Brain, Respiration and Cardiovascular Causalities in Anæsthesia

BRACCIA

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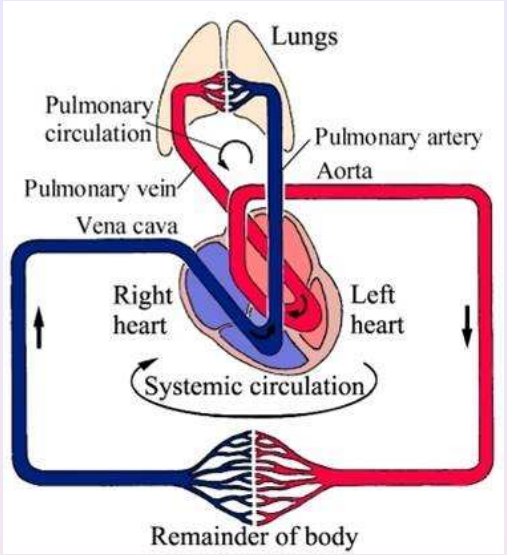
Outline

1. Introduction
   - Complexity
   - Measurements
   - Analysis
2. Anæsthesia
   - Practice & problems
   - Anæsthesia in rats
   - Anæsthesia in humans
3. BRACCIA

A NEST applying ideas from complex systems to medicine.



Complexity and human body

- Human body + brain, most complex mechanism ever to have existed –
  - 10^{13} cells, 10^{11} neurons in brain.
  - 40000 kilometres of capillaries.
- Mostly self-repairing, long-lasting.
  - E.g. heart lasts for $>$ 2 gigabeats.
- Complex signals from physiological measurements.

Challenges: (i) to understand the underlying processes by analysis of the signals; and (ii) to exploit this knowledge.

Measured quantities

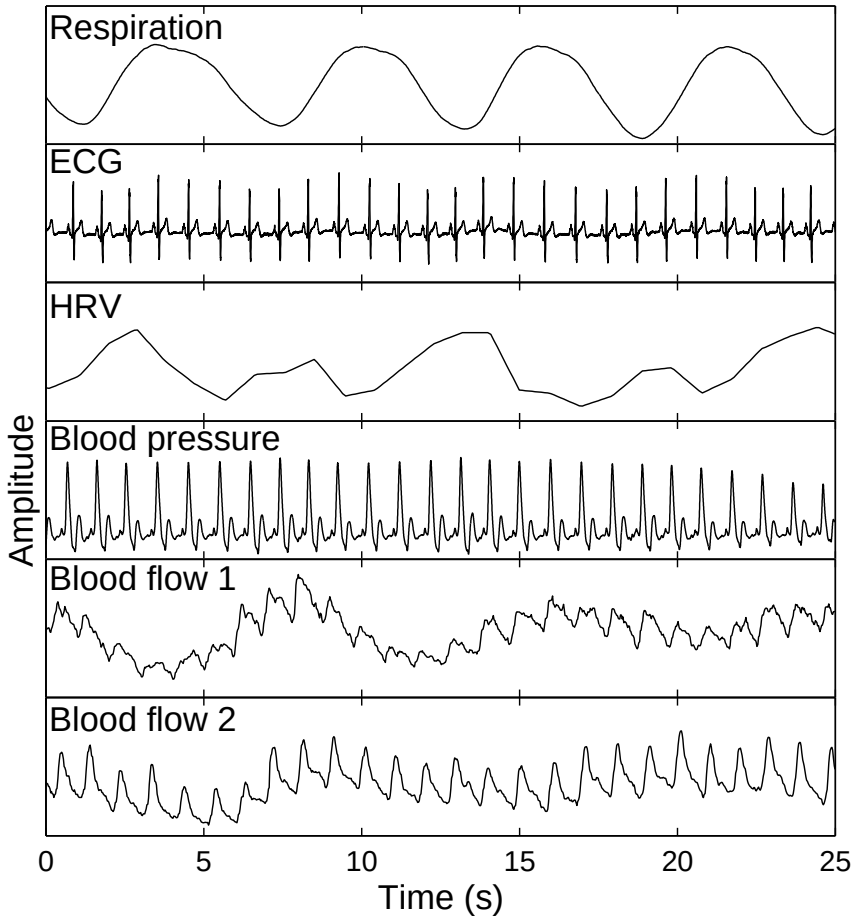
Make simultaneous measurements of several different physiological quantities, e.g. –

- Cardiac activity (from ECG)
- Respiration (belt+sensor on thorax)
- Blood pressure (sensor on finger)
- Blood flow rate (laser-Doppler flowmetry)
- Temperature (semiconductor sensor)
- Brain waves (EEG)

Typically, data are complex and oscillatory.

Data recorded over 30 minutes, noninvasively, and usually for a quiescent subject.

