Low Energy Cardioversion Using Feedback Stimuli in Human Atria

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Overview

- **Motivation**
- **Atrial cardioversion in 2D, 3D**
- **Direct solver numerical method: Progonka**
- **Beatbox**
- **Summary**

Response to small perturbation

Given a PDE with a rigidly rotating scroll wave solution:

$$C_m \frac{\partial U}{\partial t} = D\nabla^2 U - I_{ion}(r,t) + \varepsilon h(r,t)$$

$$\frac{d\vec{q}}{dt} = \vec{F}(\vec{q}, \vec{p}, U)$$

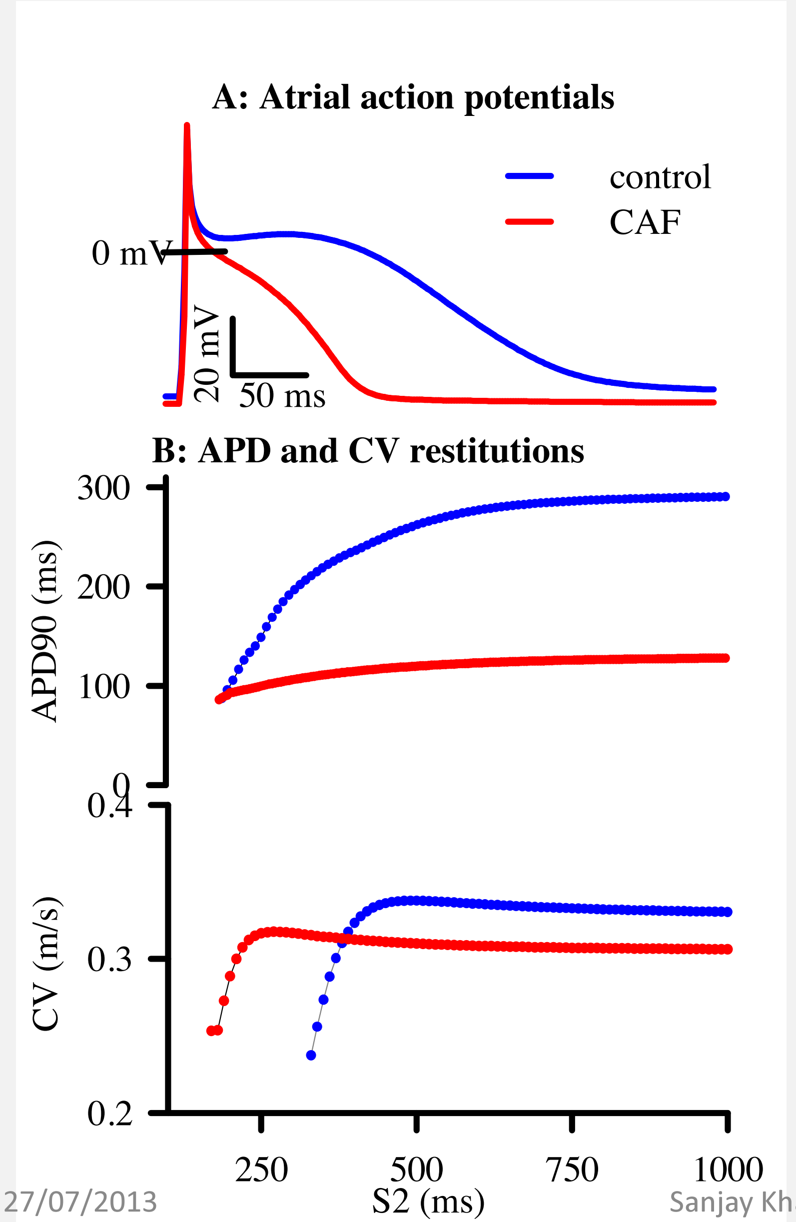
Compute & estimate time course trajectory of the scroll wave core [1,2]:

$$U_{drift}(r,t) = U_{rigid}(r) + \varepsilon g(r,t)$$

Does the theory work in 3D realistic atria?

