Ventricular Fibrillation in the Human Heart. Why is it different from fibrillation in the dog and pig heart?

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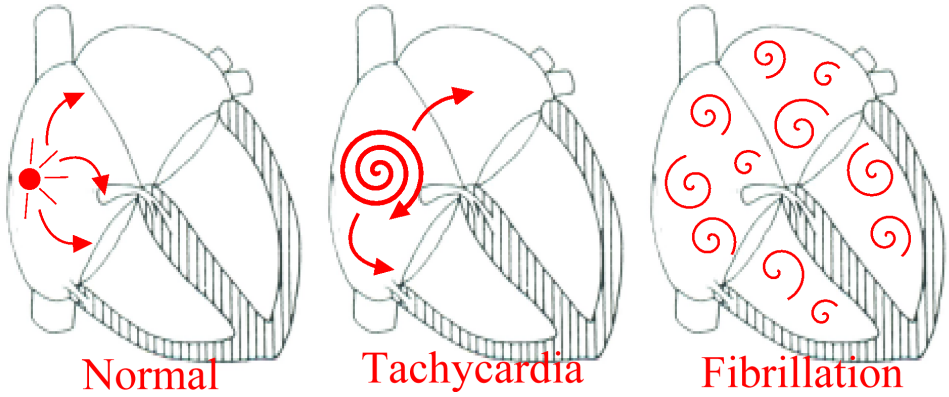
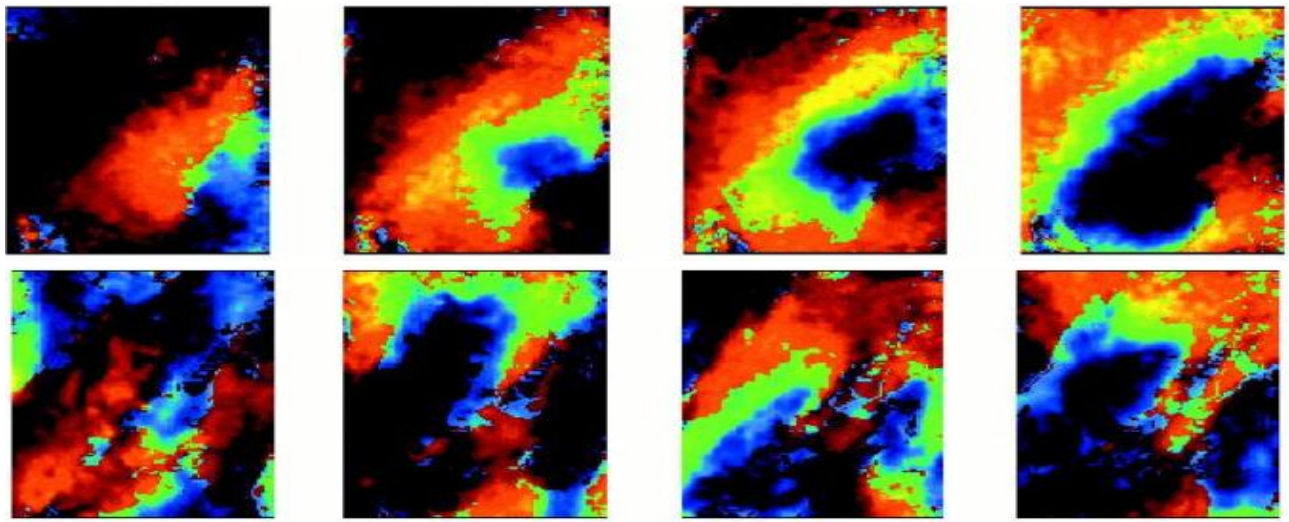
Ventricular Fibrillation and Spiral Waves

Heart is **excitable medium**: electrical wave triggers/coordinates contraction. **Arrhythmias** are caused by abnormal excitation wave.

