Long ECGs reveal rich and robust dynamical regimes in patients with frequent PVCs

SMB 2021 Annual meeting
14 June 2021

Thomas Bury

Postdoctoral researcher
Department of Physiology
McGill University

McGill UNIVERSITY

CAMBAM
Centre for Applied Mathematics in Bioscience and Medecine

In collaboration with…

Marc Deyell, MD

Zachary Laksman, MD

Claudia Lerma

Leon Glass

Gil Bub

UBC THE UNIVERSITY OF BRITISH COLUMBIA

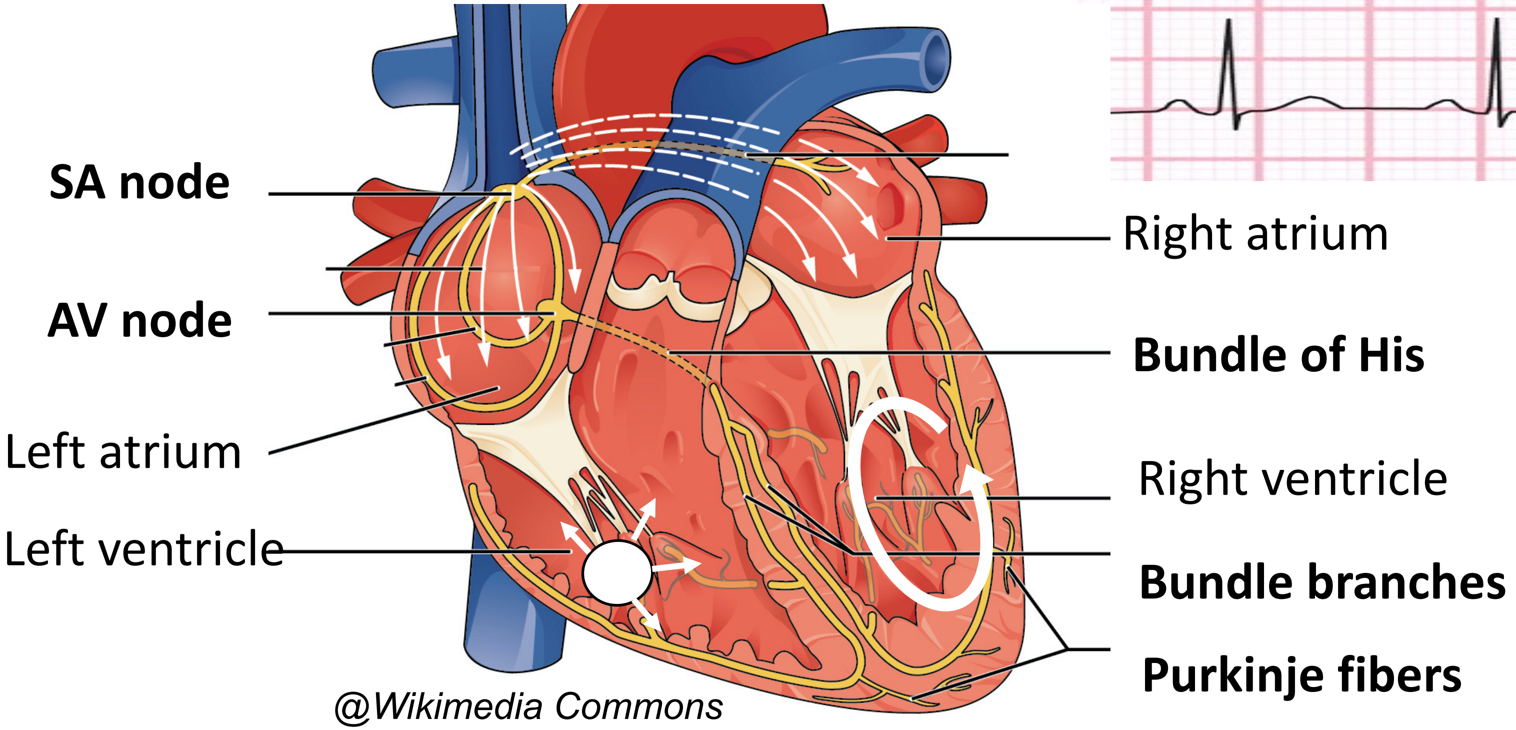
McGill UNIVERSITY

icentia™

INSTITVTO N DE CARDIOLOGIA IGNACIO CHAVEZ

Ventricular arrhythmia

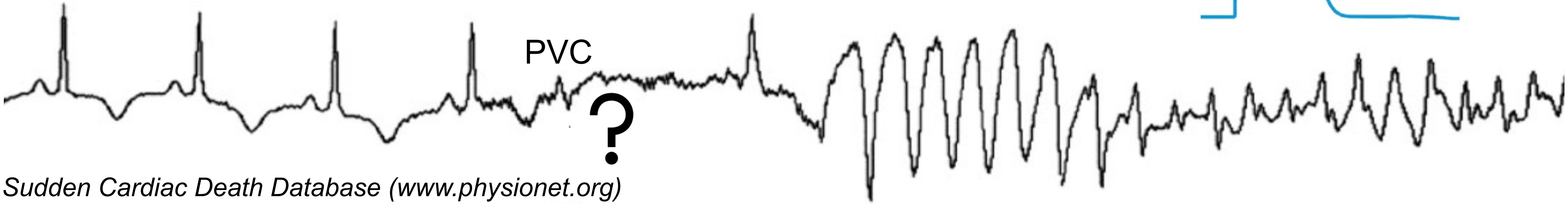
PVC = Premature Ventricular Complex



@Wikimedia Commons

Initiation mechanisms

1. Ectopic pacemaker
2. Reentry
3. Triggered activity



Sudden Cardiac Death Database (www.physionet.org)

Why analyse PVC dynamics?

