Kinds of Mechanistic Evidence

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Introduction

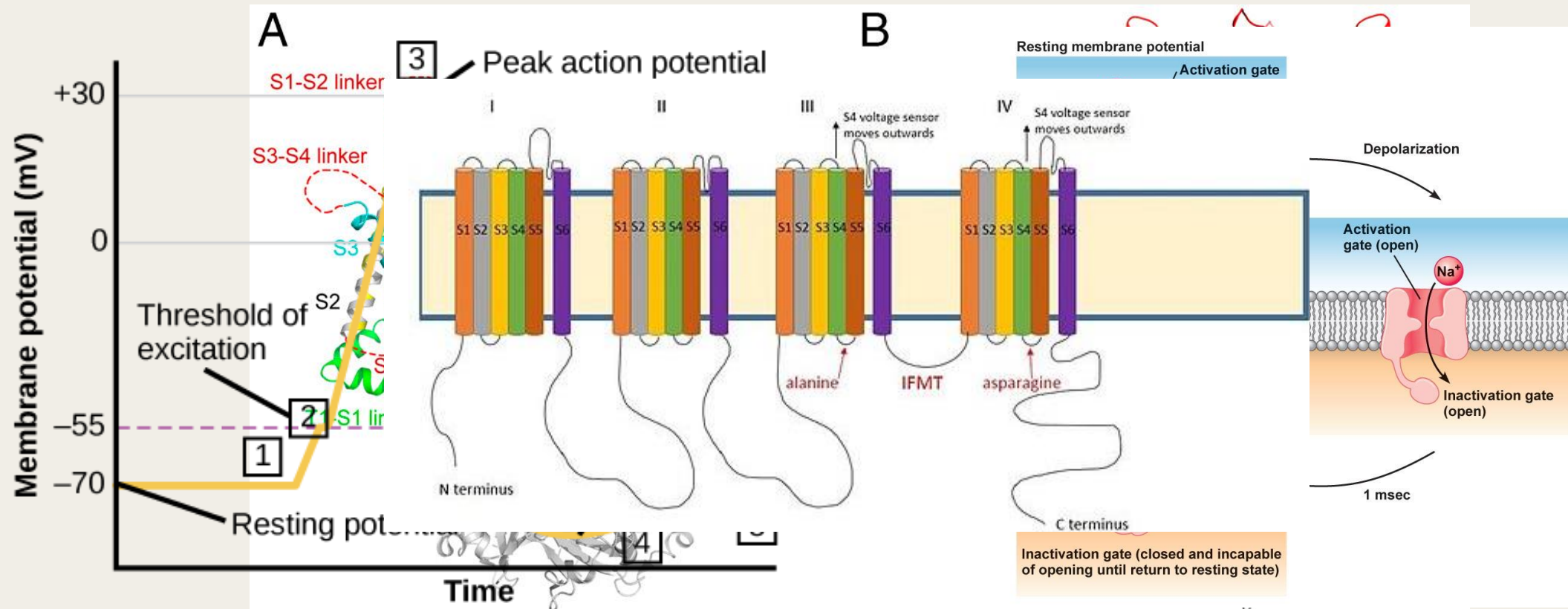Why this approach to mechanisms and medicine

Space of Possible Mechanisms, and Evidence

My Conception of Evidence

Kinds of Mechanistic Evidence

Implications of Analysis

The Discovery of The Action Potential

Chen *et al.* 2010

Mechanisms and Medicine

Correctness and Completeness

Evidence of Mechanism; Complexity of mechanism (Bechtel and Abrahamsen 2005 p.433

