3 models: Mechanisms, disease-entities and –omics

Maël Lemoine
Université de Tours
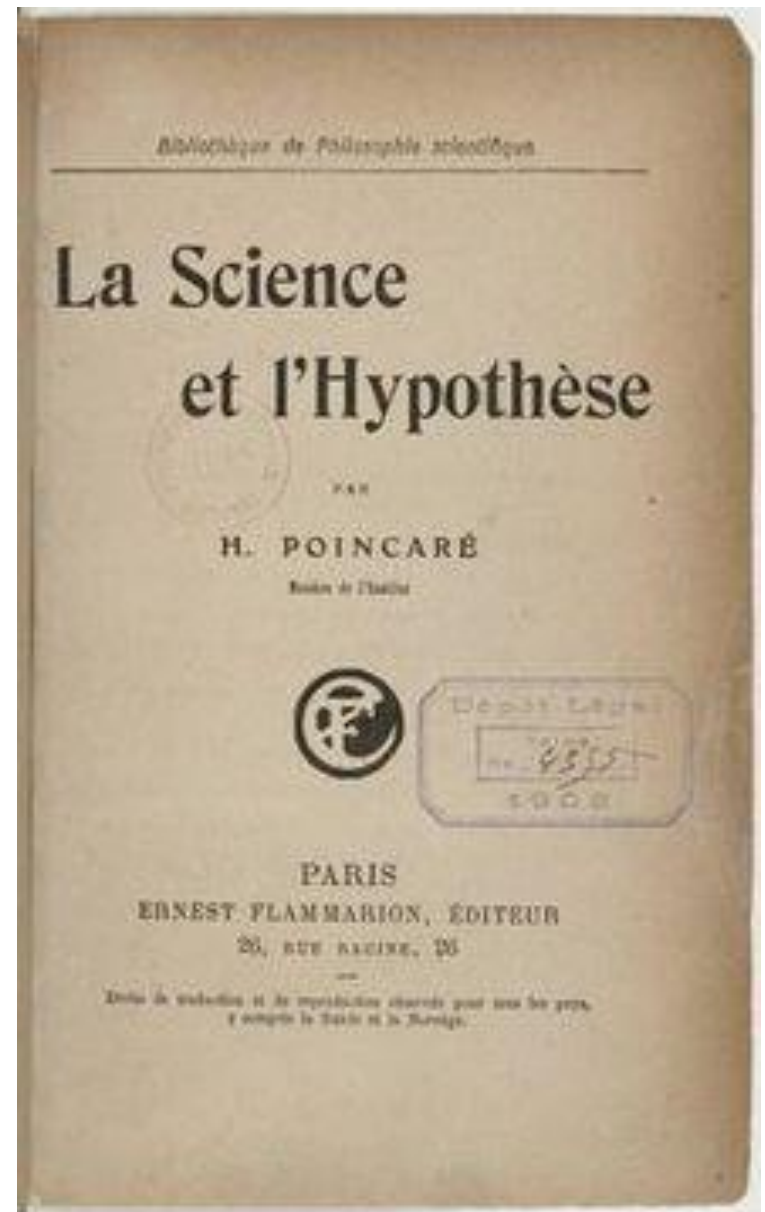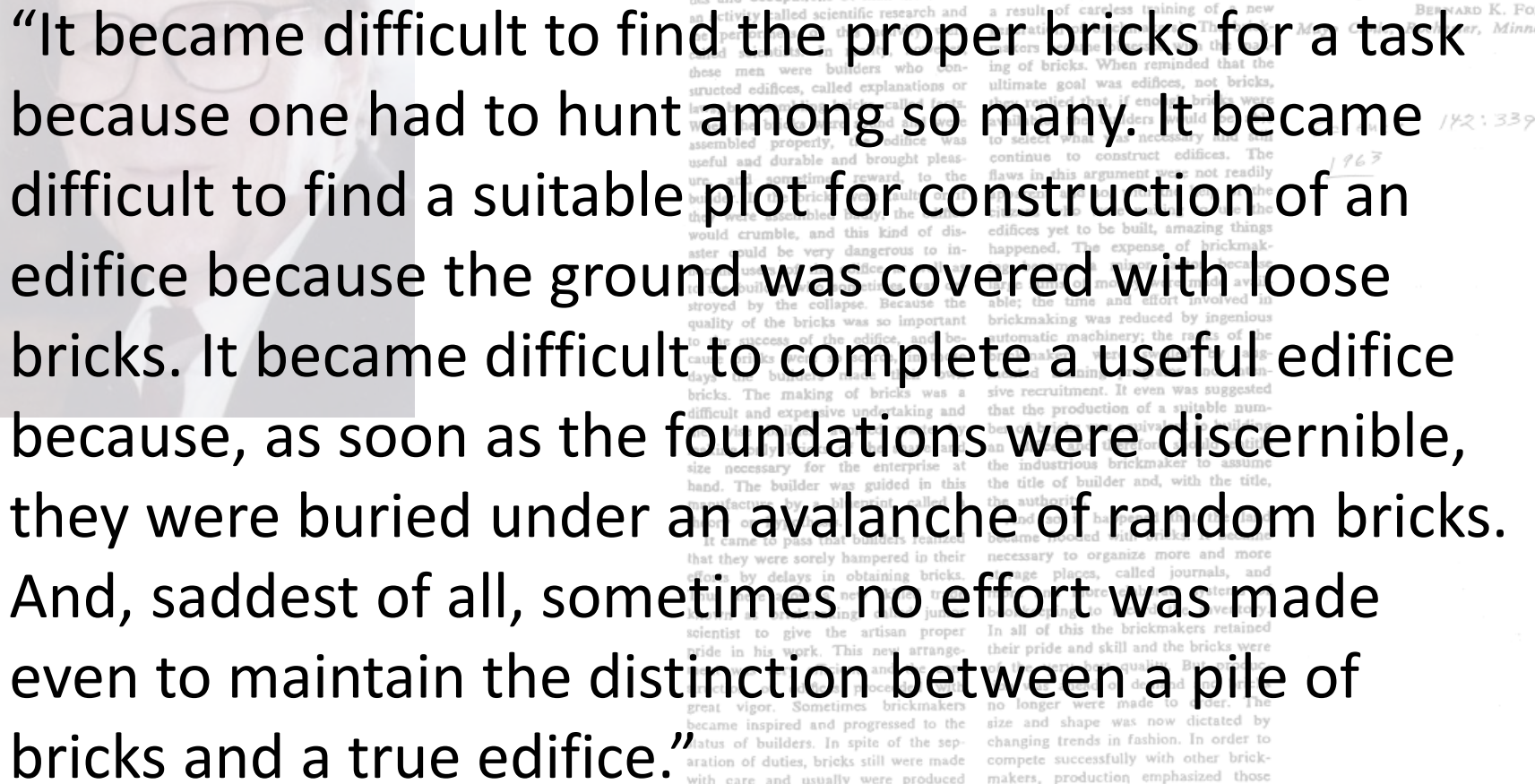
Brendan Clarke
UCL