- Frequent PVCs show increased risk of sudden cardiac death

  Dukes et al. Ventricular ectopy as a predictor of heart failure and death. JACC (2015)

- Ventricular fibrillation is often preceded by frequent PVCs

  Deyell et al. Sudden Cardiac Death Risk Stratification. Circulation research. (2015)

- Risk stratification for sudden cardiac death is still a major challenge

- PVC dynamics in patients are rich but poorly understood – still cannot reliably infer mechanism from pattern

How can we analyse PVC dynamics?

Holter monitor

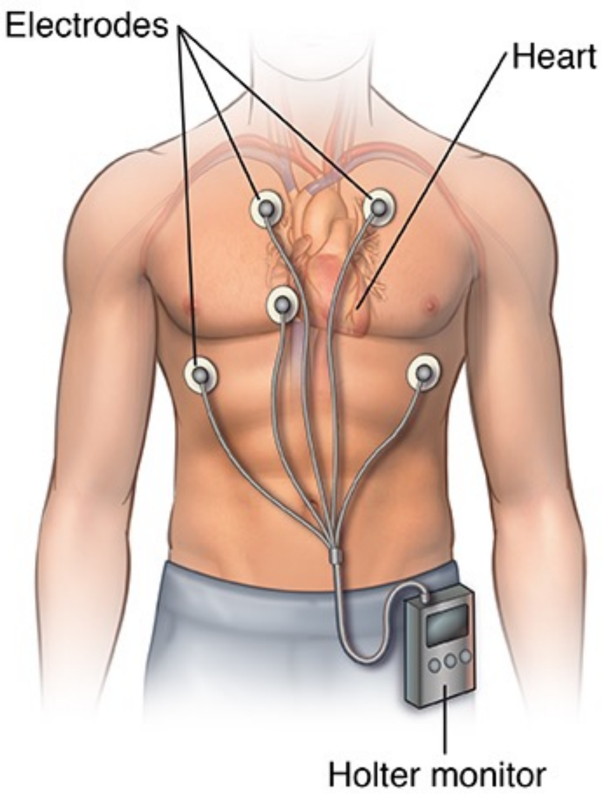
1947 - Norman Holter

Wikipedia. The original Holter biotelemetry apparatus in 1947 weighing 85 lb

1954 – Briefcase recorder

Image courtesy of National Museum of American History

1960 – Tape recorder



H L Kennedy. The history, science and innovation of Holter technology. Annals of Noninvasive Electrocard. (2006)

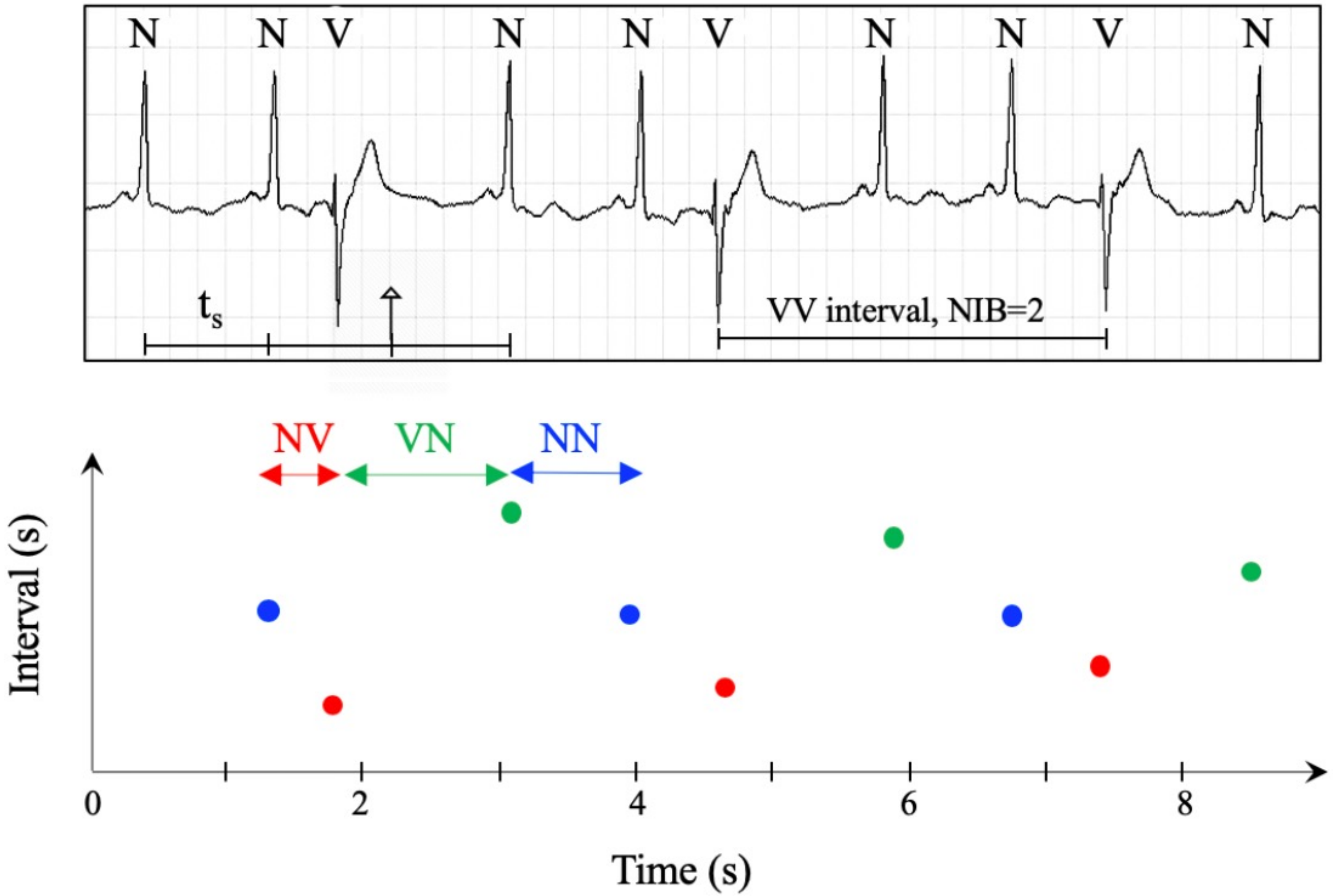
2010 onwards:

