# Mechanisms for Initiation of Cardiac Discordant Alternans

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Nonlinear waves and patterns are common structures found in multitude of biological systems, ranging from the propagation of electrical impulses along neurons to the geometrical forms present in animal coatings. Very often these waves appear in the form of propagating pulses characteristic of excitable systems. In these, a finite size perturbation can bring the system far from the stable state for a given amount of time, that typically depends on the time elapsed from the previous excitation. A well studied example is cardiac muscle, where a change in transmembrane cellular potential produces a response known as action potential, that propagates along the tissue. Many cardiac malfunctions are associated to problems in propagation, sometimes inducing the formation of rotors (spiral or scroll waves, in two or three dimensions). These structures, typical of excitable systems, are thought to underline many cases of ventricular tachycardia (VT). They also constitute the most commonly accepted building block of ventricular fibrillation (VF), a particularly malign malfunction of the heart, in which synchronous excitation is lost among different parts of the ventricle, impeding contraction, and causing death in a few minutes. The main explanation for the transition from VT to VF is related to instabilities of spirals, either in the core, causing the continuous creation and destruction of rotors, or in the waves emitted by spirals. Thus, a major challenge is to classify and understand the mechanisms that cause, first, the creation of rotors, and second, their subsequent destabilization. To this end, numerical simulations of propagation of the electrical impulse on the heart provide an invaluable tool. In computer models, unlike in real experiments, it is possible to isolate each of the possible mechanisms, and study them separately to assess their influence. Results obtained with this *in silico* models can be compared with real controlled experiments. The goal is then to construct models that help us to bridge the gap from cellular electrophysiology to propagating properties in tissue, and through whole heart models, to clinical manifestations.

Among the known precursors of life-threatening ventricular arrhythmias and sudden cardiac death are T wave alternans, defined as a periodic beat to beat change in the amplitude or shape of the ECG T wave. Although T wave alternans provide a global measure of the propagation at the whole heart level, they have been related to alternations in the duration of the excited phase (or action potential duration APD) at the single cell level, thereby establishing a causal link between electrical alternans and the initiation of ventricular fibrillation[1]. Electrical alternans may appear as concordant (all the tissue presenting the same phase of oscillation) or discordant (with out-of-phase regions distributed among tissue)[2]. Spatially discordant alternans can lead to unidirectional block that initiates reentry and ventricular fibrillation. The role played by tissue heterogeneities and heart rate changes in their initiation remains, however, unclear.

We study the mechanisms for initiation of spatially discordant alternans by numerical simulations of an ionic model spatially distributed in a one-dimensional cable and in an anatomical model of the rabbit heart. The effects of CV-restitution, ectopic beats, and the role of spatial gradients of electrical restitution properties are investigated[3]. In homogeneous tissue, the origin of discordant alternans may be dynamical, through CV-restitution, or due to a localized change in the pacing period. We also find that a sudden change of stimulation rate can initiate discordant alternans in the presence of a spatial gradient of APD-restitution without necessitating CV-restitution. The mechanism of, and the conditions for, initiation are determined based on an iterated map analysis of beat to beat changes of APD. This analysis leads to the definition of a vulnerable window for initiation of discordant alternans. Moreover, the pattern of spatially discordant alternans is found to change slowly over several beats following initiation, as reflected in ECG recordings.

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