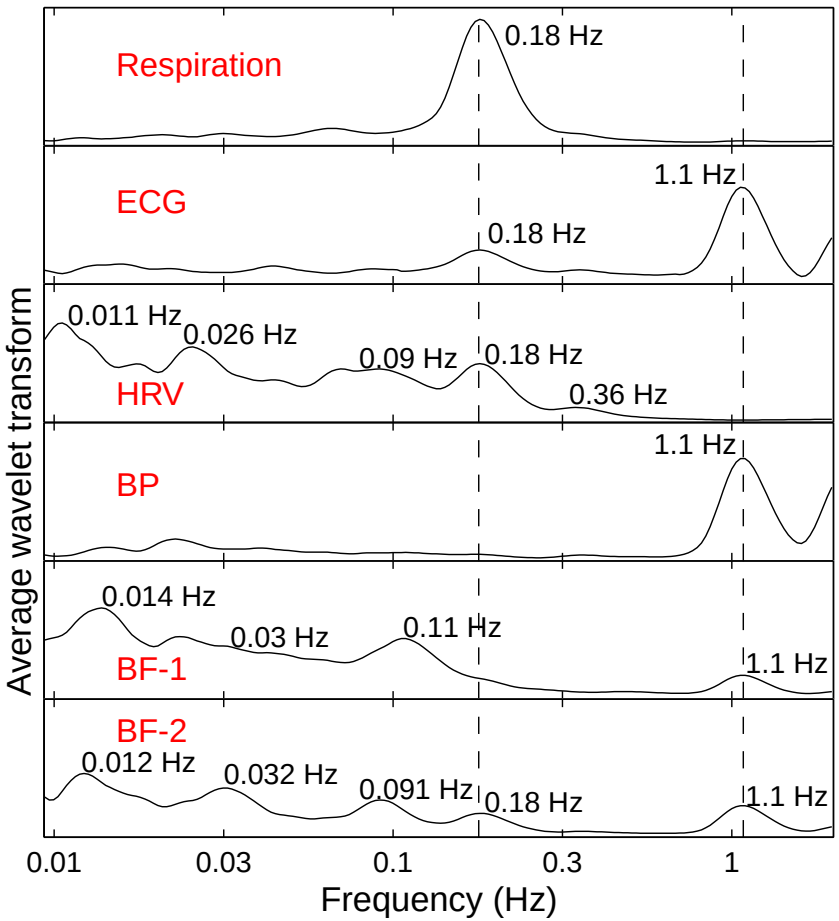
Physiological signals are complex



Note –

- “HRV” is derived from ECG
- Several frequencies evident in blood flow...

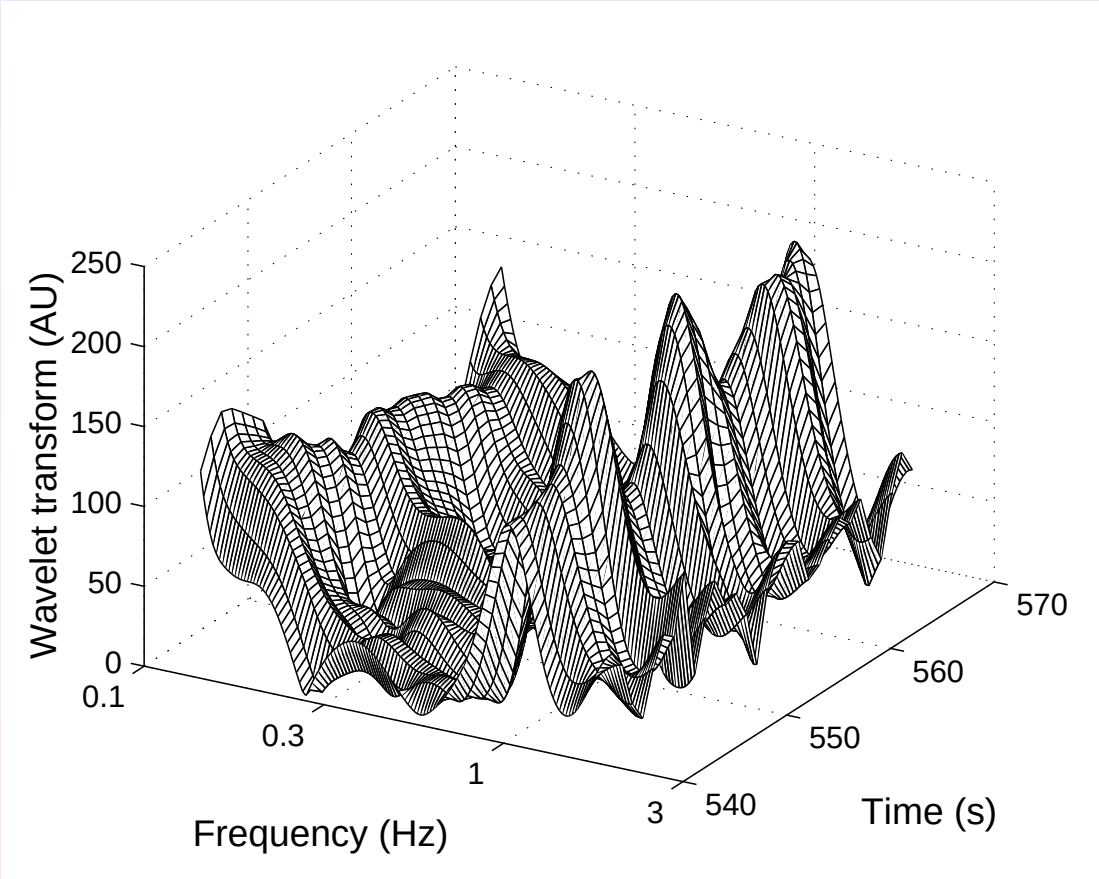
Averaged wavelet spectra



Note –

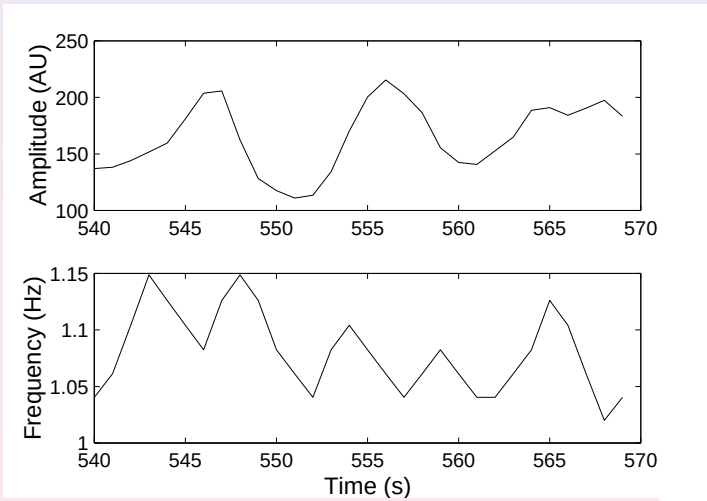
- Log frequency resolution
- Same spectral peaks in all data?
- Peaks are broad

Time–frequency wavelet transform



Time variation of maxima –

- Amplitudes
- Frequencies



Physiological origins of the rhythms?

