Modelling of epileptic seizures

Internal dynamics and network connectivity structure in a bistable setting

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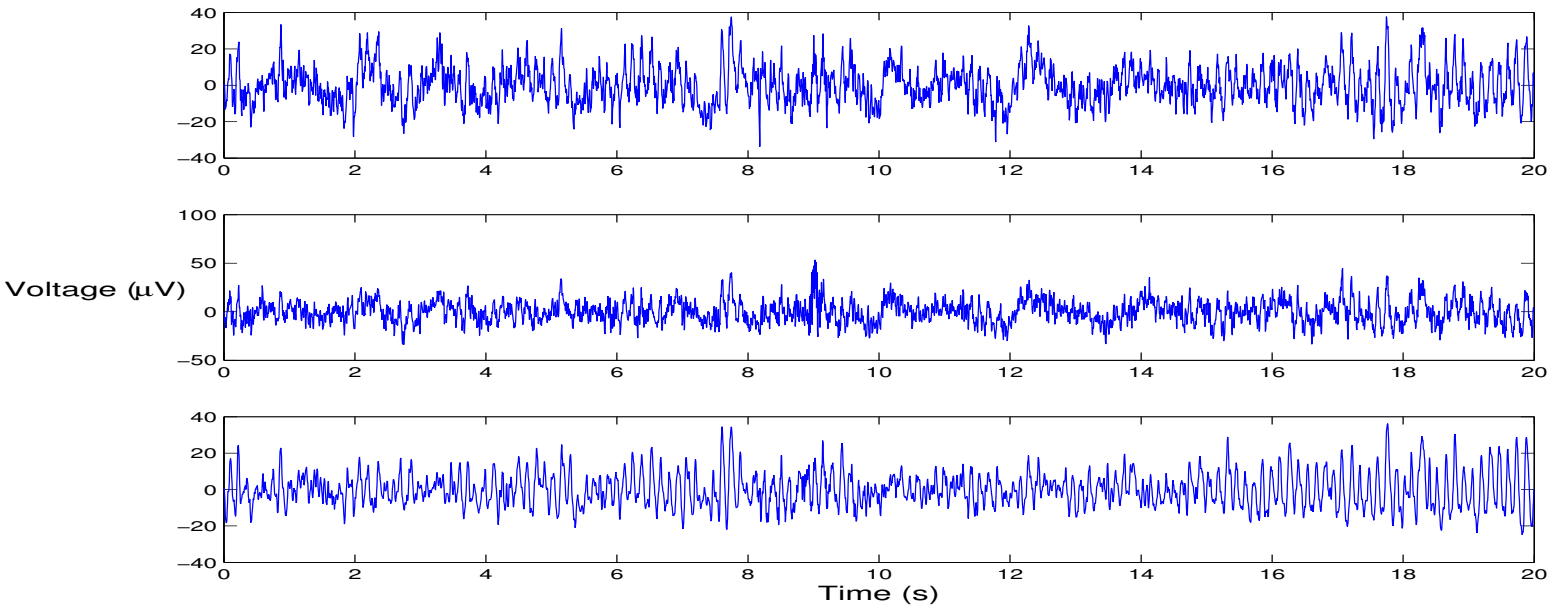
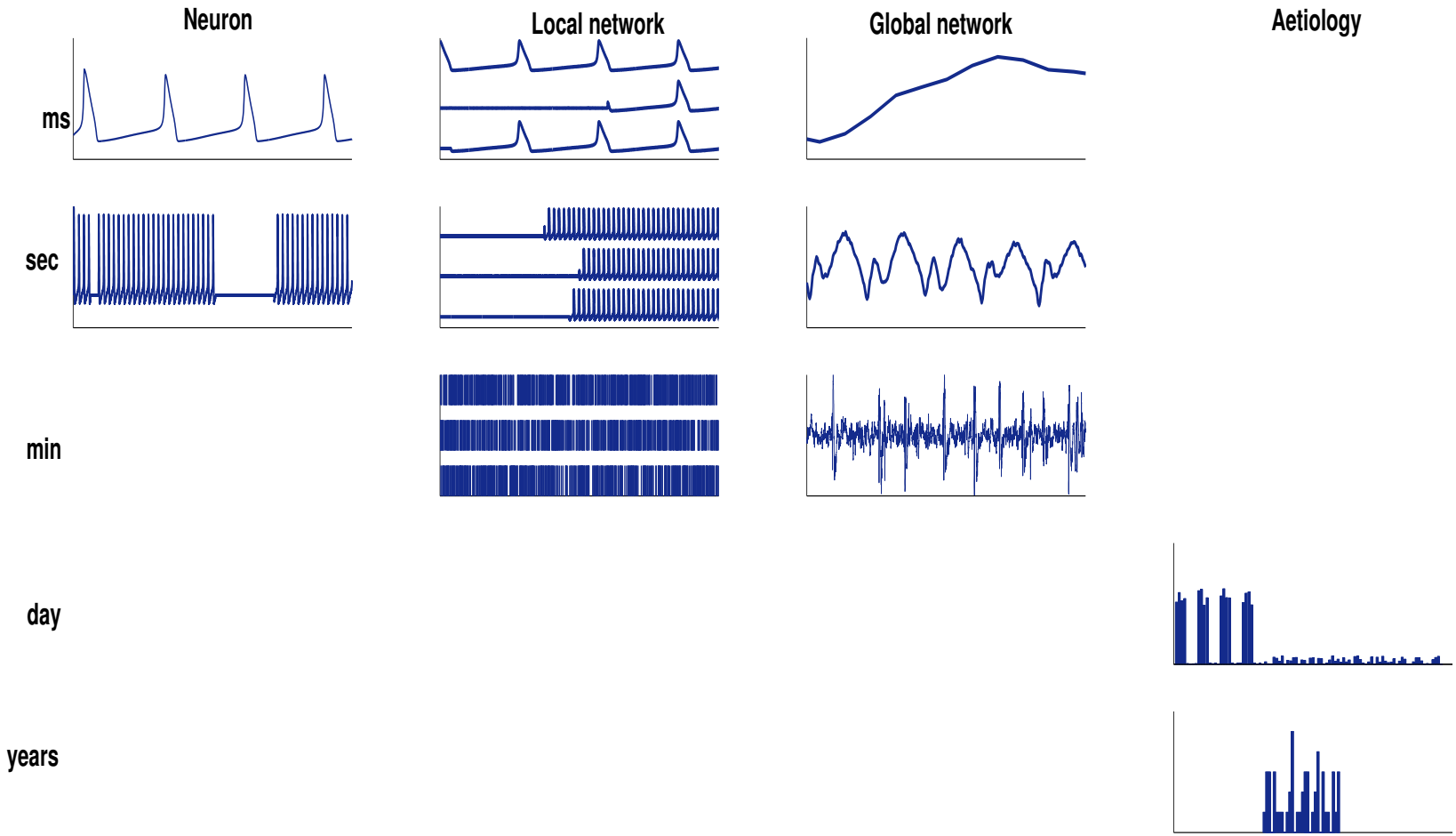