1 Biktasheva et al. PHYSICAL REVIEW E 79, 056702 2009
2 Biktasheva et al. Plos 1 2011; 6(9): e24388

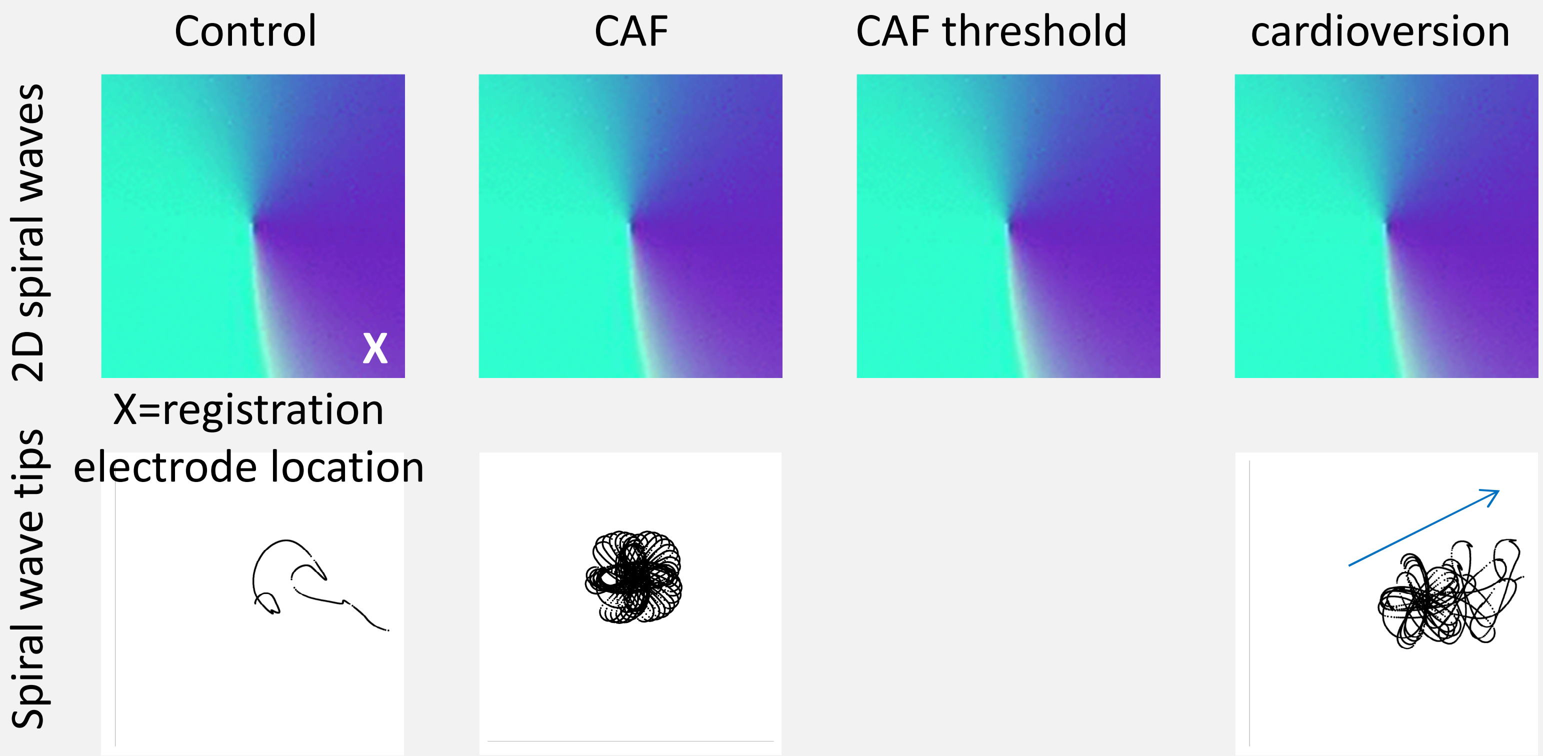
CAF abbreviates APD, increases propensity to AF



- CAF: g_{CaL} reduced by 50%, g_{K1} increased by 100%
- APD_{90} abbreviated by 47% (306 ms under control, 162 ms under CAF) [1]
- CV reduced due to CAF
- CV restitution shows increased propensity of atrial tissue to sustain high pacing rates [2]

1 Grandi et al. Circ. Res (2011); 109(9): 1055
2 Kharche et al. J Physiol. 2012 (epub ahead of print)

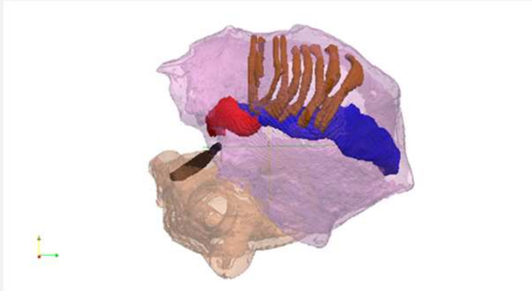
2D Re-entry and cardioversion



- **Control re-entry self-terminates quickly**
- **CAF re-entry is persistent with small meandering spiral wave core**
- **CAF threshold stimulus is 4.5 pA/pF**
- **Cardioversion in 5 s using a lower stimulus of 1 pA/pF**
- **The presented mono-domain calculations may overestimate the threshold, bidomain ongoing [1]**