lemoine@univ-tours.fr

b.clarke@ucl.ac.uk

Science is built of facts the way a house is built of bricks: but an accumulation of facts is no more science than a pile of bricks is a house

"It became difficult to find the proper bricks for a task because one had to hunt among so many. It became difficult to find a suitable plot for construction of an edifice because the ground was covered with loose bricks. It became difficult to complete a useful edifice because, as soon as the foundations were discernible, they were buried under an avalanche of random bricks. And, saddest of all, sometimes no effort was made even to maintain the distinction between a pile of bricks and a true edifice."

(Forscher 1963)

Introduction: research question

Bricks in medicine are zillions of pieces of knowledge about things, processes, properties.

They must be organised (selection) to be tractable (explanation, prediction, therapeutic action).

How have practitioners (doctors and medical researchers) organised their knowledge?

- Some say they are organised into practices (Fleck???), models (Schaffner 1986, 1993), theories (review in Lemoine 2014).

Mechanistic motive

The obvious answer is: it is organised in mechanisms (of X, Y, Z)

Yet so many things count as mechanisms that the mechanisms project (as applied to medicine) risks vacuity (diabetes diabetizes is a mechanism)

Besides, in medicine at least, nature is a gigantic mechanism of everything in nature.

And there are inference styles not involving mechanisms in medicine, which should be clearly distinguished.

Introduction: some aims

- To give a positive characterisation of ways of modelling medical knowledge
  - Including some comparative and functional work
- We want to explore and strengthen links to existing scholarship (both philosophical and medical)

- Not about the nature of disease
- Not about "the medical model"

1. Mechanisms

A description of a disease mechanism is a description of the organisation of entities and activities that collectively produce a disease. This must include a description of the pathway linking aetiological factors to symptoms via those entities and activities that describe how these aetiological factors bring about some specified pathology, and in turn how that pathology brings about symptoms.