Idea: arrhythmias caused by **spiral waves**:



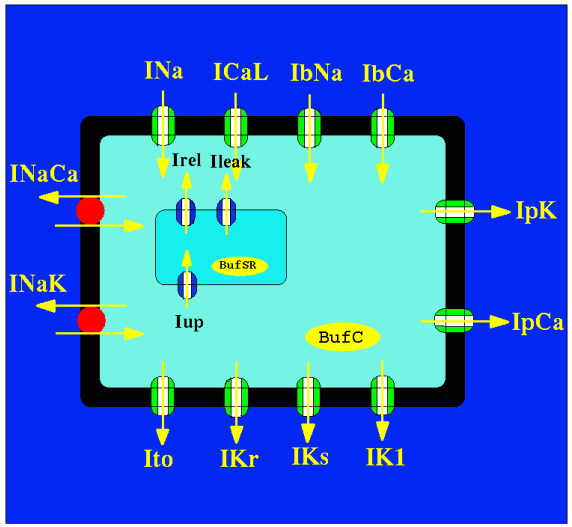
Experimental support:

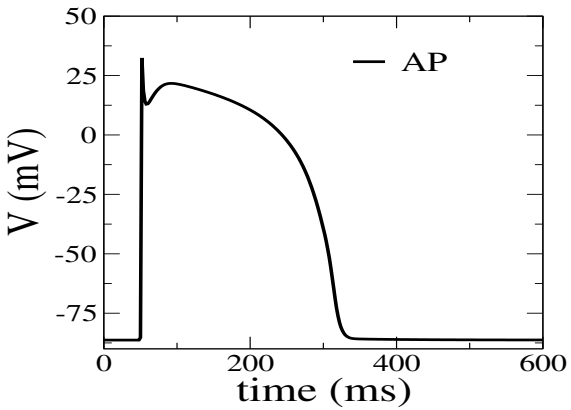


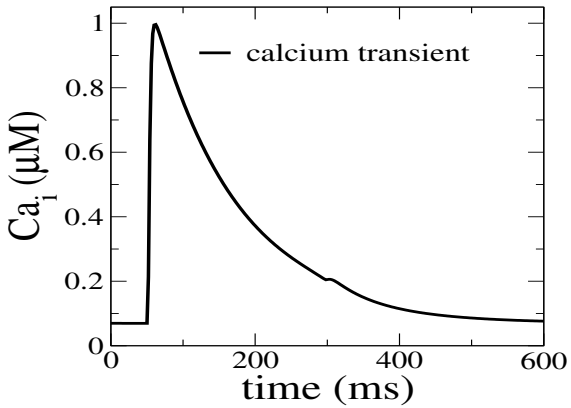
Human Ventricular Model (1)

Model for electrophysiology of human ventricular cells:
Fitted to human ion channel, cell and tissue data.

$$
\begin{aligned}
\frac{dV}{dt} &= -\frac{I_{ion}}{C_m} \\
I_{ion} &= I_{Na} + I_{K1} + I_{to} + I_{Kr} + I_{Ks} + I_{CaL} + I_{NaCa} + \ldots. \\
I_{Kr} &= G_{Kr} x_{r1} x_{r2} (V - E_K) \\
I_{rel} &= G_{rel} O (Ca_{SR} - CaSS) \\
dCa_{itotal}/dt &= -\sum I_{Ca}/(2V_c F) + I_{leak} - I_{up} + I_{rel} \\
dCa_{srtotal}/dt &= (V_c/V_{sr})(-I_{leak} + I_{up} - I_{rel}) \\
dNa_i/dt &= -\sum I_{Na}/(V_c F) \\
dK_i/dt &= -\sum I_K/(V_c F),
\end{aligned}
$$