Icentia cardioSTAT

Apple watch

ECG data processing

Cohort of 48 patients with idiopathic frequent PVCs



Beat detection algorithm

N – normal (sinus) beat

V – premature ventricular complex (PVC)

Timing – precise to 250Hz

Beat-to-beat interval plot

NV – coupling interval

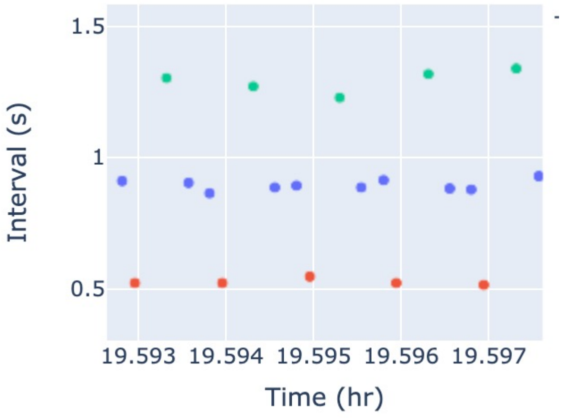
VN – compensatory pause

NN – sinus interval

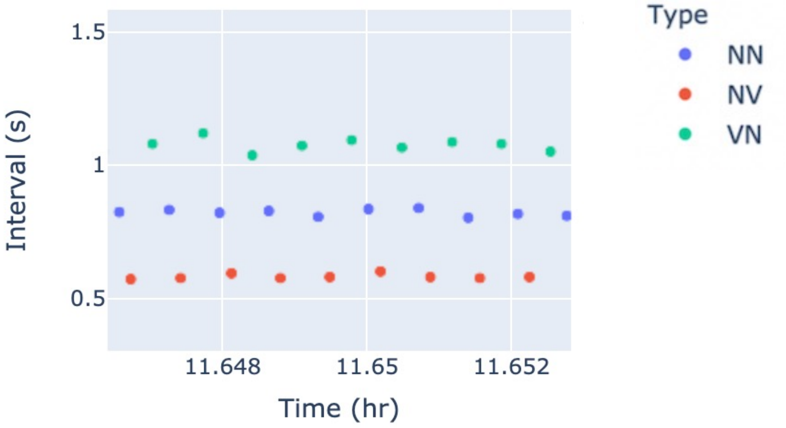
Observations in single patients

Record AC4182

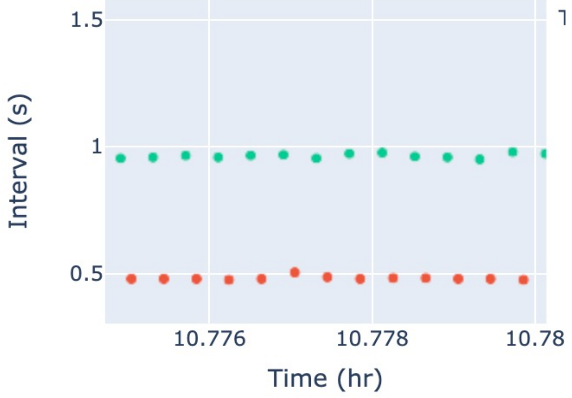
67 bpm : NIB=3



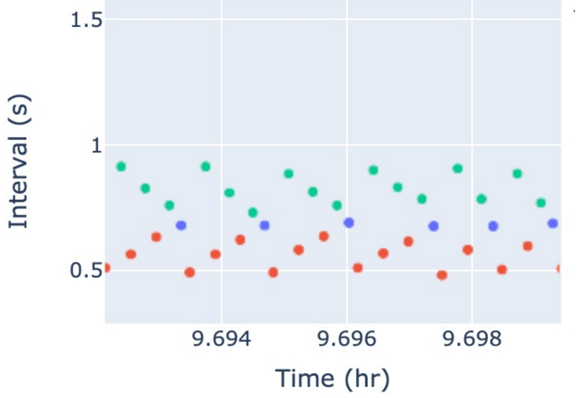
75 bpm : NIB=2



80 bpm : NIB=1



86 bpm : cycling CI



Record AC5111

Sequence of 149 NIB values

10 4 4 4 4 7 1 1 7 4
4 1 4 1 13 1 10 4 1 1
7 1 4 4 4 7 4 7 7 13
7 7 4 4 10 7 1 4 4 7
4 10 4 10 7 4 4 7 7 1
10 10 4 10 1 7 4 4 7 1
1 7 4 7 4 4 4 1 4 4
1 4 4 4 1 4 4 1 4 4
4 1 7 4 1 1 1 1 7 4
1 4 1 4 4 4 1 7 1 7
1 4 1 1 7 4 4 4 1 1
7 1 1 1 4 7 4 1 1 1
7 4 1 1 1 1 4 4 1 4
4 1 1 1 7 1 4 1 7 1
7 1 1 1 4 7 4 4 4

[1,4,7,10,13,...]

NIB=3n-2

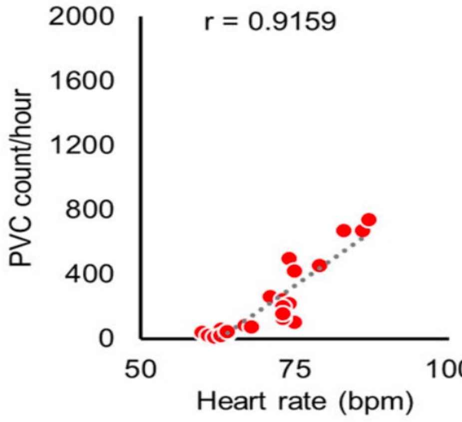
P_{random}=

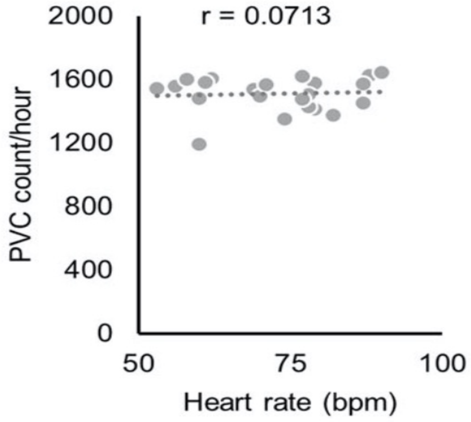
$(1/3)^{149} \sim 10^{-72}$

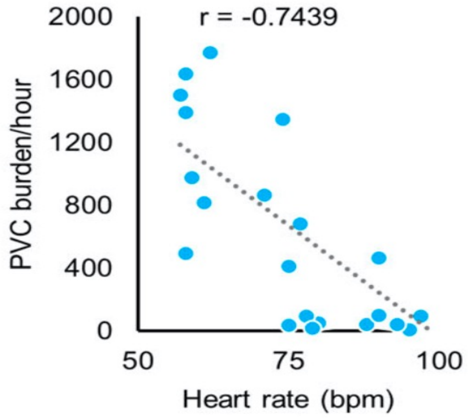
PVCs as a function of heart rate

416 patients, 24-hour Holter

50% | 36% | 14%





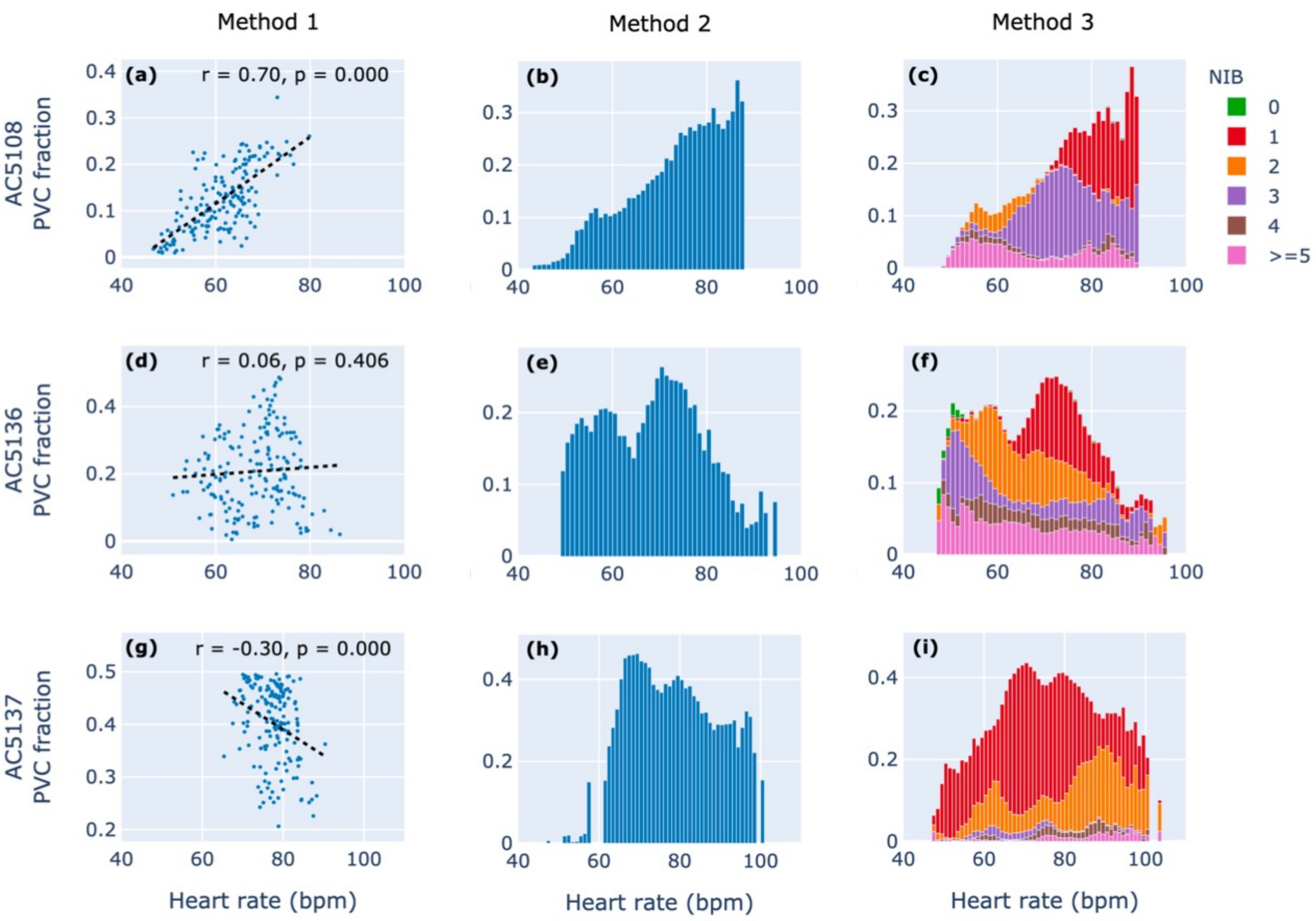


Prescribed beta blockers

Follow-up Holter

Decrease in PVCs | No effect | Increase in PVCs

Hamon et al. Premature ventricular contraction diurnal profiles predict distinct clinical characteristics and beta-blocker responses. J Cardiovasc Electrophysiol. (2019)



Method 1 (standard approach)

- *Hourly* averaging of HR
- %PVC computed within each hour

Method 2

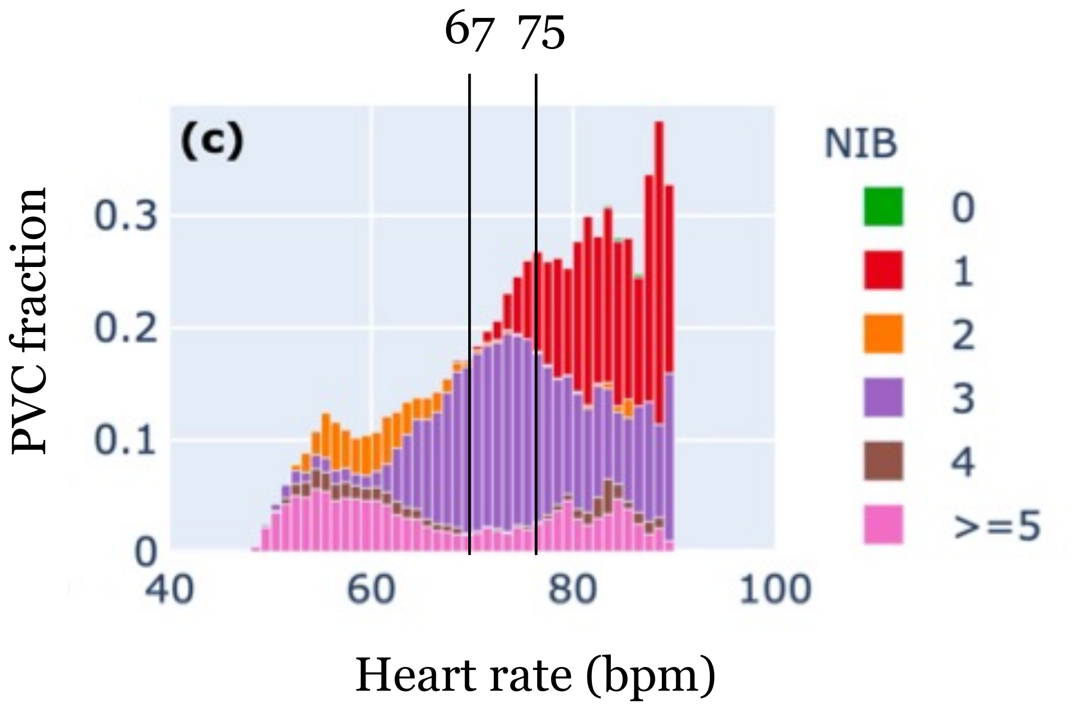
- *Minute* averaging of HR
- %PVC computed across entire record for each HR