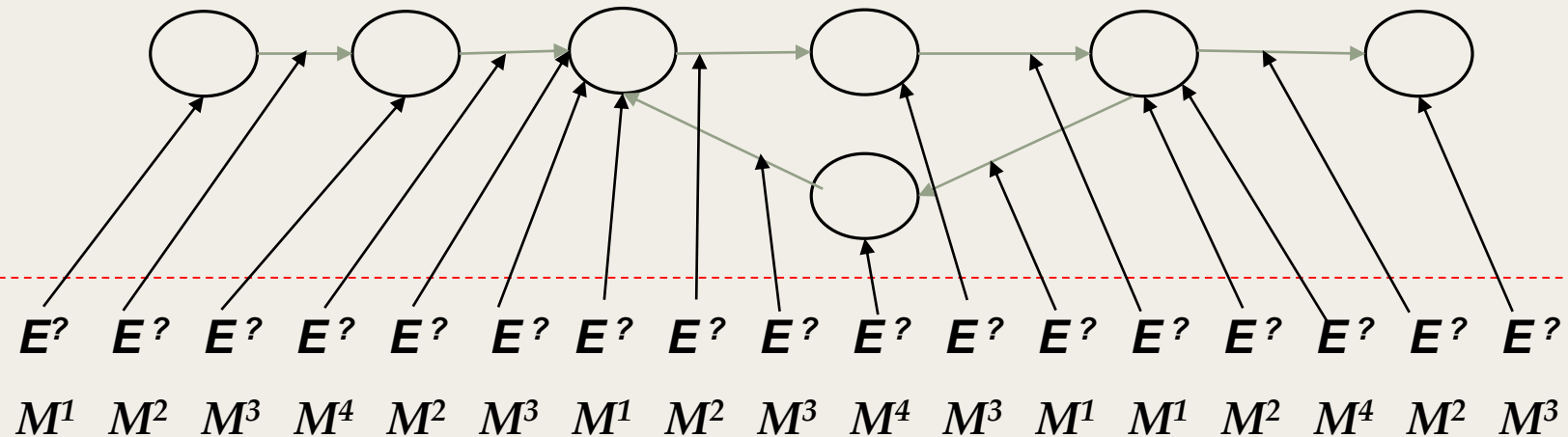Howick 2011; Clarke *et al.* 2014), and Heterogeneity of method (Baetu 2015c p.16)

Mechanisms *as* evidence: How to assess a whole mechanism *as* evidence

Mechanisms and Medicine

Mechanisms as Evidence; How to assess?

Clinical Decision

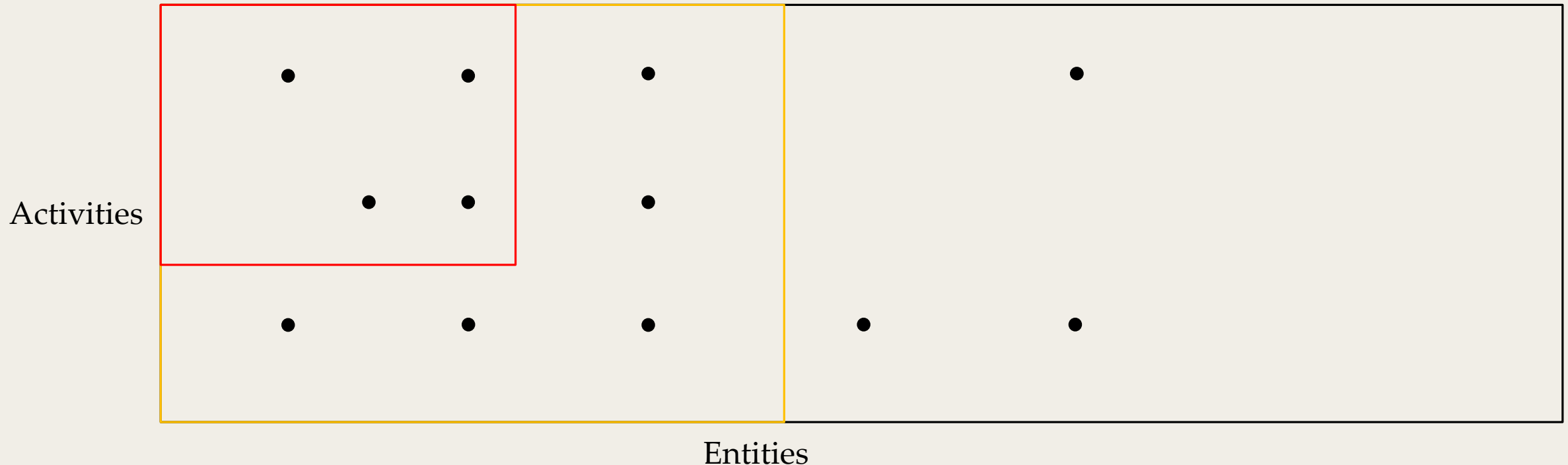*Evidence of Mechanism; Complexity, and Heterogeneity of Method*

E? E? E? E? E? E? E? E? E? E? E? E? E? E? E? E? E?