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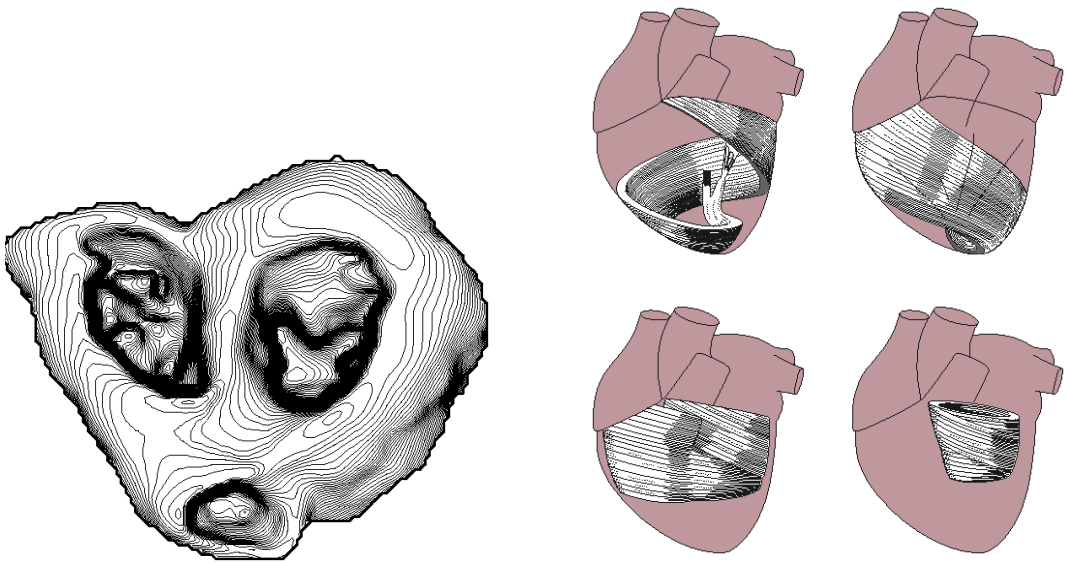
Human Ventricular Model (2)

Model for the **anatomy** (domain) and **fiber direction field** (diffusion tensor) of the ventricles: $\frac{\partial V}{\partial t} = -\frac{I_{ion}}{C_m} + D_{ij}\frac{\partial^2 V}{\partial x^2}$



Numerical details:
Finite difference explicit forward Euler integration, $\Delta x = 0.25mm$, $\Delta t = 0.02ms$, 13.5 million grid points, 19 variables per point.
MPI parallellisation, runtime of 3 days on 20 processors.

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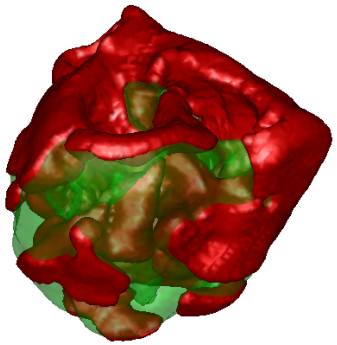
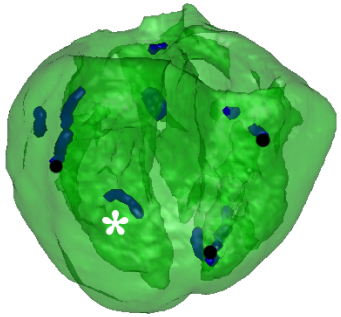
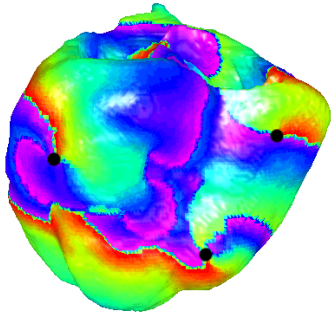
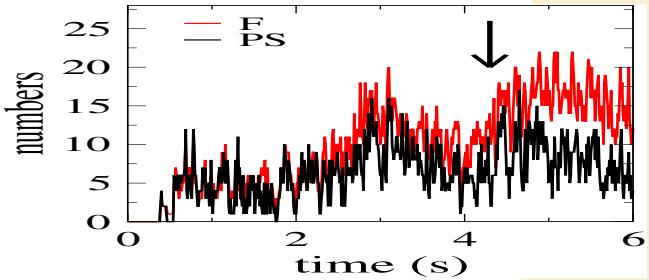
Results: VF in the human ventricles