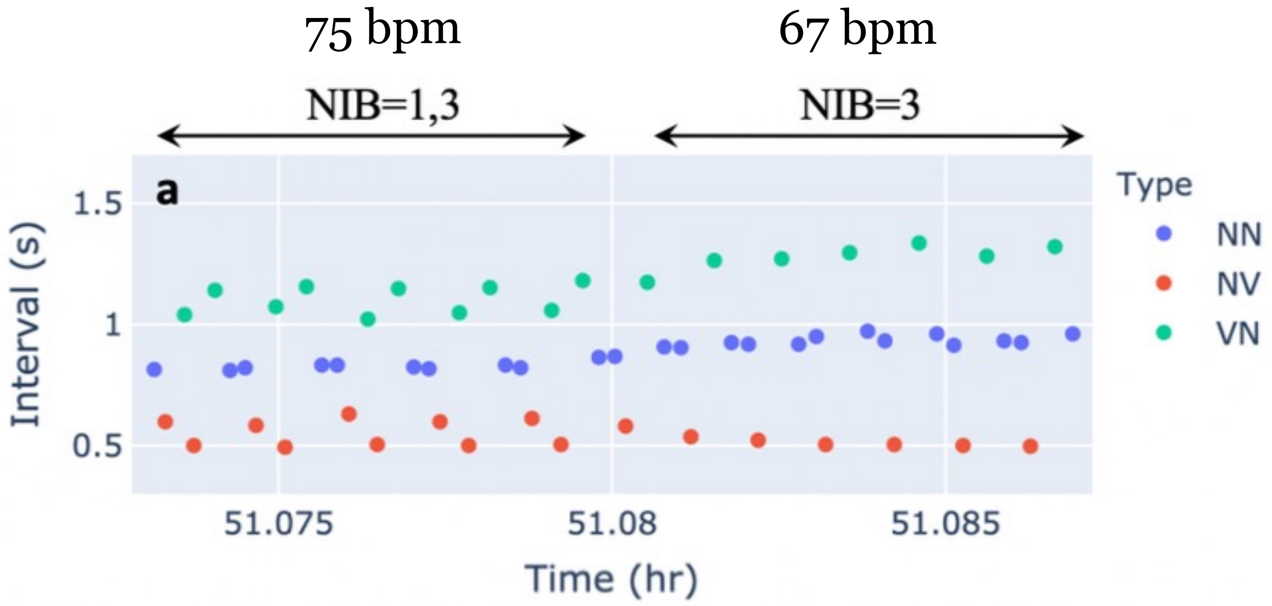
Method 3

- *Rolling* window averaging of HR
- Relative occurrence of NIB values

Over different 24 hour periods

Bifurcation behaviour of AC5108

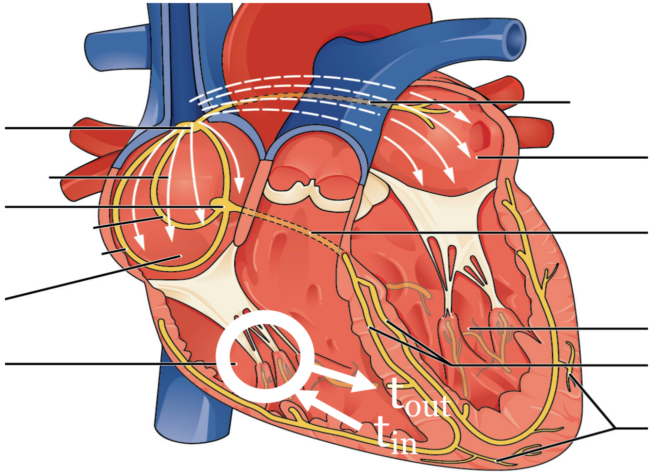




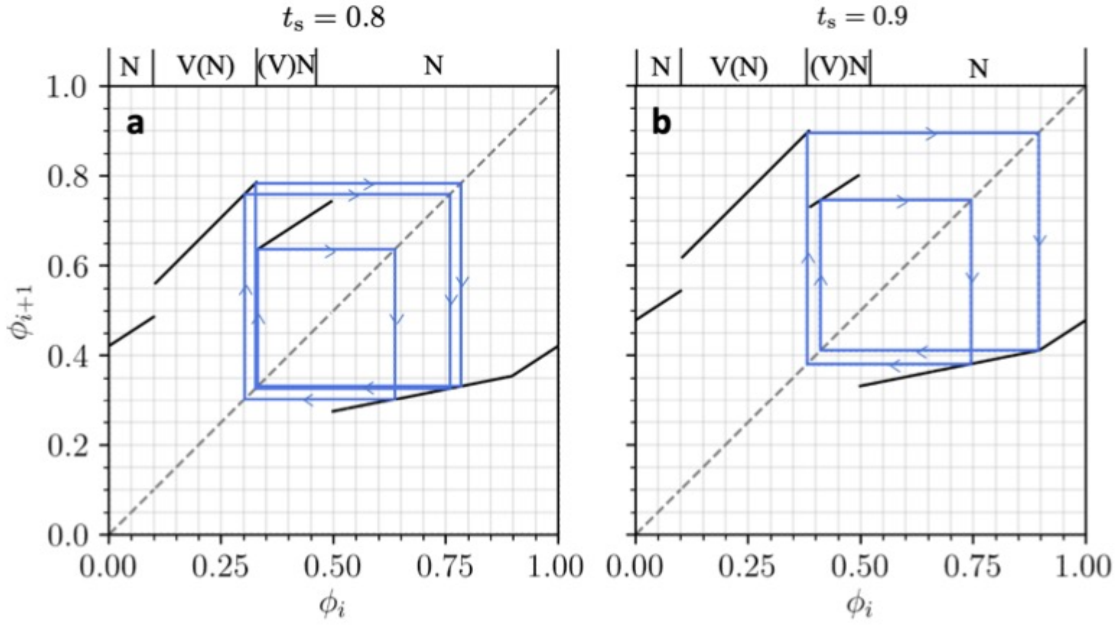
What mechanism gives rise to these robust patterns?

