

# MULTI-SCALE UNFOLDING HOMOGENIZATION METHOD APPLIED TO BIDOMAIN AND TRIDOMAIN ELECTROCARDIOLOGY MODELS

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In this work [1, 2], we present a novel microscopic tridomain model describing the electrical activity in cardiac tissue with dynamical gap junctions and then we apply the periodic unfolding method to derive the macroscopic tridomain model.

For this, we assume that the periodic domain  $\Omega$  occupied by the cardiac tissue is constituted by two intracellular media  $\Omega_{i,\varepsilon}^k$  for  $k = 1, 2$  connected by gap junctions  $\Gamma_\varepsilon^{1,2}$  and by an extracellular medium  $\Omega_{e,\varepsilon}$ , from which comes the name tridomain: Each intracellular medium  $\Omega_{i,\varepsilon}^k$  and the extracellular medium  $\Omega_{e,\varepsilon}$  are separated by a cell membrane  $\Gamma_\varepsilon^k$  (the sarcolemma).

In this case, we add some additional equations to this model, as well as several conditions on these gap junctions. After a scaling procedure, we obtain the microscopic tridomain model composed of:

- a quasi-stationary conduction equation for each intracellular electric potential  $u_{i,\varepsilon}^k$ ;
- another one for the extracellular electric potential  $u_{e,\varepsilon}$ ;
- while on the interface of the cell membrane and gap junctions, certain conditions of continuity and dynamic coupling are prescribed and satisfied by the transmembrane potential  $v_\varepsilon^k = (u_{i,\varepsilon}^k - u_{e,\varepsilon})|_{\Gamma_\varepsilon^k}$ , the junction potential  $s_\varepsilon = (u_{i,\varepsilon}^1 - u_{i,\varepsilon}^2)$  and the recovery variable  $w_\varepsilon^k$  for  $k = 1, 2$ .

As a first step [1], we establish the global existence and uniqueness of the weak solutions to our microscopic tridomain model using the Faedo-Galerkin method, and an appropriate compactness argument. As a second step [2], we derive the macroscopic tridomain model using the unfolding homogenization method [3]. To prove the convergence of the

nonlinear terms, we use the unfolding boundary operator and the Kolmogorov-Riesz type compactness argument. At the limit when  $\varepsilon \rightarrow 0$ , we show that the solution of the microscopic model converges, in an appropriate sense, to the unique solution  $(u_i^1, u_i^2, u_e, w^1, w^2)$ , with  $v^k = u_i^k - u_e$  ( $k = 1, 2$ ) and  $s = u_i^1 - u_i^2$ , of the macroscopic tridomain system (of reaction-diffusion type):

$$\begin{aligned} \sum_{k=1,2} \mu_j \partial_t v^k + \nabla \cdot (\widetilde{\mathbf{M}}_e \nabla u_e) + \sum_{k=1,2} \mu_k \mathcal{I}_{ion}(v^k, w^k) &= \sum_{k=1,2} \mu_k \mathcal{I}_{app}^k, & \text{in } \Omega_T := (0, T) \times \Omega, \\ \mu_1 \partial_t v^1 + \mu_g \partial_t s - \nabla \cdot (\widetilde{\mathbf{M}}_i \nabla u_i^1) + \mu_1 \mathcal{I}_{ion}(v^1, w^1) + \mu_g \mathcal{I}_{gap}(s) &= \mu_1 \mathcal{I}_{app}^1, & \text{in } \Omega_T, \\ \mu_2 \partial_t v^2 - \mu_g \partial_t s - \nabla \cdot (\widetilde{\mathbf{M}}_i \nabla u_i^2) + \mu_2 \mathcal{I}_{ion}(v^2, w^2) - \mu_g \mathcal{I}_{gap}(s) &= \mu_2 \mathcal{I}_{app}^2, & \text{in } \Omega_T, \\ \partial_t w^k - H(v^k, w^k) &= 0, & \text{in } \Omega_T, \end{aligned}$$

completed with appropriate initial and edge conditions where  $\mu_k = |\Gamma_k|/|Y|$ ,  $k = 1, 2$  (resp.  $\mu_g = |\Gamma^{1,2}|/2|Y|$ ) is the ratio between the surface membrane (resp. the gap junction) and the volume of the reference cell. In addition,  $\widetilde{\mathbf{M}}_j$  for  $j = i, e$  represent the homogenized conductivity matrices while  $\mathcal{I}_{ion}$ ,  $\mathcal{I}_{gap}$ ,  $\mathcal{I}_{app}$ , denote ionic, gap and applied currents, respectively.

## References

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