Introduction

- **Epilepsy:** increased predisposition to recurrent seizures
- **Seizure:** abnormal synchronous behaviour in the brain
- **Symptoms**: wide variety (sensory/motor/cognition...)
- **Cause**: pathological region? often unknown...
- **Treatment**: AEDs/surgery...
- No unifying miscroscale mechanism (genetic, synaptic) explaining seizure-generation
- **Interplay between dynamic properties of localised regions (macro-scale) and overall network structure**

Complexity: scales



Overview

IGE-data

- Scalp EEG (King's College, Chowdury & Richardson):
  - 35 people with IGE (19 seizure-free)
  - 42 first-degree relatives
  - 40 healthy controls
- 20 second epochs eyes closed, resting state (inter-ictal)
- Hypothesis: networks derived from EEGs will show abnormal network properties in patients with IGE and an endophenotype in their first-degree relatives
- Directed graphs: phase-locking factor & "beta-weights" (Benjamin, 2012)

Results: comparison amongst groups

Significant differences in alpha-low [6 – 9] Hz:

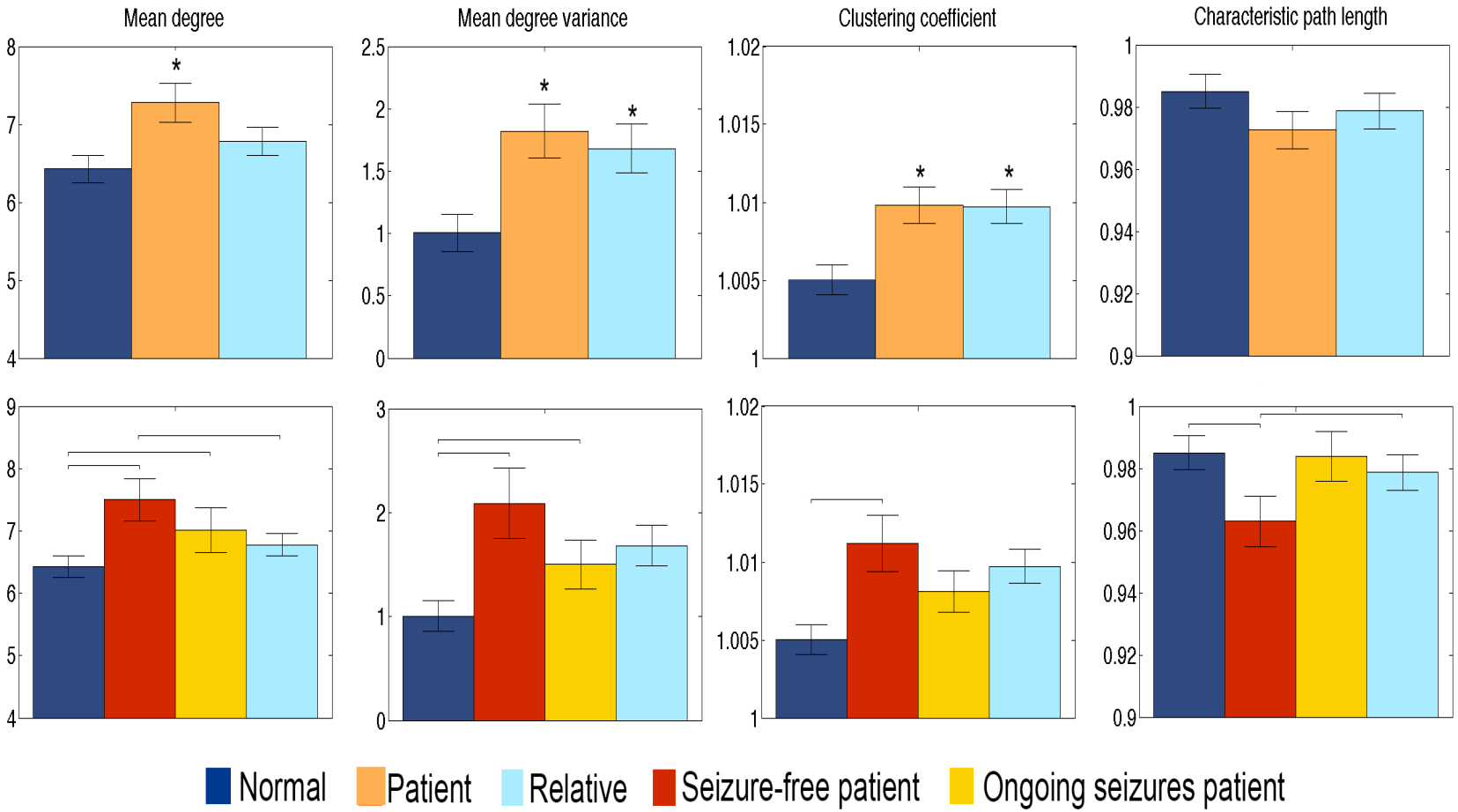


Figure: (Chowdury et al., under review)

Results

- **Evidence of endophenotype:** comparison of brain network properties across controls, patients, and relatives reveals a brain network endophenotype characterised by both unusually over-connected brain regions and under-connected brain regions (Chowdury et al, under review).
- Is this the strongest way to analyse the data?
- Limited by the number of subjects?
- Develop models to describe/predict/understand the data

Models of seizure onset

Seizures: mediated by a disruption to the dynamic balance between excitation and inhibition leading to hyperexcitable networks (McCormick, 2001). Transitions from healthy state to unhealthy epileptic state:

- Bifurcation: parameter-driven transition (Destexhe, 1998)
- Multi-stability: switching between coexisting stable states (Kalitzin, 2010)
- Intermittency: intrinsic unstable dynamics causing autonomous transitions (Goodfellow, 2013)
- Crucial question: biological detail/phenomenology (network/mass/field/...)