∼Hz	Process
1.0	Heart – obvious
0.2	Respiration – obvious?
0.1	Myogenic activity of smooth muscle – same *in vitro*
0.04	Neurogenic activity – absent after denervation
0.01	Endothelial vasodilation – NO dependent
(0.007)	(Endothelial vasodilation – endothelin dependent)

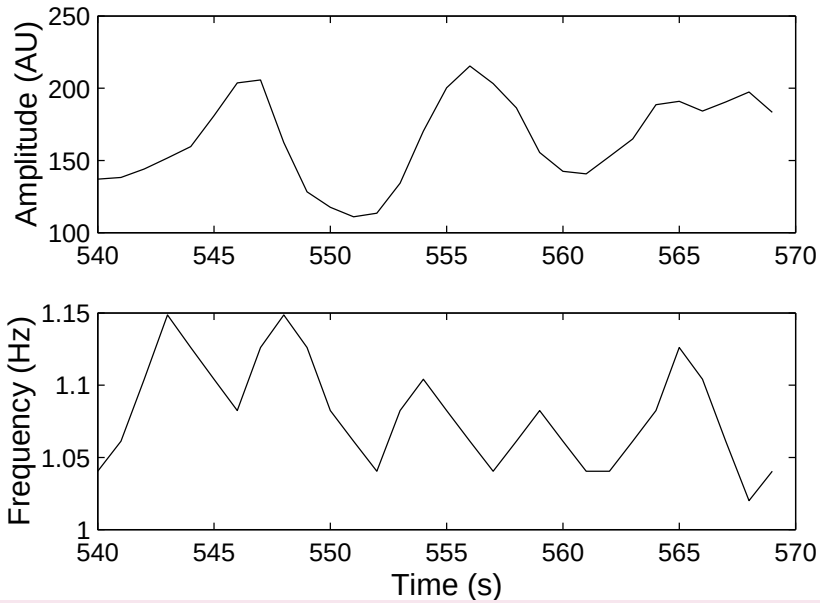
Our interest centres especially on –

- Relative amplitudes
- Couplings

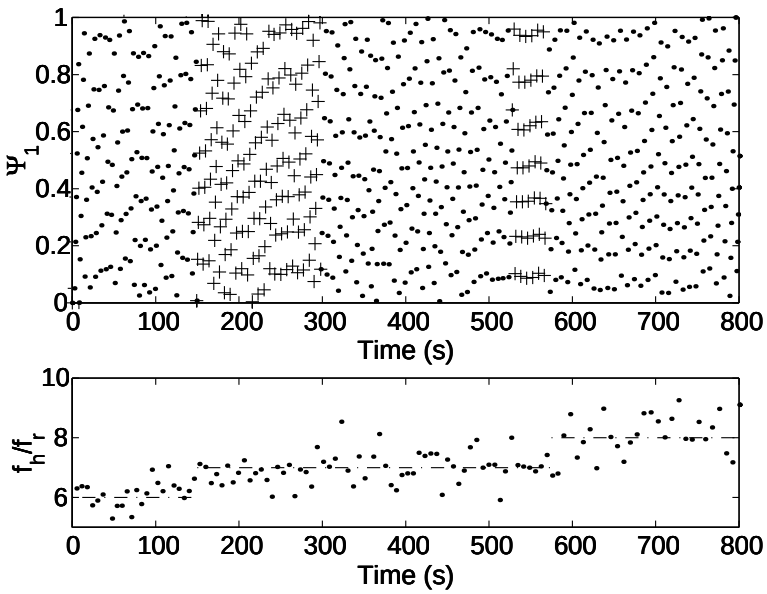
between respiratory, cardiac, and cortical (EEG) oscillations, which seem to reflect the state of the organism...

Evidence of inter-oscillator couplings?

Modulation



Synchronization



- Closely analogous to coupled-oscillator phenomena seen elsewhere in physical science and engineering.
- Relative values of oscillator amplitudes and couplings reflect state of the system, so...
- Maybe there are changes with depth of anæsthesia?

Anæsthesia

- A chemical perturbation of the organism results in a temporary loss of consciousness.
- Mysterious – mind/body relationship etc.
- Certain nervous pathways blocked.
- Important – needed for surgery.

"...the anæsthetist is still unable to measure the depth of anæsthesia in order to prevent inadvertent awakening during anæsthesia."

C.J.D. Pomfrett, *Brit. J. Anæsthesia*, 1999.

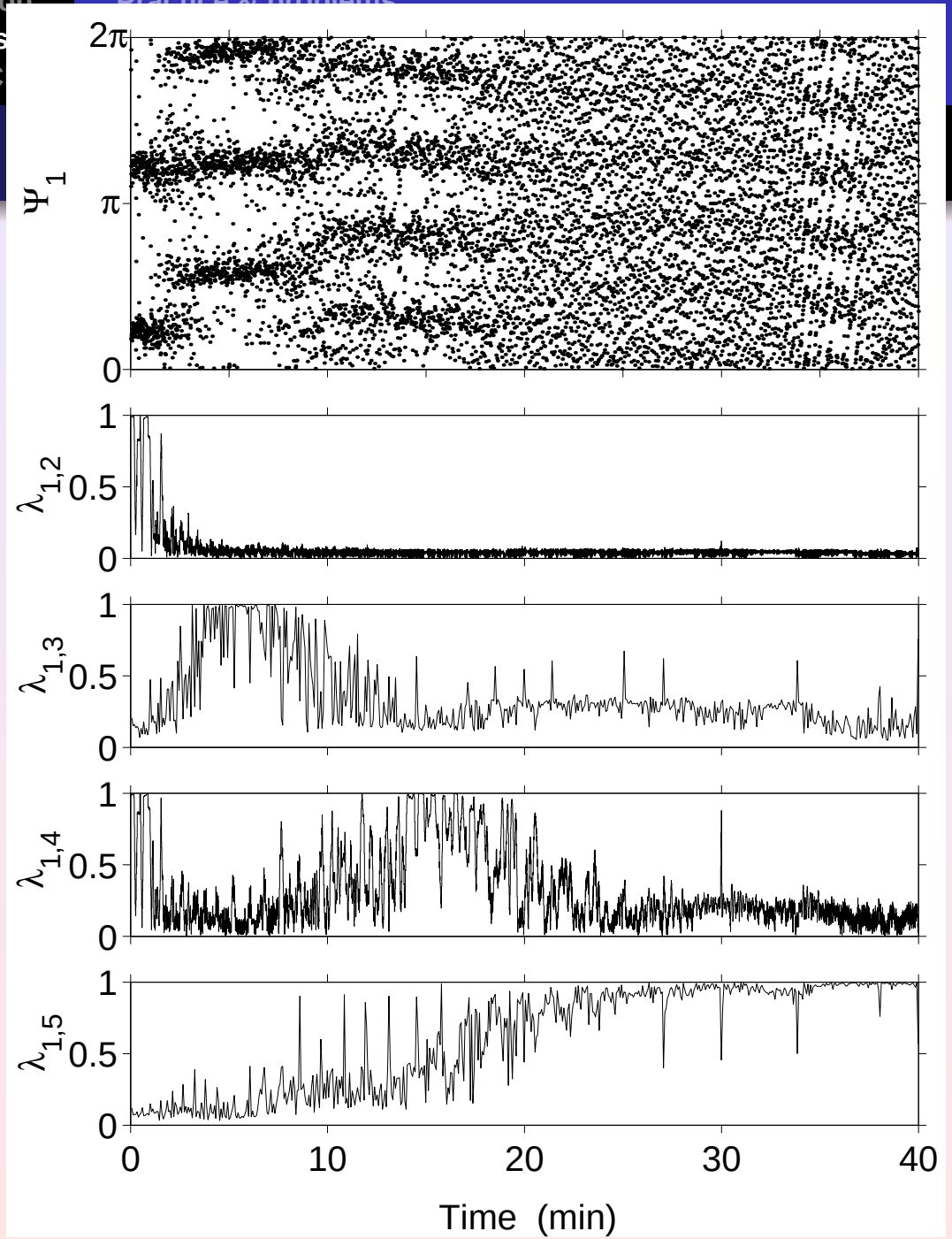
Incidence of awareness in anæsthesia

Author	Date	Sample	Awareness %
Hutchinson	1960	656	1.2
Harris	1971	120	1.6
McKenna	1973	200	1.5
Wilson	1975	490	0.8
Liu *et al*	1990	1000	0.2
Lennmarken & Sandin	2004	1238	0.9

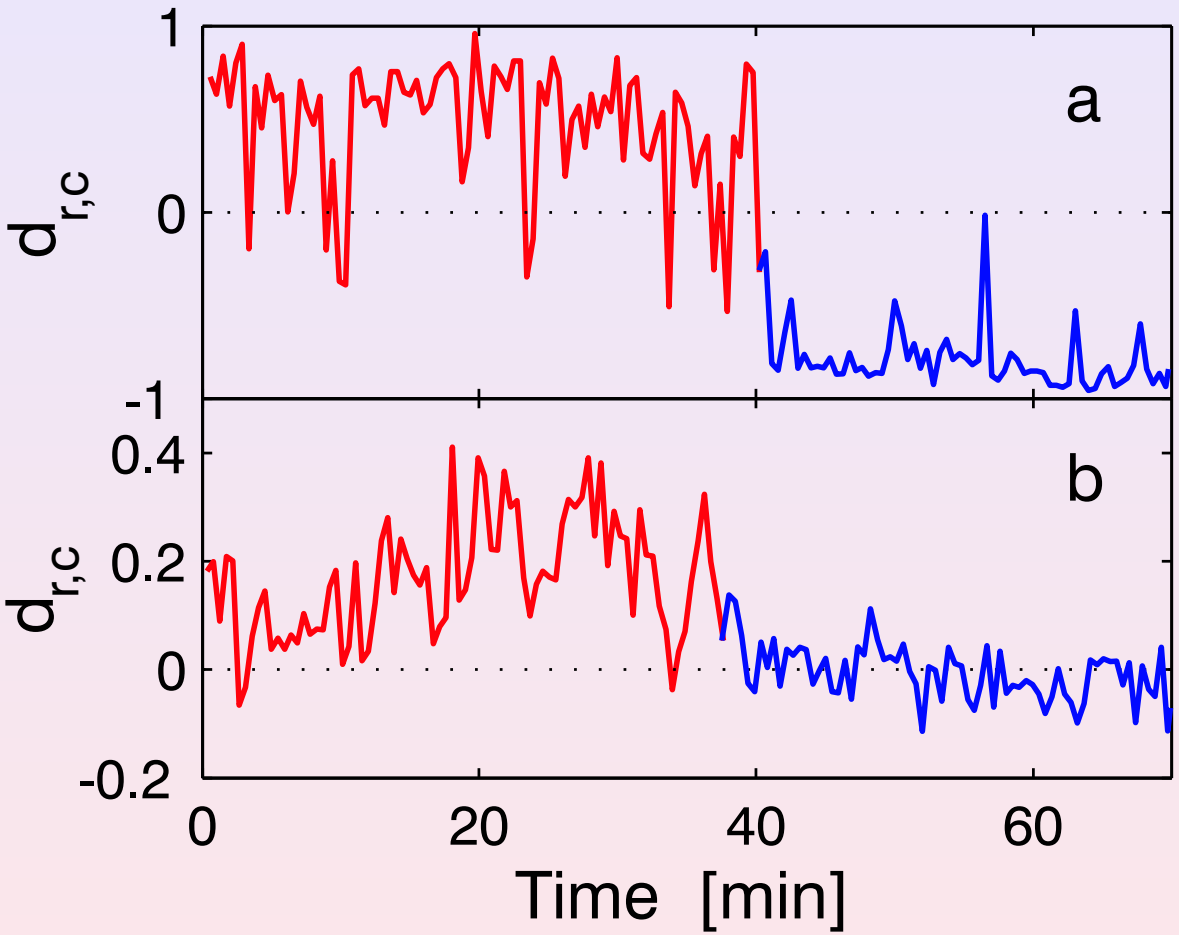
- Too much anæsthetic $\Rightarrow$ bad for patient.
- Too little anæsthetic $\Rightarrow$ awareness.
- So need a reliable measure of depth of anæsthesia.
- Can coupled oscillator picture help?