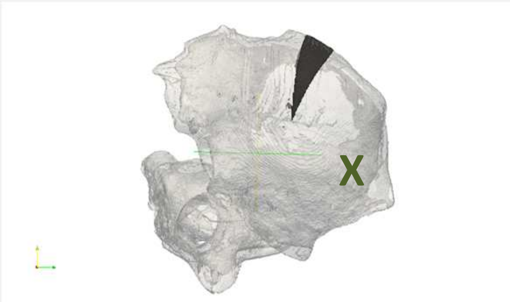
Morgan et al. Biophys. J. 2009; 96: 1364–1373.

3D re-entry and cardioversion

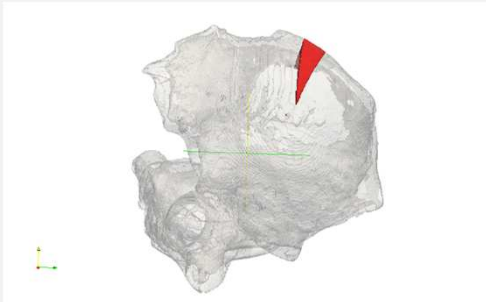


Seemann et al. Phil Trans A. (2006)

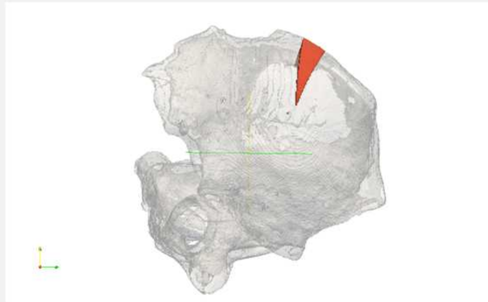
A: Control



B: CAF threshold



C: Cardioversion

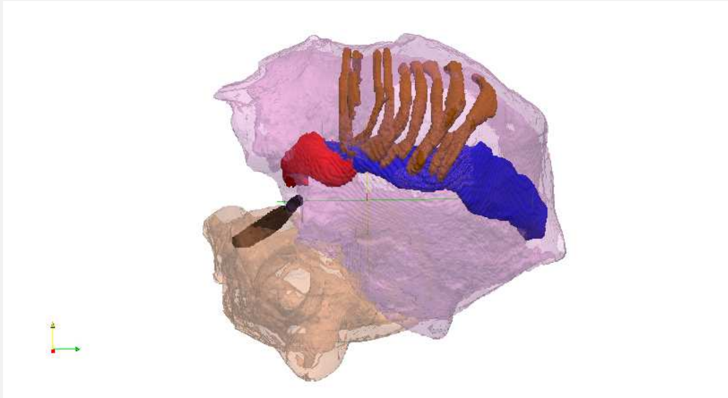


- Control scroll waves self-terminate
- CAF scroll waves meander, are pinned, but persistent throughout 10 s
- Cardioversion is effective in 9 s
- Major differences in 2D and 3D:

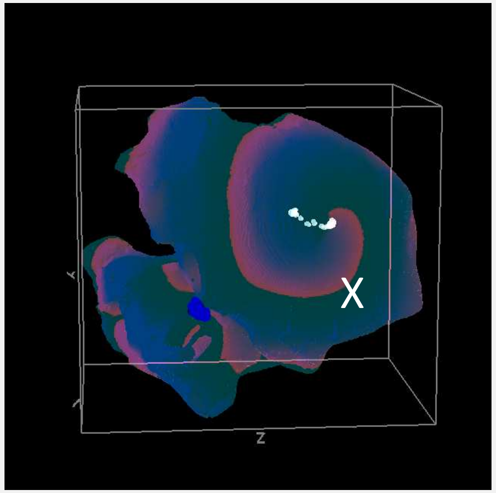
  The 3D geometry provides perturbations in location specific wall thickness affecting local drift velocity and direction;

  Pinning occurs when initiation is close to blood vessel openings or locations with large geometric heterogeneity;

