Team: Abishek Myrthy and Jonas van den Brink

Project summary. Due to its diversity and multifactorality in nature, the origin of atrial rhythm disturbance is still incompletely understood. However, remodelling has long been implicated as a basis for re-entrant arrhythmia in the atria. In this context, "remodelling", can be considered to include, but is not limited to, the diverse micro- and macro-structural, neurohumoral, and electrical alterations in cardiac cells and tissue resultant from a variety of pathogenic etiologies. In this project, the student team will use mathematical modeling employing systems of nonlinear ODEs, PDEs, and finite element models to investigate the role of pathological remodelling on vulnerability to arrhythmias in atrial tissue as mediated by (a) alterations in tissue conductivities (to represent e.g. fibrotic changes) and (b) changes in cellular electrophysiology (to represent e.g. alterations in ion channel and calcium machinery expression following periods of atrial fibrillation).

Main objectives:
(a) Cellular electrophysiology and reentrant arrhythmia. Translate several models using e.g. gotran and modify select parameters to examine model restitution under dynamic protocols and finally induction in a two-dimensional tissue construct.
(b) Fibrosis and reentrant arrhythmias. Use numerical simulations to show that reduced electrical diffusion due to fibrosis can lead to heterogeneous conduction patterns that can lead to re-entrant arrhythmia in a 2D tissue construct.

The project logically follows 0D (cell) ODE models to 2D (tissue) models (introduced during Wednesday, Thursday, and Friday of lectures this week, 18-19-20 June, in Oslo) of propagation:

Tasks (general):
1. Implement "chosen" cell models -- these will be:
   A. Koivumäki, et al 2011 (healthy atrial myocyte)
   B. Koivumäki, et al 2014 (chronic atrial fibrillation myocyte)
   C. Fenton-Karma model parameterised for (A)
   D. Fenton-Karma reduced model parameterised for (B)

2. Simulate action potentials in A-D. *More details to follow re: e.g. stimulation protocols.*

3. Implement a finite difference solution for solving propagation in 1D for all 4 models. Calculate CV for each.

   Suggested deadline: 27.06.2014

4. Simulate a planar wave in 2D (FEM monodomain solver) using all 4 models.

5. S1-S2 spiral wave induction

   Suggested deadline: 04.08.2014

6. Addition of structural heterogeneties via alteration of regional cell-cell coupling (conductivities in FEM monodomain model); what affect does this have on (a) spiral wave period? (b) ease of induction?

7. Addition of ionic heterogeneities via alteration of ionic conductances (to be defined and chosen a priori) (a) spiral wave period? (b) ease of induction?

Suggested deadline: End of course in La Jolla

NB!

1. Importantly, knowing that you both are relatively savvy in the use of research code/scripting, we have decided to make this project tool-independent, meaning that you can decide to use any languages/tools you would like, given that you agree on the approach. This does not imply, of course, that you will not receive necessary software assistance, but simply that you have the freedom to choose what you think works best, what you would like to try out, or what you might want to use in the future. Examples in the course centred around matlab, gotran, and fenics, but you are under no obligation to use any of these if another option is preferable.

2. Also importantly, this project is now both ambitious and rather vague. Therefore, the aim is to determine desired directions during discussion on Wednesday 25, and the the exact direction for the remainder of the project after completion of step #2, above.