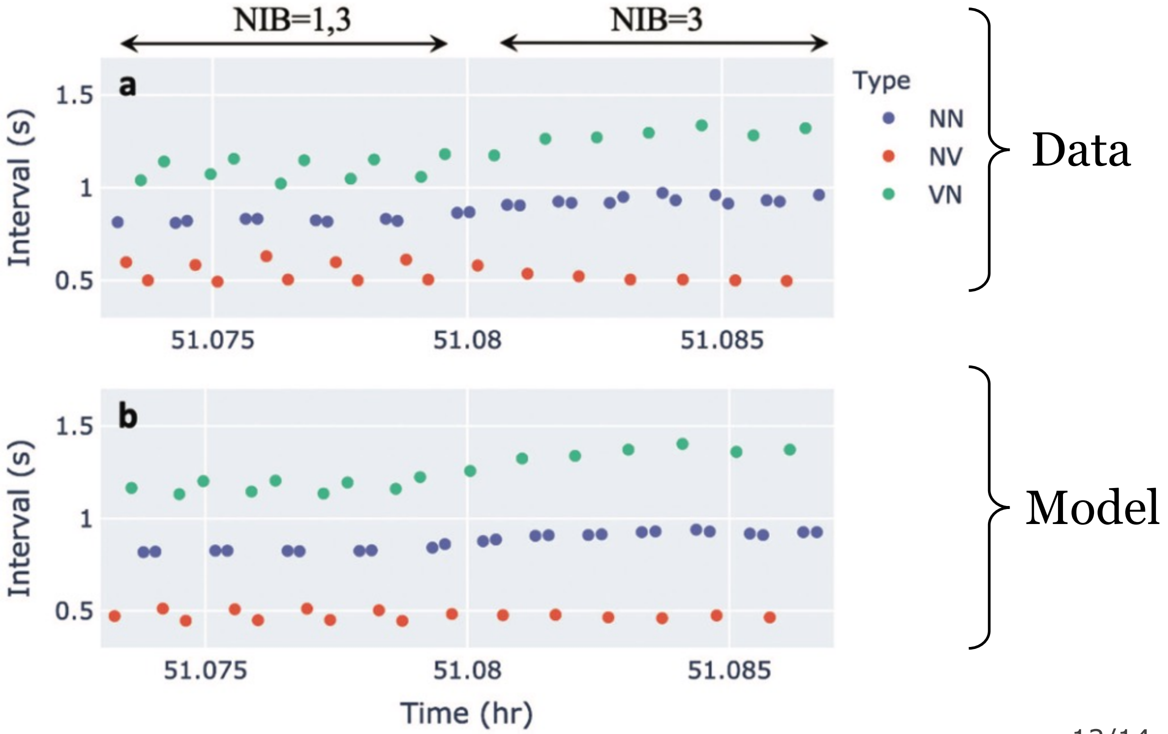
Goal: Find a model based on physiological principles that reproduces this behaviour

Model: Modulated parasystole with conduction delay



$$\phi_{i+1} = \begin{cases} \phi_i + \frac{t_s}{t_e} + 1 - f(\phi_i + \frac{t_{in}}{t_e}) & 0 \le \phi_i < \frac{t_{out}}{t_e}, \\ \phi_i + \frac{t_s}{t_e} & \frac{t_{out}}{t_e} \le \phi_i < \frac{t_{out}+t_s-\theta}{t_e}, \\ \phi_i + \frac{t_s}{t_e} + 1 - f(\phi_i + \frac{t_{in}}{t_e}) & \frac{t_{out}+t_s-\theta}{t_e} \le \phi_i < 1. \end{cases}$$

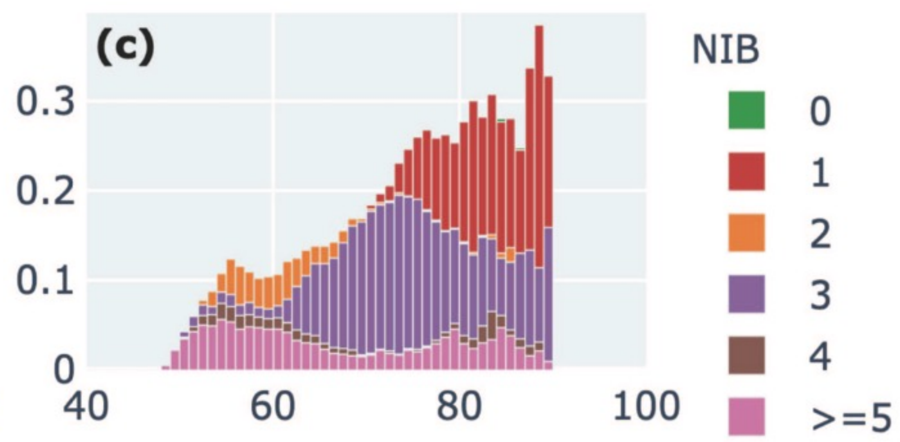




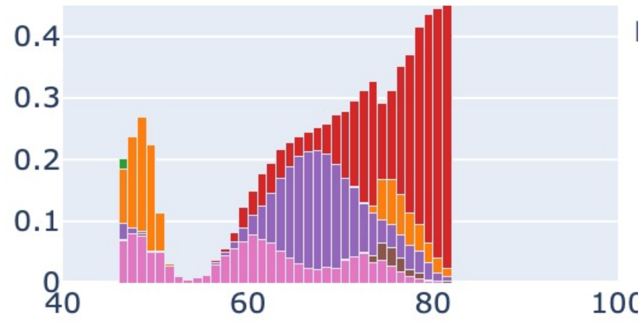
Model: Modulated parasystole with conduction delay

