

# Cellular Heterogeneity in the Atria: An in-silico Study in the Impact on Re-entries.

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In silico modelling is increasingly relied upon to gain new insights into the underlying mechanisms of atrial fibrillation. Due to the complex nature of the atria, in silico models typically exclude cellular heterogeneity. One question that remains unanswered is the impact of cellular heterogeneity on AF mechanisms and in the vulnerable window (VW). This study aims to present the impact of cellular heterogeneity on the AF mechanisms and susceptibility to re-entry behaviour.

Cellular heterogeneity was introduced using the population of models approach and calibrated on a regional basis based on 5 biomarkers: APA, RMP, and  $APD_{20,50,90}$ . A comparable regionally homogeneous atrial model was created as a control. 9 rapid-paced ectopic beats were applied to a 2mm radius of tissue in 2 locations in the LA to induce a re-entry. The re-entrant path, frequency, and vulnerable window were compared between the two models at these two EB locations. SA stimulation was discontinued at EB onset to observe the re-entrant pattern.

Results showed a slight increase in frequency of re-entry due to cellular heterogeneity (5.66Hz versus 5.73Hz for the homogeneous and variable models respectively). In both cases, the re-entrant pattern was established through the coronary sinus (see Figure). In the Homogeneous model, ectopic beats applied to the centre of the LA resulted in re-entrant activity from an EB onset of 105-323ms, with a VW of 218ms. Cellular heterogeneity increased the VW to 270ms (105-375ms). In the second EB location, sustained re-entry was observed in the homogeneous model for an EB onset from 105-341ms. Cellular heterogeneity increased this window to 105-382ms. In both cases, cellular heterogeneity resulted in an increase in the VW of 41-51ms (17.4-23%).

At both EB locations, the window for re-entry was significantly increased due to cellular heterogeneity whereas re-entrant pathways were unchanged, with re-entrant frequency slightly increasing with heterogeneity.

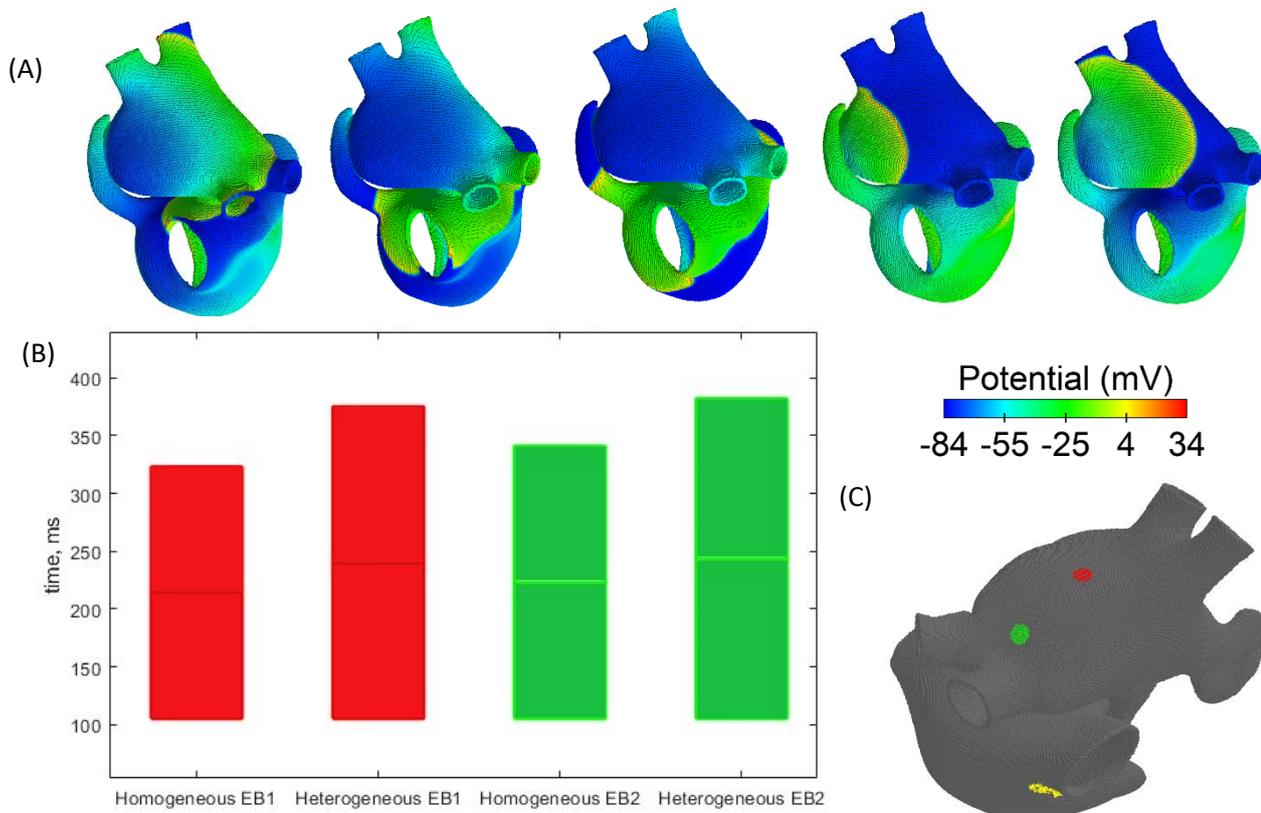


Figure 1: Re-entry behaviour in the atria. (A) shows the path of re-entry with the associated scale below. (B) shows the vulnerable window for the homogeneous and heterogeneous atrial models when ectopic beats were applied to the left of the LA (green) and the centre of the LA (red). (C) shows the EB locations associated with (B) and the SA node in yellow.