M^1 M^2 M^3 M^4 M^2 M^3 M^1 M^2 M^3 M^4 M^3 M^1 M^1 M^2 M^4 M^2 M^3

Space of Possible Mechanisms (SOPM)

Craver and Darden's (2013) version.

Complexity of mechanism results in needing reasoning strategies; many such strategies searching through SOPM.

SOPM and Evidence

Differentiation by:

SOPM – Questions about constraints (Craver and Darden 2013).

Mechanism Literature – Method; Object; Relation to Explanation.
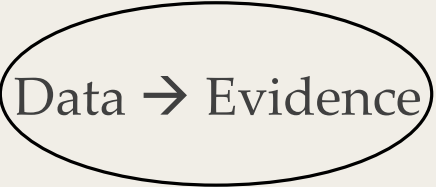
Evidence as one-size-fits-all concept.

Extend the account by looking at evidence *as* evidence.

Evidence

Bogen and Woodward 1988:

Experiment → Observation (Detection) → Data → Evidence → Explanation

How does data *serve* as evidence?

Evidence

Functionalist conception (Brown 2015)– whatever the function is of evidence, defines it.

Following Bird (2010; 2016): evidence are propositions that can be inferred from to Knowledge (K).

Evidence are propositions about data that are inferred from to K. This is how data *serves* as evidence.
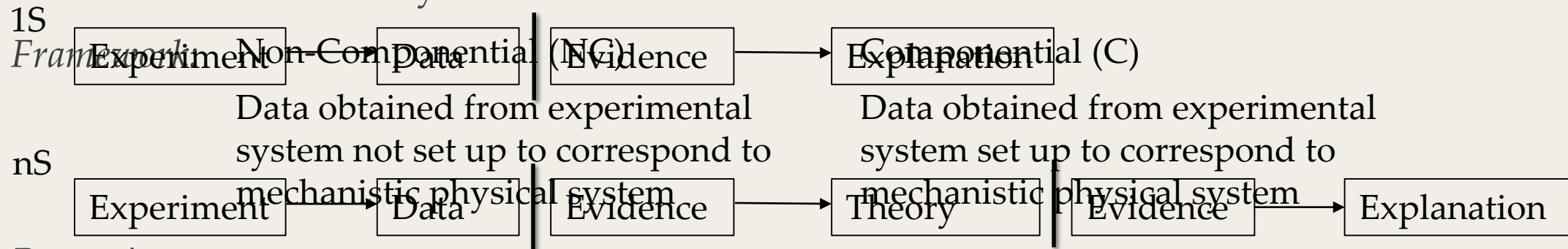
The role, then, is to be inferred from to knowledge.

The constitution of evidence is *how* this role is carried out. This is epistemic; no change in physical state.

Properties of *how* evidence is inferred from to knowledge are the properties of evidence *as* evidence.

Properties of Evidence

In mechanistic discovery the main are:

1S

Framework:

Non-Componential (NC) → Componential (C)

| Experiment | → | Data | | Evidence | → | Explanation |

Data obtained from experimental system not set up to correspond to mechanistic physical system

Data obtained from experimental system set up to correspond to mechanistic physical system

nS

| Experiment | → | Data | → | Evidence | → | Theory | → | Evidence | → | Explanation |

Reasoning:

Multiple-Step (nS)

1-Step (1S)

Data from experiment does not serve as evidence. Theory/Explanation is the evidence.