$$\phi_{i+1} = \begin{cases} \phi_i + \frac{t_s}{t_e} + 1 - f(\phi_i + \frac{t_{in}}{t_e}) & 0 \le \phi_i < \frac{t_{out}}{t_e}, \\ \phi_i + \frac{t_s}{t_e} & \frac{t_{out}}{t_e} \le \phi_i < \frac{t_{out}+t_s-\theta}{t_e}, \\ \phi_i + \frac{t_s}{t_e} + 1 - f(\phi_i + \frac{t_{in}}{t_e}) & \frac{t_{out}+t_s-\theta}{t_e} \le \phi_i < 1. \end{cases}$$

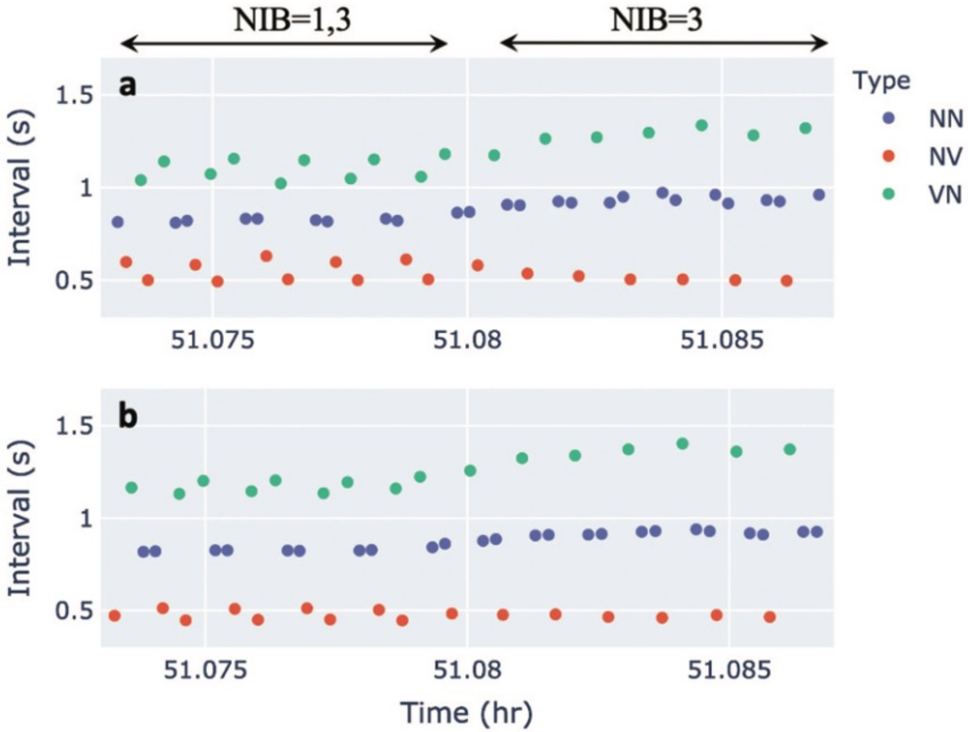
Data



Model



Heart rate



Data

Model

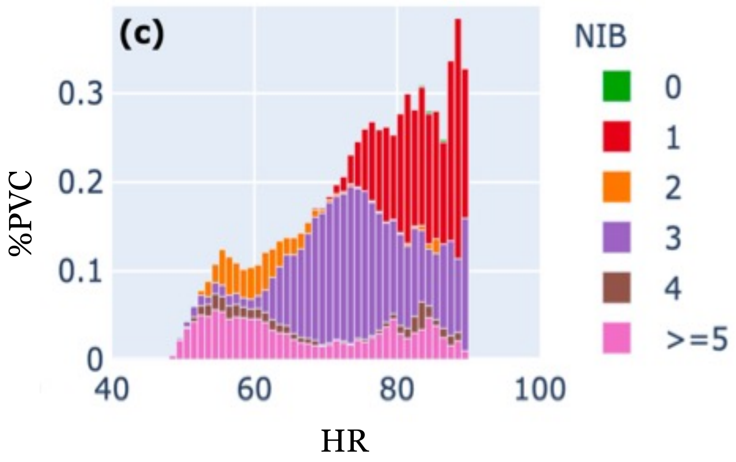
Bury et al. "Long ECGs reveal rich and robust dynamical regimes in patients with frequent ectopy." *Chaos: An Interdisciplinary Journal of Nonlinear Science* 30.11 (2020): 113127.

Take-home points

- New opportunities for large-scale analysis of PVC dynamics

- Patients with unexplained PVCs exhibit **diverse** bifurcations in cardiac rhythm as a function of heart rate

- Facilitates the development and calibration of mathematical models – a dynamics-based personalised medicine.



Questions/comments?