Bistable model

Transitions from healthy state to unhealthy epileptic state:

- Brain network ictogenicity (BNI): enduring interictal propensity for a brain network to generate seizures
- "Healthy" people (can) have seizures as well (though not epilepsy)
- Allow a paradigm for growing out of epilepsy (IGE)
- Successful treatment/surgery alters BNI
- Phenomenological approach based on bistability:
  - Non-seizure state: stable fixed point (noisy)
  - Seizure state: oscillatory, synchronized activity
- Reduction of a detailed network approach (Suffczynski, 2004)

Benjamin model

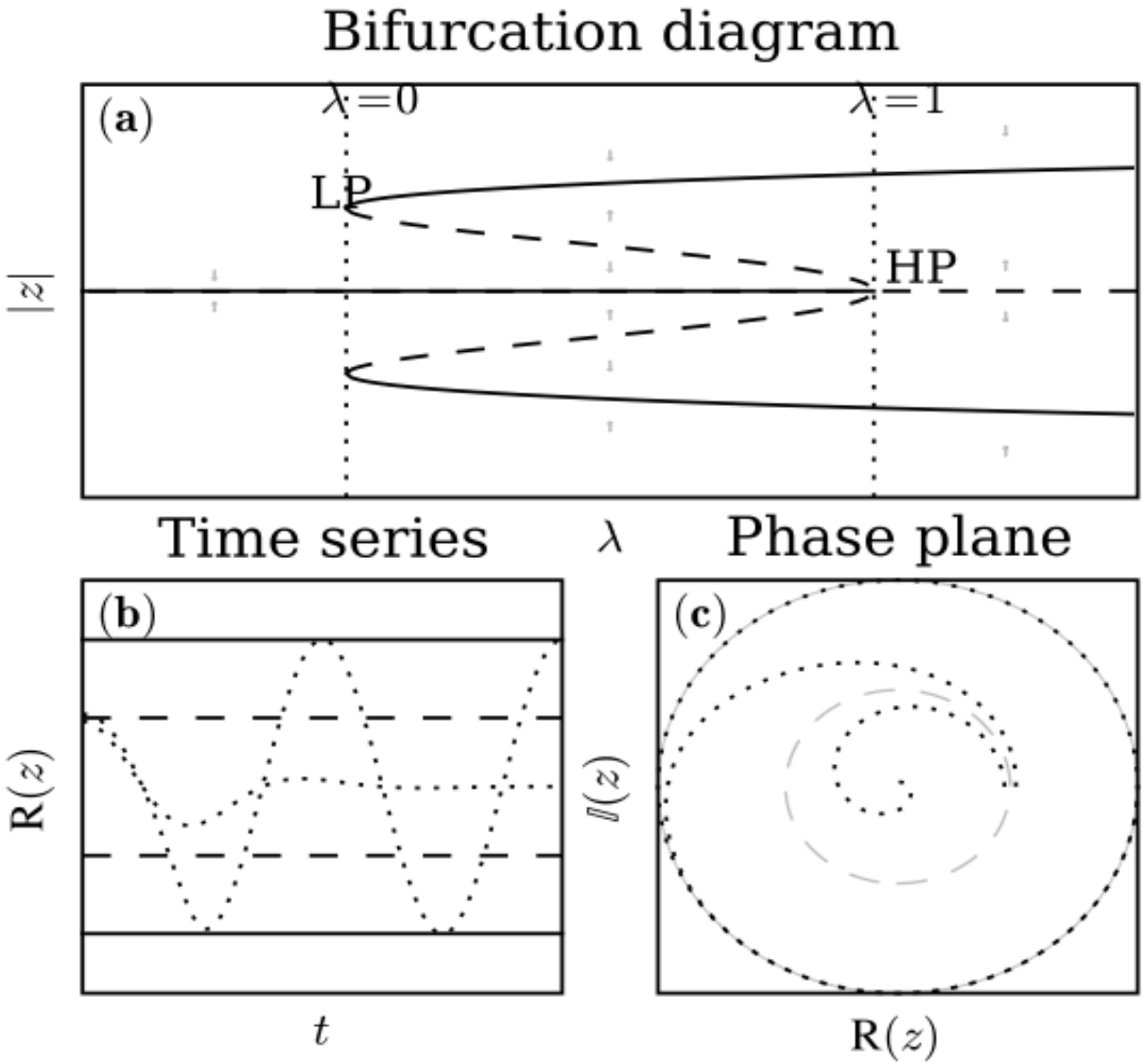
General idea: describe the onset of a seizure mathematically as transitioning from a stable fixed point to a stable limit cycle in a bistable regime caused by noise.