Rats

- Initially, study rats.
- *a* Administer anæsthetic;
  b Measure;
  c Anæsthesia lasts
  $\sim$100 min.
- Synchronisation effects are much stronger in anæsthesia.
- Starts wearing off after typically 40–50 min.
- Can also calculate direction of the coupling...



Cardio-respiratory directionality in rats



Musizza et al, to be published

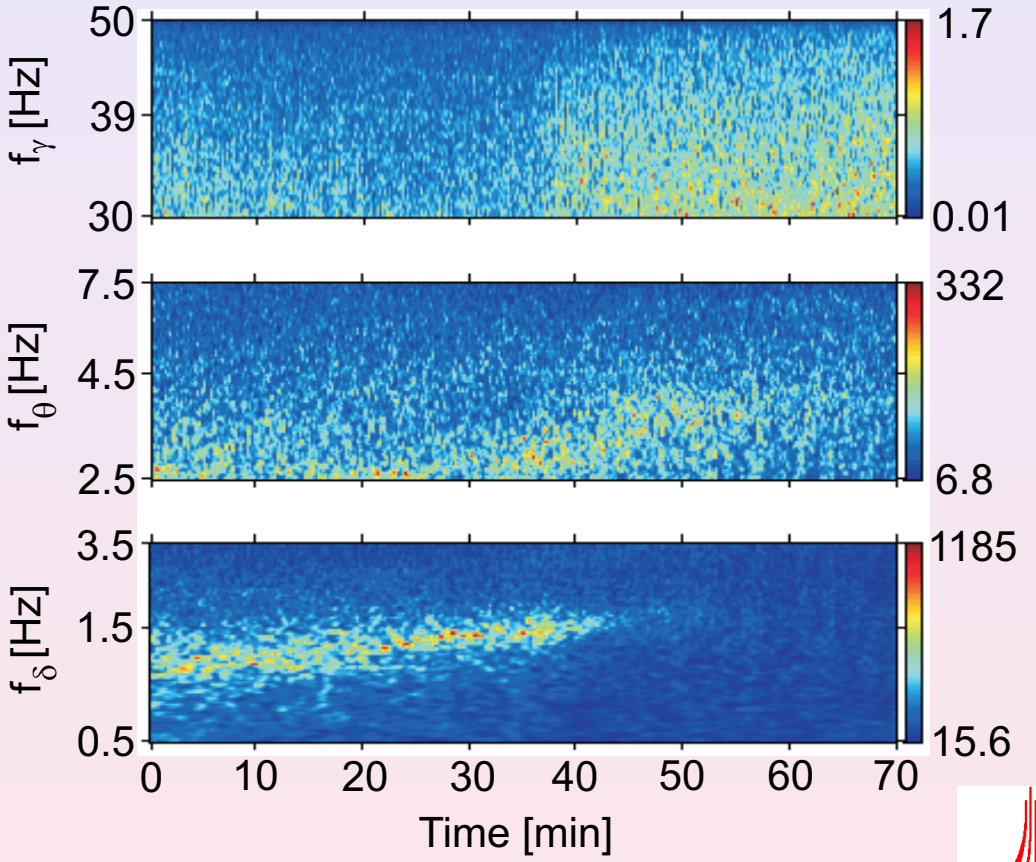
Technique of Rosenblum *et al* *PRE* **65**, 041909 (2002)

Technique of Paluš & Stefanovska *PRE* **67**, 055201 (2003)

NB Deep $\rightarrow$ light anæsthesia transition at $\sim$40 minutes.

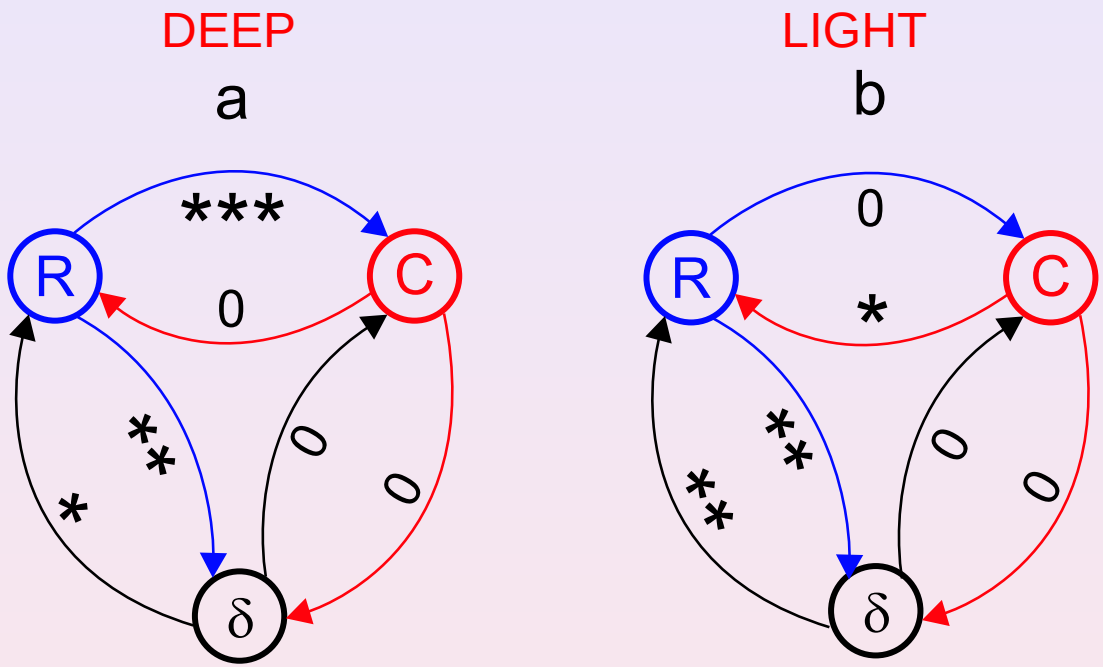
Cardio-respiratory-EEG in rats

- Use wavelet transform to follow frequency evolution of different EEG waves.
- Marked decrease occurs in δ–wave amplitude, at deep-light anæsthesia transition.
- Increase in γ-wave, θ-wave, frequencies.



Cardio-respiratory-δ directionality, in rats

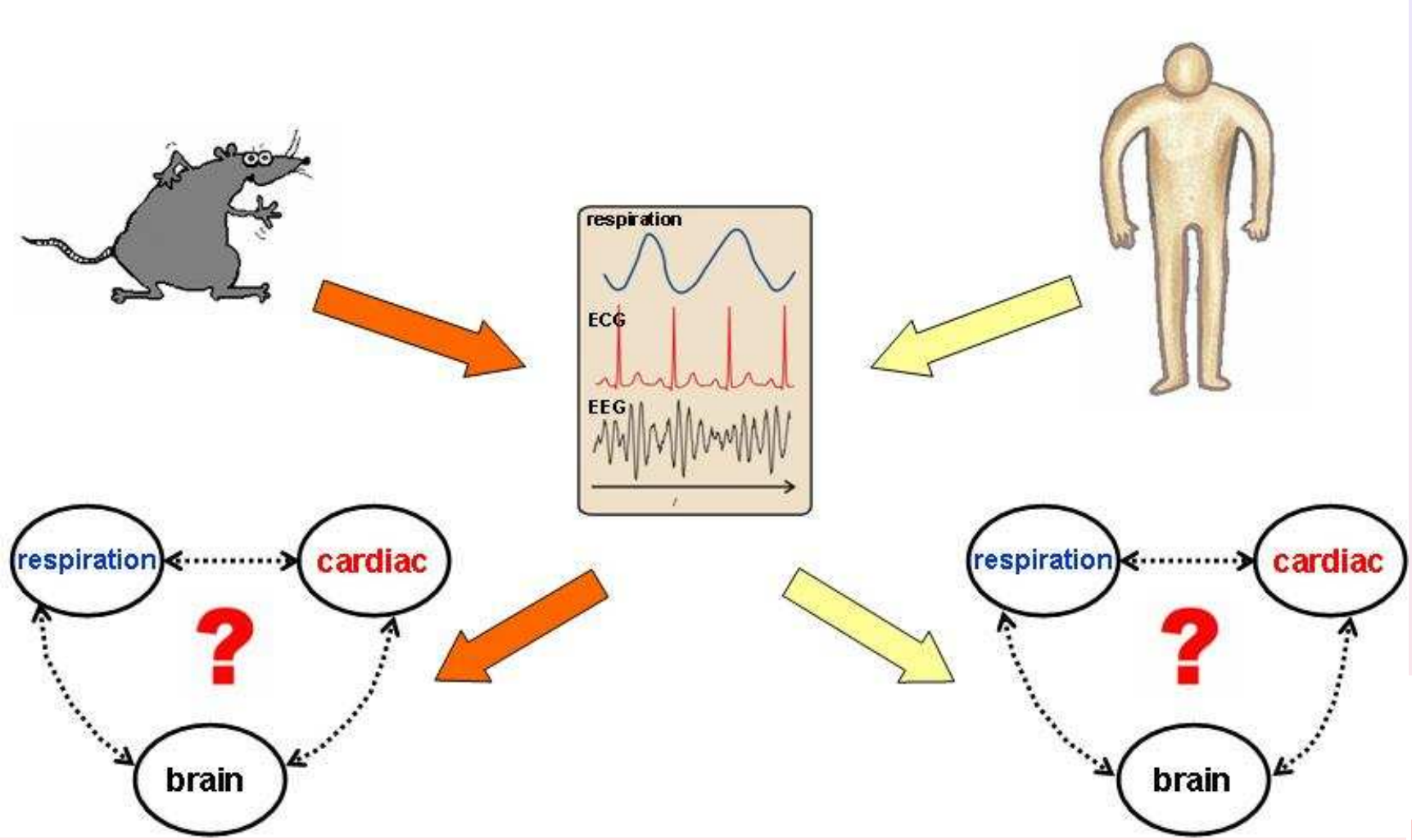
- Definite changes in pattern of interaction at deep→shallow anæsthesia transition.
- Mainly qualitative at present.