Data from experiment serves as evidence: 1 inferential step to serve

Strength of Justification (Use):

For SOPM this by strength of constraints resulting in different mechanisms schemas

| Potential | Possible | Weakly-Plausible | Strongly-Plausible | Actual |

Kinds of Mechanistic Evidence

Strength/ Constraints	Framework: NC Reasoning: nS	Framework: C Reasoning: 1S
Potential	Phenomenal Characterisation Evidence (PCE)	
Possible	Theoretical Evidence (TE)	
Weakly-Plausible		Observational Evidence 1 (OE1)
Strongly-Plausible		Observational Evidence 2 (OE2)
Actual		Simulation Evidence (SE)

Some Kinds

TE | Experiment → Data → Evidence → Theory | Evidence → Explanation
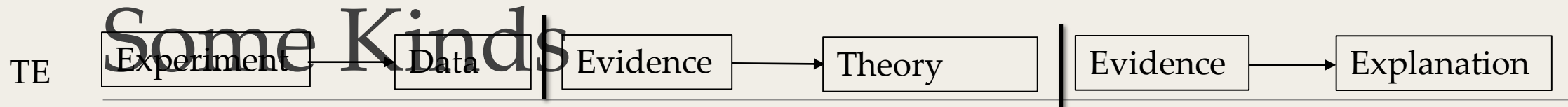
THEORETICAL EVIDENCE (TE)

Non-Componential

n-Step Inference

Limits possible components

"one typically begins with a prior knowledge about the kinds of entities and activities that might be involved in such phenomena in a given type of organism of system" (Craver and Darden 2013 p.67)

But, as the propositions are inferred from (or justifies belief) to K, it is not Background Knowledge.

TE IN AP

"[T]*hermodynamic dilemma*", posed by

"*[the] energetic cost of placing four positive gating charges of the S4 segment in a transmembrane position…and [the] outward movement of these gating charges through a hydrophobic environment [that] would be energetically prohibitive*" (Catterall 2010 p.919)

Physical theory used to infer from to knowledge.

Some Kinds

| Experiment | → | Data | → | Evidence | → | Explanation |

Evidence → Explanation
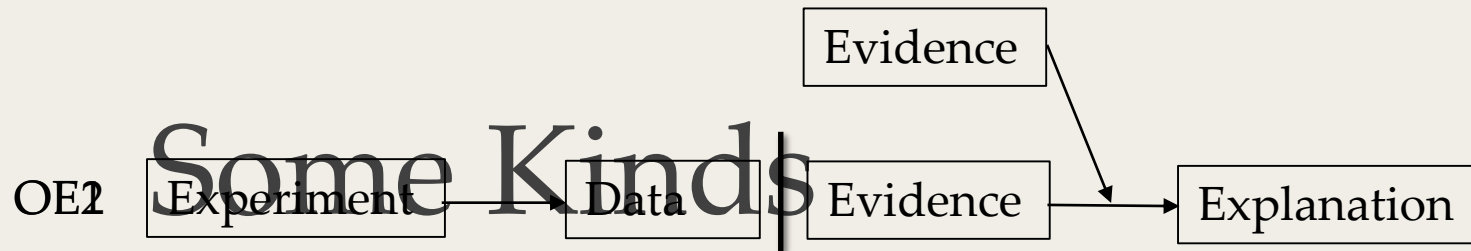
OE

Componential

1-Step Inference

But, can be subdivided:

OE1: Other evidence needed to infer to K

Irrespective of quality of method, if evidence base stops here then can only be weakly-plausible

OE2: Seen (detected) without other justifying inference – strongly plausible

OE1 IN AP

Mutagenic studies used in search for S4 mechanism (Armstrong and Hille 1998). Knocking out certain proteins stopped action – using TE from biochemistry can infer to certain action.

Irrespective of how good the methods are that produce this evidence, the margin for error in the inferential process is too high to be strongly plausible.

OE2 (e.g. X-Ray Crystallography) does not need extra evidence.

Implications

Again, assessing by evidence, not methodology.

When assessing quality of evidence of mechanism, looking at methodology can work. When putting mechanism together this becomes more difficult. Must look at errors of inference when making an explanation, rather than errors in methodology.

When an explanation is itself used as evidence, this will be non-observational evidence. First step is identifying this as evidence, and the properties it has *as* evidence. Assessment of the evidence can hopefully be built off of it.

Conclusion

Extended SOPM to included kinds of evidence, differentiated by properties of the evidence itself.

Properties of evidence are those which allow data to serve as evidence by by inferring from propositions about the data to knowledge.

This also extends what counts as evidence to the non-observational.

5 Kinds of Evidence; including those which would ordinarily be counted as Background Knowledge.

Forms a basis to assess evidence of mechanism, and mechanism as evidence; both of which will rely on inference and inferential evidence

THANK YOU FOR LISTENING

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