Simulation results: $\sim$ 7 PS $\sim$ 10 spiral waves

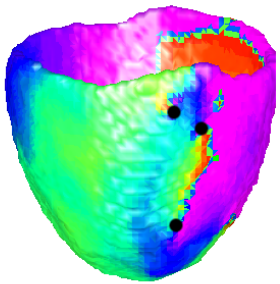


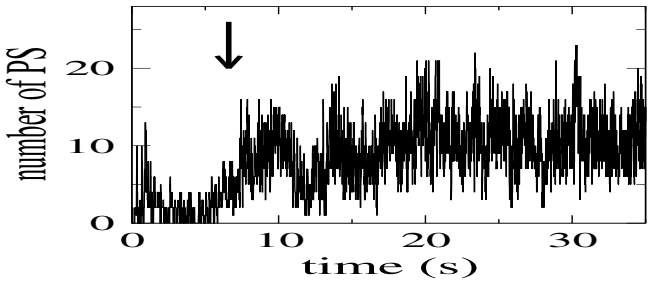




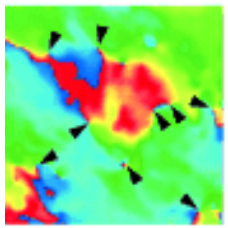


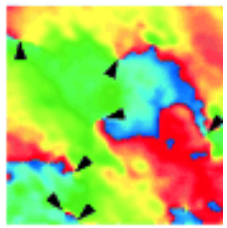
Clinical results in humans: $\sim$ 8 PS





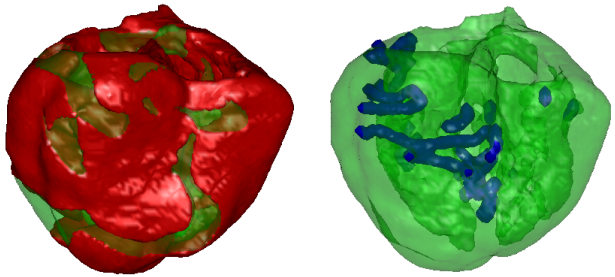
Experimental results in pigs and dogs: $\sim$ 50 PS



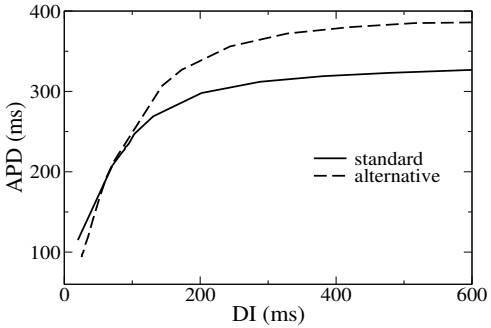


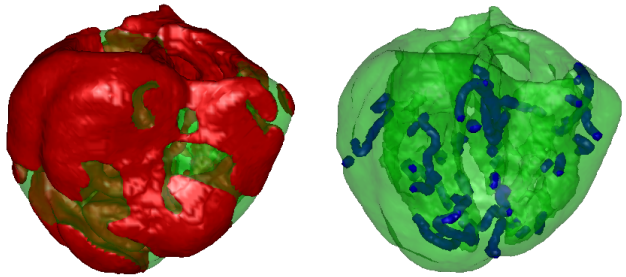
Results: What determines complexity wave patterns

Anisotropy: 1.5 fold increase

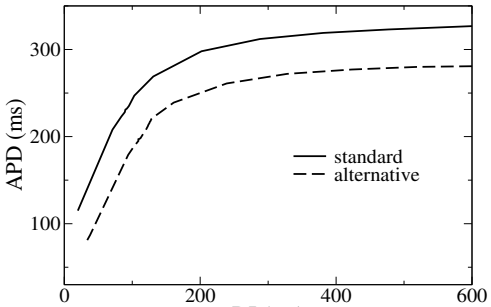


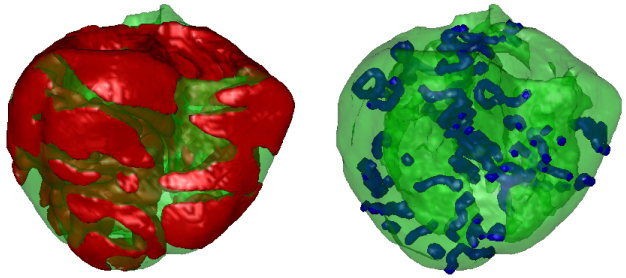
APD restitution slope: 2 fold increase





Minimum APD: 5 fold increase





Conclusion

Our quantitative model for human VF agrees well with clinical data.

Number of spirals in human VF $\sim$5 fold smaller than in pig/dog VF. Difference in minimum APD best potential explanation.

Experimental support: