I	I	I	I				

EIKID: Id of the eikonal
EIKPST: Part set id on which the Eikonal model is solved.
EIKSNS: Node set id used as a seed for Eikonal propagation.
EIKSDF: Id of the define function used for the seed activation time

Card 2	1	2	3	4	5	6	7	8
Variable	FTYPE	FT	FA					
Type	I	I	F					

FTYPE: Foot current type
FT: Foot current duration (see equation 7)
FA: Foot current amplitude (see equation 7)

Card 3	1	2	3	4	5	6	7	8
Variable	SOLVETYPE							
Type	I							

SOLVETYPE: Eikonal solve type

EQ.0: Simple eikonal, computes only activation times, for one cycle (see section 4.1)

EQ.1: Time-stepping multifront eikonal. Allows for simulating several cycles and reentries (see section 4.2)

8.4 *EM_MAT_003

Card 1	1	2	3	4	5	6	7	8
Variable			SIGMA11	SIGMA22	SIGMA33			
Type	I							

Card 2	1	2	3	4	5	6	7	8
Variable	SIGMA12	SIGMA13	SIGMA21	SIGMA23	SIGMA31	SIGMA32		
Type	I							

SIGMA11,…: when using an eikonal solver, i.e. EMSOL= 14,15 or 16, these variables represent the wave velocity tensor, i.e ($v_l(x)$, $v_t(x)$, $v_n(x)$) in equation (2)

9 Summary

We presented the new „simple“ and „TSMF“ eikonal solvers available in LS-DYNA. These solvers can be coupled to full ionic ODE's or „spline“ ionic model for a full time dependant EP solution, through the RE- and RE+ models. Like the mono/bi-domain models previously introduced in LS-DYNA, these new eikonal-based models allow computing the transmembrane potential and other state variables of the ionic model, so that they can be coupled with the mechanics (and CFD) for a multiphysics cardiac simulation in LS-DYNA. The advantage is that the eikonal model can be used on coarser meshes, with larger time steps hence reducing considerably the computation time, as presented in section 7. These eikonal-based models can be used on the full cardiac electric system, including the bundle of His, the left and right bundle branches, and the Purkinje network. The TSMF solver allows the simulation of reentry phenomena, which are very important in the understanding of cardiac arrhythmia.

10 Bibliography

[1] L'Eplattenier, P. et al: "Cardiac electrophysiology using LS-DYNA", 15th International LS-DYNA Users Conference, Detroit, 2018

[2] Ganellari, D. et al: "A massively parallel Eikonal solver on unstructured meshes", Computing and Visualization in Science (2018) 19:3–18

[3] C.M. Costa, C.M. et al, "Automatic parameterization strategy for cardiac electrophysiology simulations", in: Computing in Cardiology Conference, CinC, 2013, IEEE, 2013, pp. 373–376

[4] Neic, A, et al, „Efficient computation of electrograms and ECGs in human whole heart simulations using a reaction-eikonal model“, Journal of Computational Physics 346 (2017) 191–211

[5] Colli Franzone, P., Guerri, L., & Rovida, S. (1990). Wavefront propagation in an activation model of the anisotropic cardiac tissue: asymptotic analysis and numerical simulations. *Journal of mathematical biology*, *28*, 121-176.

[6] Gillette, K., Gsell, M. A., Strocchi, M., Grandits, T., Neic, A., Manninger, M., ... & Plank, G. (2022). A personalized real-time virtual model of whole heart electrophysiology. *Frontiers in Physiology*, *13*, 907190.

[7] Antzelevitch, C. et al, "Overview of Basic Mechanisms of Cardiac Arrhythmia", Card. Electrophysiol. Clin. 2011 Mar 1; 3(1): 23–45.

[8] K. H., W. J., ten Tusscher, A.V. Panfilov, *Alternans and spiral breakup in a human ventricular tissue model*, Am. J. Physiol. Heart Circ., Physiol 291: H1088-H1100, 2006.