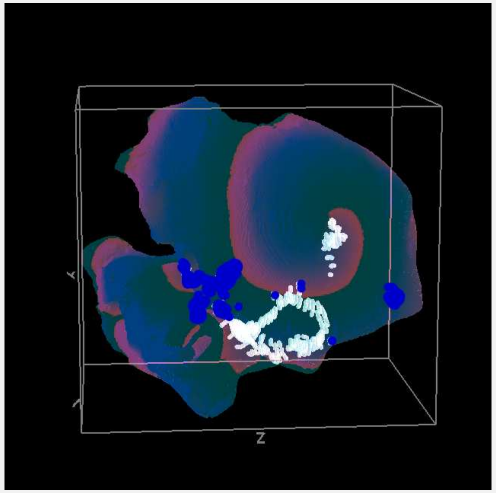
  Meander of scroll waves is influenced by external stimulation as well as geometry: calculation of response functions should consider both perturbations



CAF2 [1] no Stim



CAF2 with 1 pA/pF stim.



CAF2 without any stimulation (left) and with 1 pA/pF stimulation right. In the right hand panel, the registration electrode is located at the “X” marker. For a long duration, the re-entry persists above the terminal crest location. Then it jumps below the terminal crest, and continues in a few loops as indicated by the loop formed by the filament trace. The stimulation successfully eliminated the scroll waves in 15 seconds. The scroll wave exited the tissue by meandering vertically downwards where a very large blood vessel hole is present.

1 Morgan et al. Biophys. J. 2009; 96(): 1364–1373.

Alternating Directions PDE Solver: Ongoing Development

PDE is:

$$C_m \frac{\partial U}{\partial t} = D\nabla^2 U - I_{ion}(r,t)$$

$$\frac{d\vec{q}}{dt} = \vec{F}(\vec{q},\vec{p},U)$$

With Neumann b.c.s., an unconditionally stable implicit scheme using Alternating Directions Implicit method is D'yakonov method:

$$\left(1-\frac{\gamma}{2}\delta_x{}^2\right)U^* = \left(1-\frac{\gamma}{2}\delta_x{}^2\right)\left(1-\frac{\gamma}{2}\delta_x{}^2\right)\left(1-\frac{\gamma}{2}\delta_x{}^2\right)U_n - I_{ion}{}^n / C_m$$

$$\left(1-\frac{\gamma}{2}\delta_y{}^2\right)U^{**} = U^*$$

$$\left(1-\frac{\gamma}{2}\delta_z{}^2\right)U^{n+1} = U^{**}$$

$$where$$

$$\gamma = Dk / C_m h$$

- **Unconditional stability, improved accuracy in comparison to fully explicit solver**
- **Boundary conditions are taken into account in conjunction with the PDE**