Complex stochastic differential equation describing a generalised Hopf bifurcation:

$$\frac{dz}{dt} = (\lambda + i\omega)z + \sigma z\,|z|^2 - \kappa z\,|z|^4 + \alpha\,(\eta_1(t) + i\eta_2(t)) \qquad (1)$$

- λ: bifurcation parameter
- $\sigma, \kappa > 0$: dynamical parameters
- α: noise amplitude (Gaussian white noise)
- ω: frequency of oscillations

Bistable regime: generalized Hopf-bifurcation



Network structure & internal dynamics

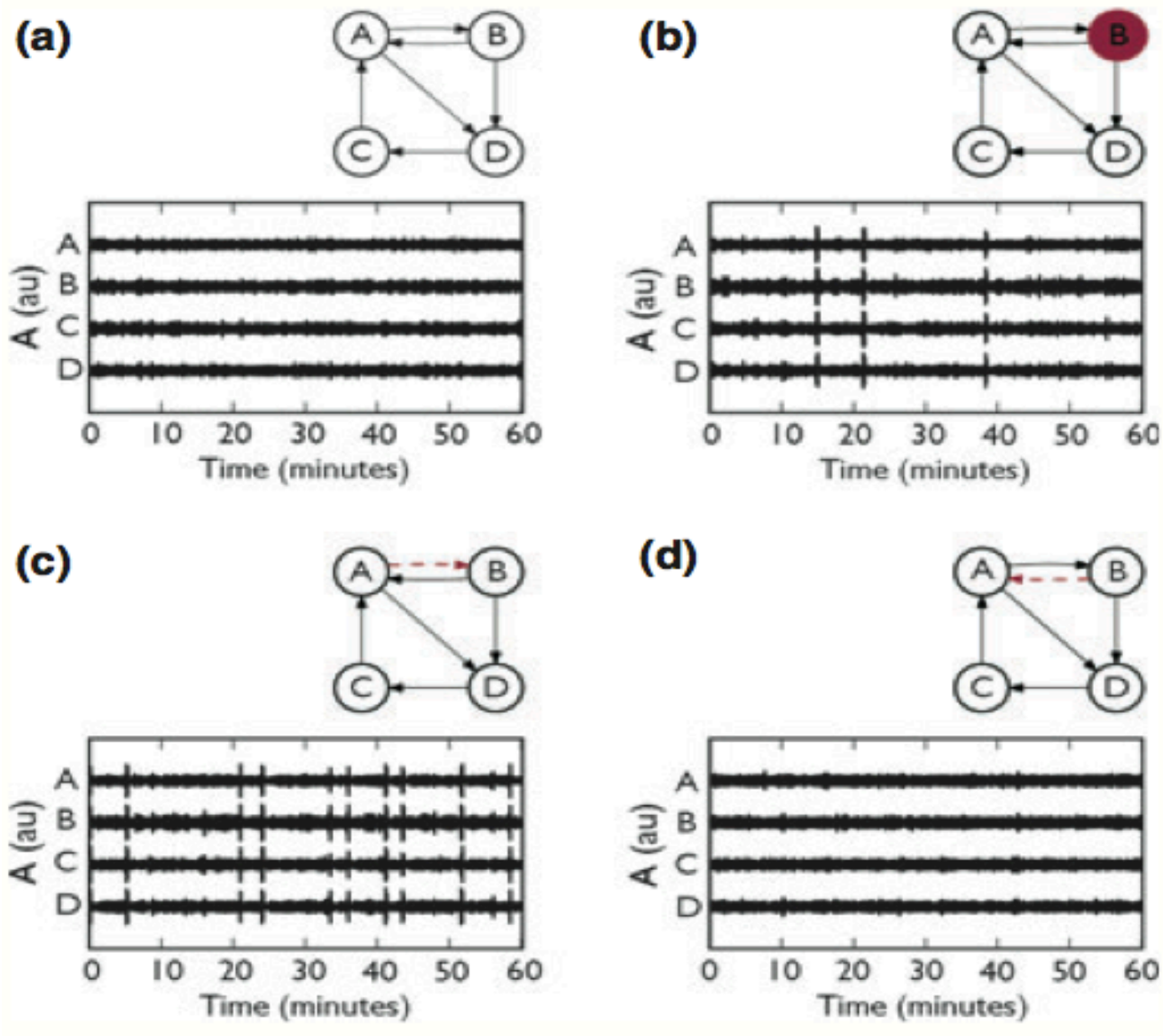


Figure: (Terry, 2012)

Current questions: network structure & dynamics

- Edge-removal/escape-times/seizure-rate
- Double-well potential; unequal depth?
- Coupling (type/strength)
- Loss of stability
- Relation between network-parameters and behavior (MacKay, Neiman 1995)
- (Jirsa,2014); invariant properties

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