10 Are Cardiac Waves Relevant to Epileptic Wave Propagation?*

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10.1 Introduction

The mechanisms of cardiac fibrillation and of the epilepsies differ markedly. Also, there are many kinds of fibrillation and many epilepsies. Yet some collective parallels stand out. Their tissue substrates (heart muscle, brain neocortex and sub-cortical nuclei) both involve electrically active cells connected to neighbors, and both aberrations are electrical modes that seem alternative to the normal modes in the same tissue without change of parameters. The onset and offset of each is an abrupt switch from or back to the normal mode, both can be evoked by electrical stimulation at 10–100 Hz and current density around 20 mA/cm², and both can be terminated by a brief stimulus. In the case of fibrillation a single harsh direct-current shock of several milliseconds' duration is in fact the only known acute therapy. In the case of epilepsy, Gluckman et al. [590] report prompt suppression of epileptiform activity in hippocampal slices using much smaller 60 Hz AC fields, and it is well known that a single brief sensory stimulus given close to seizure onset often appears to abort it [110]. Both fibrillation and epilepsy look quite irregular electrically, yet both have dominant periodicities in the 3 to 10 Hz range, and both processes seem to be determined at least in part by propagation geometry on the scale of centimeters. But they differ in that fibrillation seems to be a geometrical mode of normal propagation between cells of just one kind through only excitatory electrical connections, whereas epilepsies involve feedback loops between distinctive cell populations through both excitatory and inhibitory synapses. The dispersion curves of cardiac propagation (the dependence of speed on periodicity) do not much resemble those proffered for waves contributing to the EEG [144,147].

That said, the aim of this chapter is to present what is known of cardiac fibrillation in a way that may assist theorists of the epilepsies in drawing their own conclusions about helpful or misleading analogies between the two phenomena.

* My efforts have been supported by the US National Science Foundation since 1967, currently from the Applied Mathematics program. I thank John Milton and Ivan Osorio for thoughtful reading and critique which improved the 11 June 1999 manuscript in several places, and Jeff Reznik for direction to recent literature.
10.2 Different Molecular Mechanisms of Propagation

Do propagating activations in any CNS tissue resemble those in heart muscle? This seems a silly question. The answer might seem obviously “No, not at all: heart muscle is a relatively uniform electrical syncytium like a 3-dimensional squid axon, but brain tissues are composed of neurons connected through excitatory or inhibitory chemical synapses.” Yet among the diverse non-synaptic communication modes referred to as “volume transmission” in the CNS [591], there are some rather like those encountered in heart muscle. Some of these slow communications involve calcium-induced calcium release, and the like for potassium. Hippocampal glial networks are thought to be well coupled by gap junctions [592], as heart cells are. Non-synaptic propagation seems implicated in some forms of epilepsy [592–594]. And the CNS abounds with commissures, fasciculi, and association tracts of diverse lengths and speeds; along these fast-lane projections action potentials propagate in much the same way as they do in normally beating heart muscle.

There are basically two kinds of propagating signal in the CNS:

- The fastest propagations are mediated by electrotonic currents. These traverse single-cell arborizations that may bypass several cells, or long fiber tracts that bypass many thousands to end at a remote synapse. Whether myelinated or not, the axon’s intracellular mechanism is Hodgkin-Huxley-like: local “reactions” (the voltage–dependence of ionic channels affecting local membrane voltage) electrotonically connected by “diffusion” of electrical potential through a conductive medium. Then final passage to the target cell is synaptically mediated; and

- The slowest propagations, e.g. calcium waves or laterally spreading depression, are mediated by local diffusion of ions or molecules through the gap junctions linking adjacent cells, or through the extracellular medium. Such chemically mediated impulse propagation is familiar to physical chemists in much simpler systems, e.g., the Belousov-Zhabotinsky reagent.

A mixture of these two modalities is familiar in the heart. Excitable cells in heart muscle connect to several immediate neighbors through electrically conductive gap junctions; there is nothing like arborization to contact remote neighbors, nothing like chemical synapses, and no postsynaptic membrane to respond by inhibition or excitation: these connections are only excitatory. Adjacent cells are also relatively similar in structure and function in heart muscle. Excitation conducts through a volume of such connected cells much as it does across a uniform sheet of excitable membrane. Transmembrane potential in the various tissues of the heart plays exactly the role of chemical concentration, Hodgkin–Huxley-like channel kinetics plays exactly the role of chemical reactions, and electrotonus plays exactly the role of molecular diffusion. From the viewpoint of dynamical equations, these are exact correspondences, not loose analogies.