(Musizza et al, to be published)

- Current techniques adversely affected by strong noise (phase dynamics), or where the frequency ratio becomes large (information theory).

Are humans like rats?



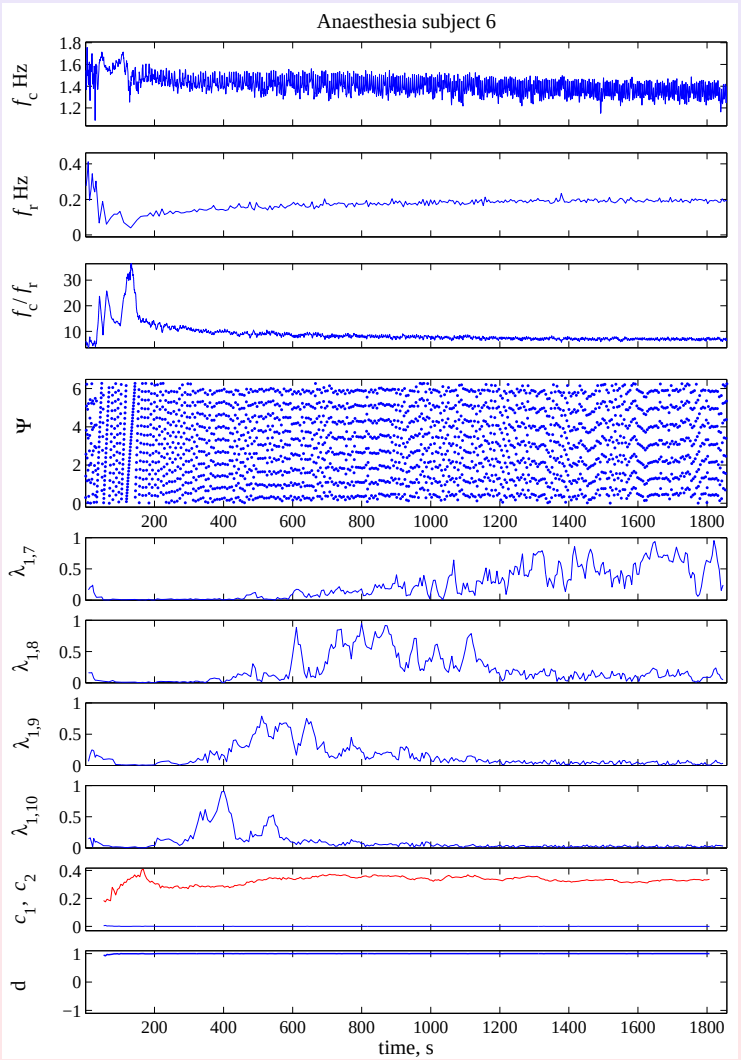
Anæsthetised humans – preliminary study

To see if changes in synchronization phenomena, like those in rats, also occur in humans – with Andy Smith, Mike Entwistle, Bojan Musizza, Andriy Bandrivskyy –

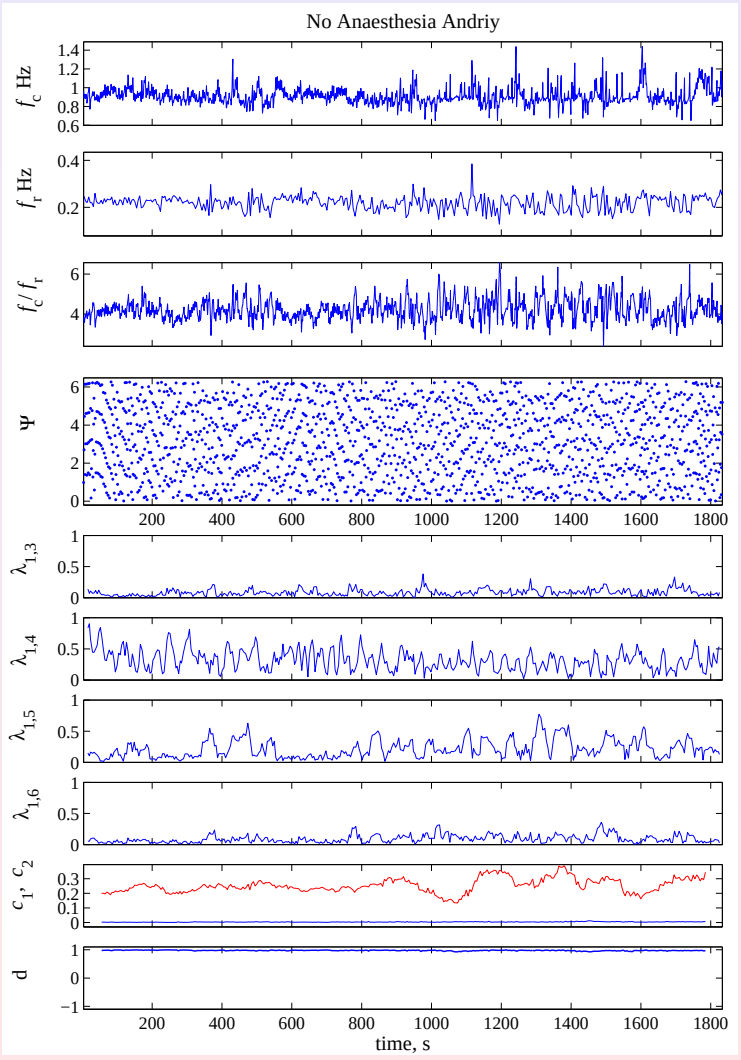
- Study volunteers – healthy males aged 25–40.
- Measure for 30 minutes prior to minor surgery in Royal Lancaster Infirmary.
- Record ECG, respiration, EEG (blood pressure and temperature).
- Look for evidence of cardio-respiratory-cortical synchronization, and information about coupling directions...
- Compare with measurements on wakeful humans.