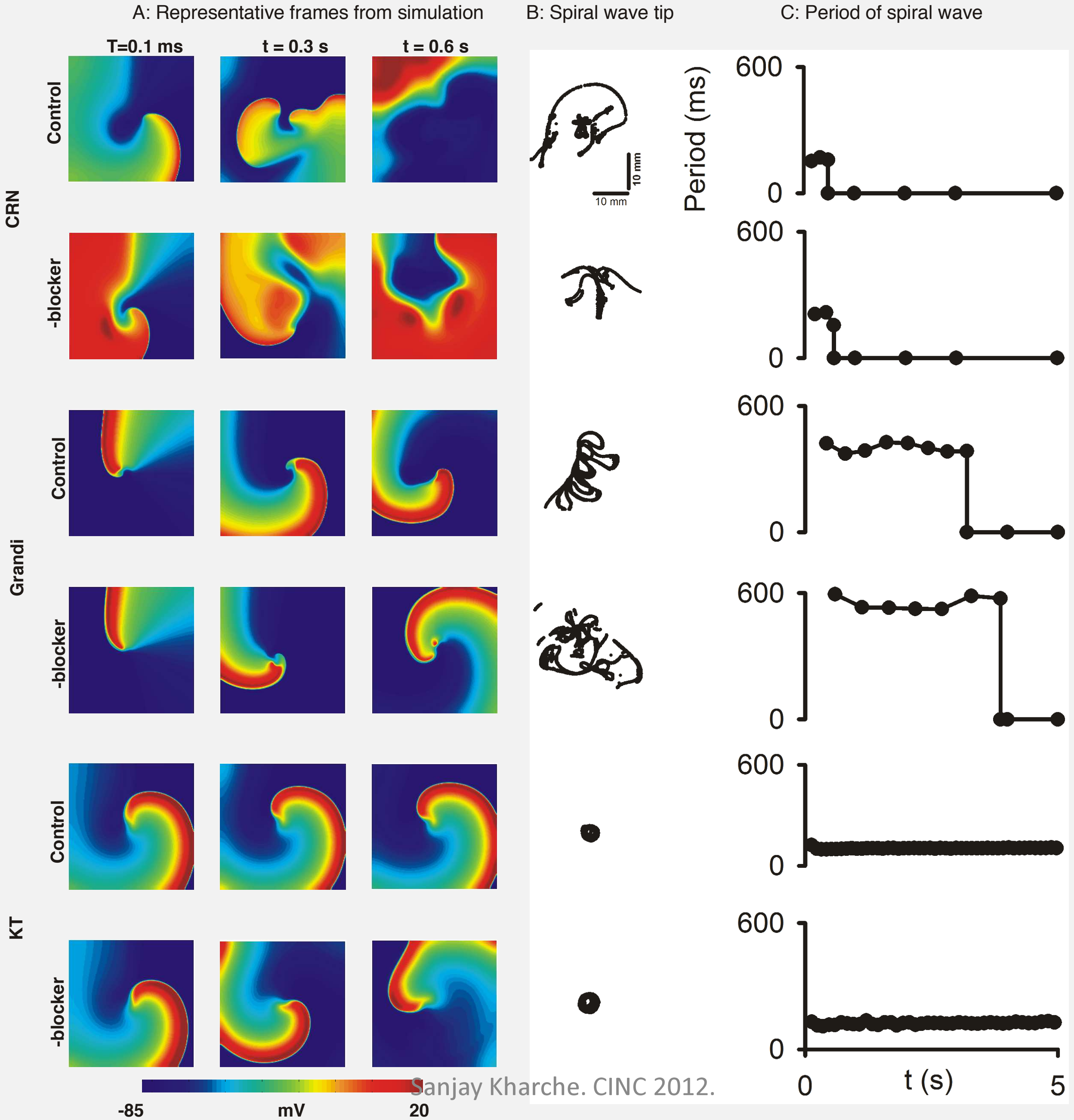
Keener and Bogar. Chaos. 1998; 8(1): 234
Heidenreich et al. Int. J. Num. Met. Eng. 2010; 82(8): 1022

Interlude: Application of the Implicit Solver

CRN
(type 1 AP)

GRANDI
(type 3 AP)

KT
(type 3
with T-
tubules)



Kharche et al. (In preparation)

Beatbox Formalism Paradigm

Input	Simulation	Output
	Serial or parallel (MPI) Beatbox bbs simulation script	
CellML → Beatbox Cell models repository	Forward Euler, RK4 ODE solvers	Run-time on screen output (serial mode)
Beatbox 1D, 2D, 3D tissue models repository	FD parabolic PDE solvers	File outputs ASCII and ppm formats
	FD elliptic PDE solvers	
DT MRI → Beatbox Anatomical models repository	Mathematical measurements and analyses: APD, CV, Restitution Curve, filament tracing, and others.	