Anæsthetised v. wakeful human

Anæsthetised



Wakeful



Initial human anæsthesia data

- Humans rather like rats, in that –
  - Cardiorespiratory synchronisation much stronger than in waking state.
  - Respiration drives heart in deep anæsthesia.
- Note (i) have not yet examined the same subject in both anæsthetised and wakeful states, (ii) only steady anæsthesia investigated to date, (iii) have not yet examined transition to light anæsthesia or wakefulness.
- But there is clear potential for basis of new kind of depth-of-anaesthesia monitor...
- Research going forward under BRACCIA, started 1 June 2005.

NEST with 8 teams, broad scientific expertise

Team leader	Institute	Expertise
Stefanovska	Universities of Ljubljana & Lancaster	Nonlinear dynamics
McClintock	Lancaster University	Stochastic dynamics
Smith	Royal Lancaster Infirmary	Clinical anæsthesia
Hasler	Swiss Federal Inst of Tech, Lausanne	Networks
Ribarič	University of Ljubljana	Neurobiology, rats
Raeder	Ulleval Hospital, Oslo	Clinical anæsthesia
Kurths	Potsdam, Inst of Complex Systems	Synchronisation
Paluš	Prague, Inst of Computer Sciences	Information theory

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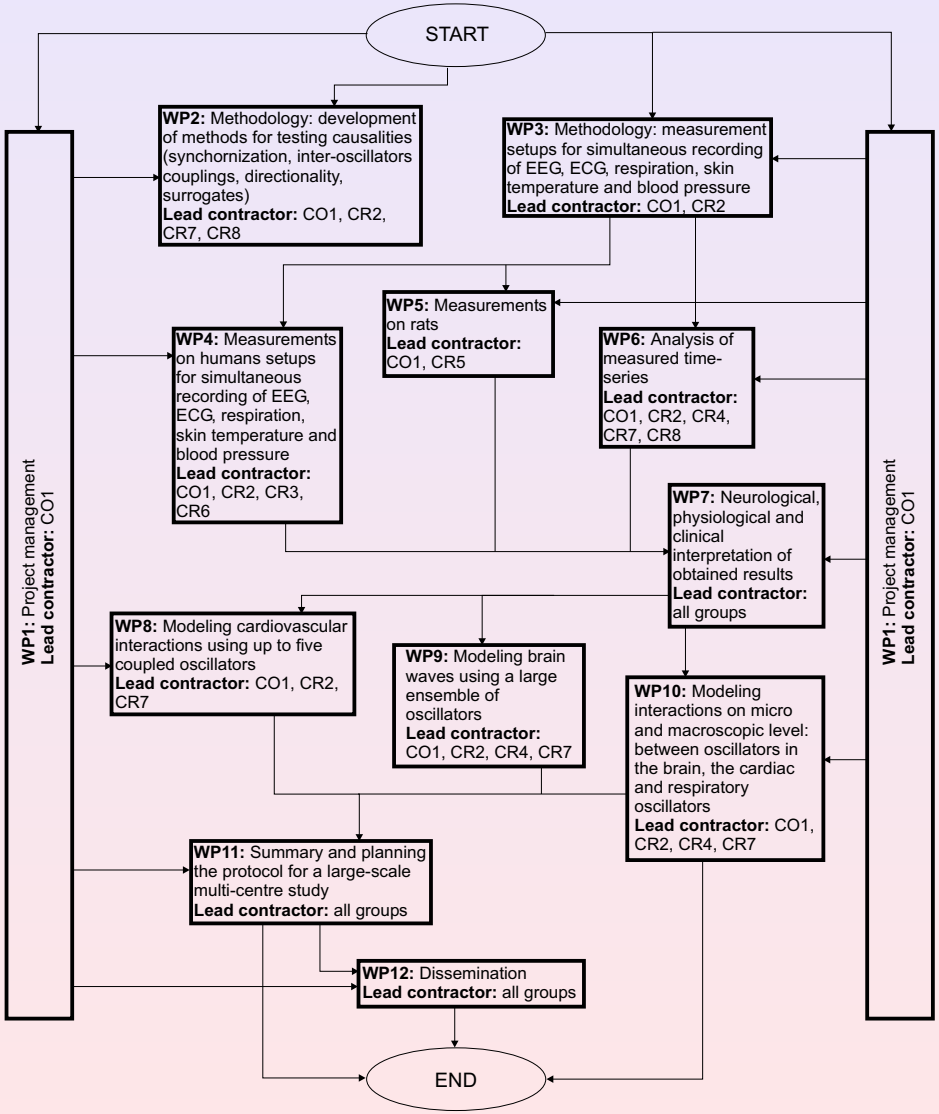
The plan. . .



Acknowledgements & References

Acknowledgements

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Selected references

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