Post-processing
Netpbm, EZView, VTK

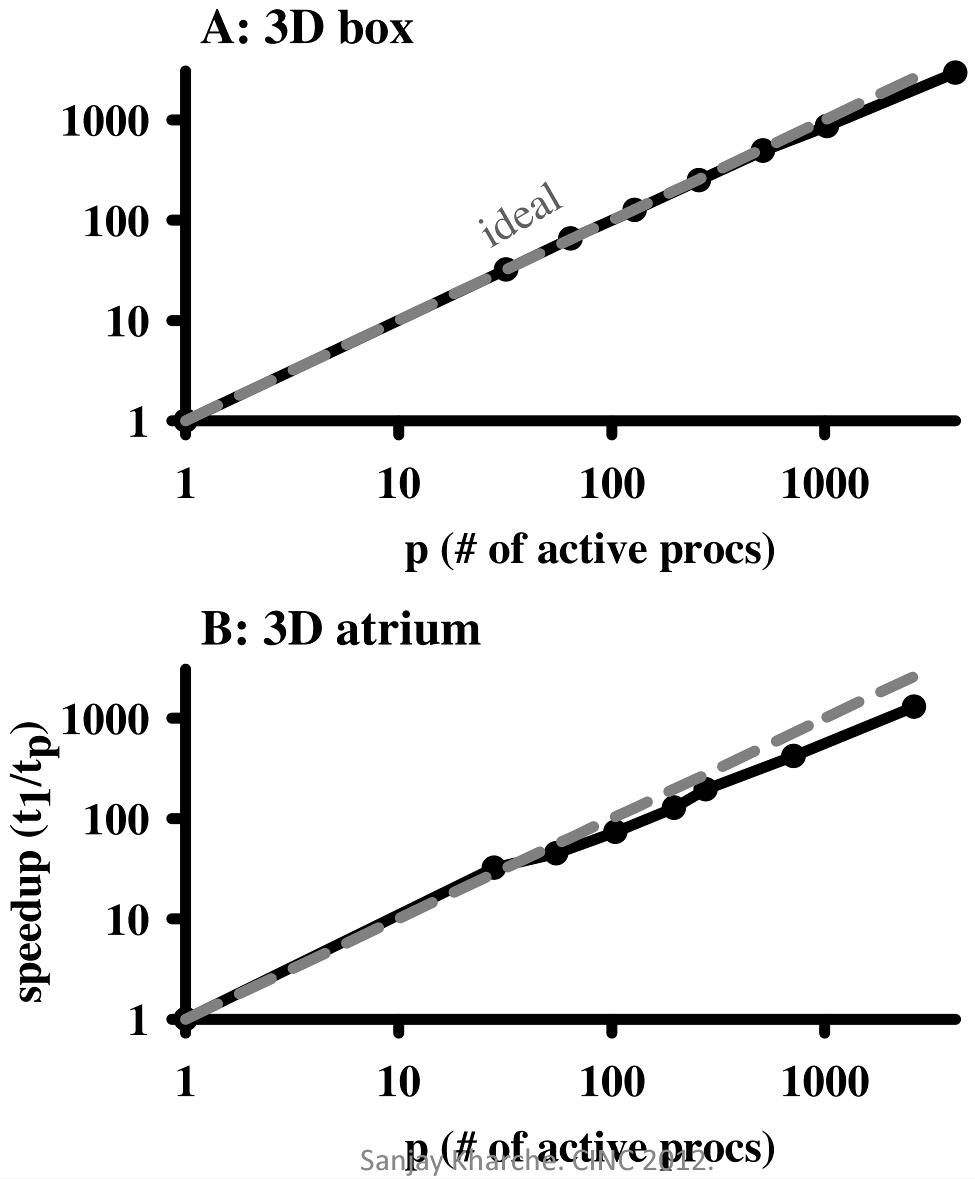
- Extensible, alienable, flexible
- No dependencies

Sanjay Kharche. CINC 2012.

A sample BeatBox script

```
<fhn.par>                                              // model pars are read in from file fhn.par
state geometry=ffr.bbg                                 // file ffr.bbg describes the tissue geometry
def real T; def real begin; def real out; def real end;   // real vars control works of “devices”
// The computation
diff v0=[u] v1=[i] Dpar=D Dtrans=D/4 hx=hx;            // anisotropic diffusion
k_func when=force pgm={u[i]=u[i]+force};
euler v0=[u] v1=[v] ht=ht ode=fhncubpar={eps=eps bet=@[b] gam=gam Iu=@[i]};
// Output
ppmout when=out file="[0]/%04d.ppm" mode="w"           // every “out” timesteps
record when=end file=[0].rec when=end v0=0 v1=1;       // ascii dump in the end of run
stop when=end;
end;
```

Beatbox Scaling



Summary

- The 3D atria consist of heterogeneities: wall thickness, fibre orientation, curvature
- Low energy cardioversion can be a successful strategy in the 3D atria

Ongoing work

- Improved domain decomposition
- Implicit solvers: mono-domain and bidomain
- Binary parallel file i/o and large data visualisation
- Available as a SVN repo: svn co --anonymous=YourUserName https://beatbox-trac.epcc.ed.ac.uk/svn/trunk . *(password: beatbox)*
- Mailing list: BEATBOX@JISCMAIL.AC.UK
- Detailed documentation and support from authors

Acknowledgements

This project is supported by the UK EPSRC.

Beatbox

Solution:

- **software package following the modular philosophy,** including a collection of most modern realistic models of cardiac excitation.
- the **built in script interpreter**
- **High performance computing**
- "BeatBox - HPC Environment for Biophysically and Anatomically Realistic Cardiac Simulations", EP/I029664/1, **£260K** (FEC), Co-I

Virtual Heart.

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k_func when=force pgm={u[i]=u[i]+force};
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