1a. Mechanisms conference

Fuller: abstractness, incompleteness,

Illari: to avoid vacuity, define which explanations are not mechanistic (from Dupré)

Straif: policy functions of mechanisms

Aronson: mechanisms from/for

Rocca: the airbag example

2. The disease-entity model

The *disease-entity model*: a conceptual model of reasoning about disease, the causes of disease, and the relationship between diseases and symptoms (without worrying too much about causation)
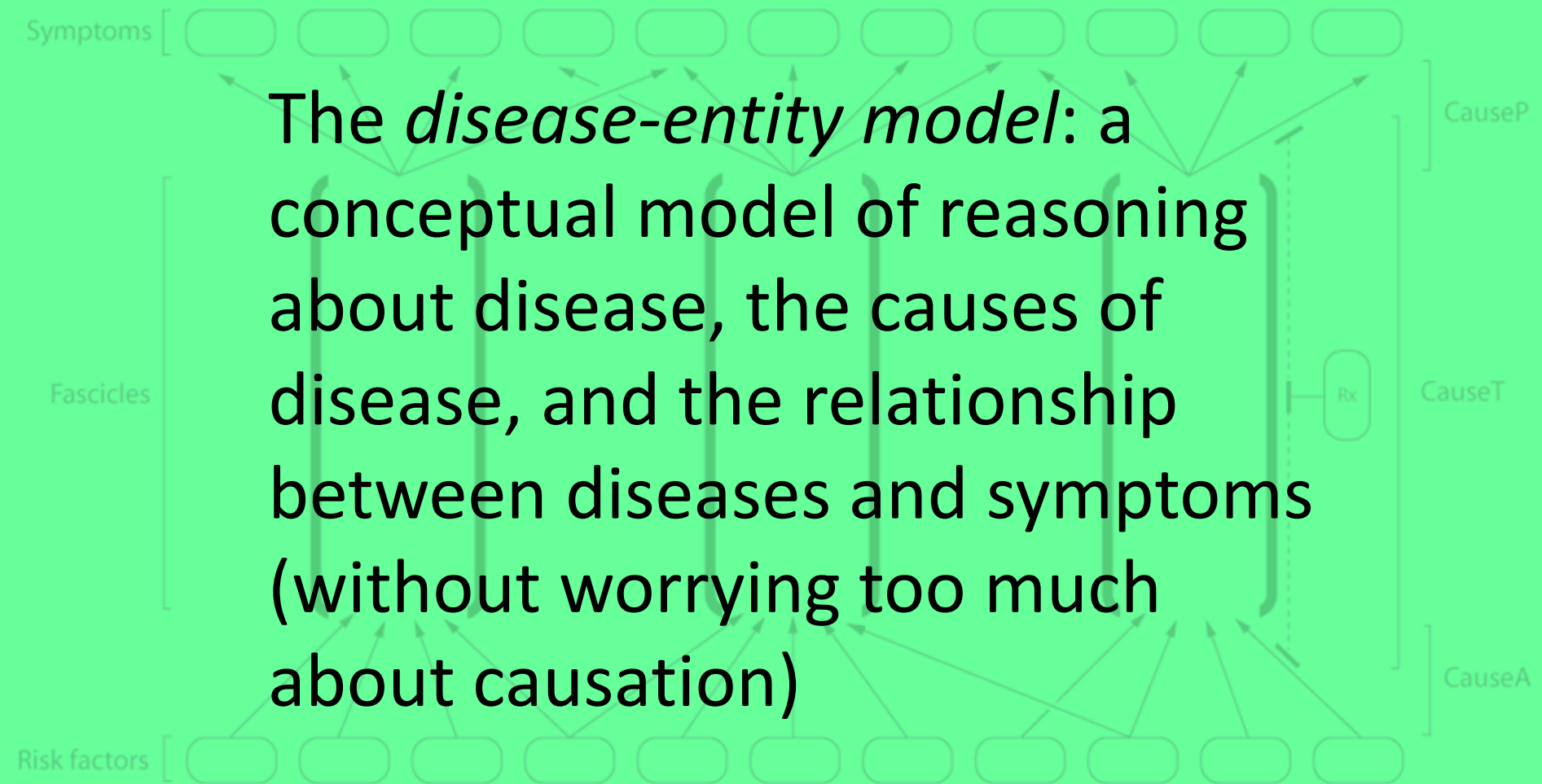
Inferences about disease without good causal knowledge

Inappropriate immune system activation in the eye, leading to protein deposition in anterior chamber of the eye (Flare, cells, keratitic precipitates)

Risk factors: HLA-B27 status
Mechanism: ?? (although ??molecular mimicry)

Treatment: steroid eye-drops, preventing the development of inflammation

A hypopyon in HLA-B27 uveitis. Half of all cases of acute anterior uveitis are HLA-B27-positive.

2a. Three distinct multifactorial causal narratives

Folk-causal relation
- No "proper" theory of causation here
- Causal narratives

3 types of causal narratives
- CauseA
- CauseP
- CauseT

CauseA: a (presumptively causal) link between some set of risk factors, and a pathogenic fascicle.

This is the aetiological narrative that describes the development of a specified fascicle from some set of risk factors.

Symptoms

CauseP

Fascicle

Rx

CauseT

CauseA

Risk factors
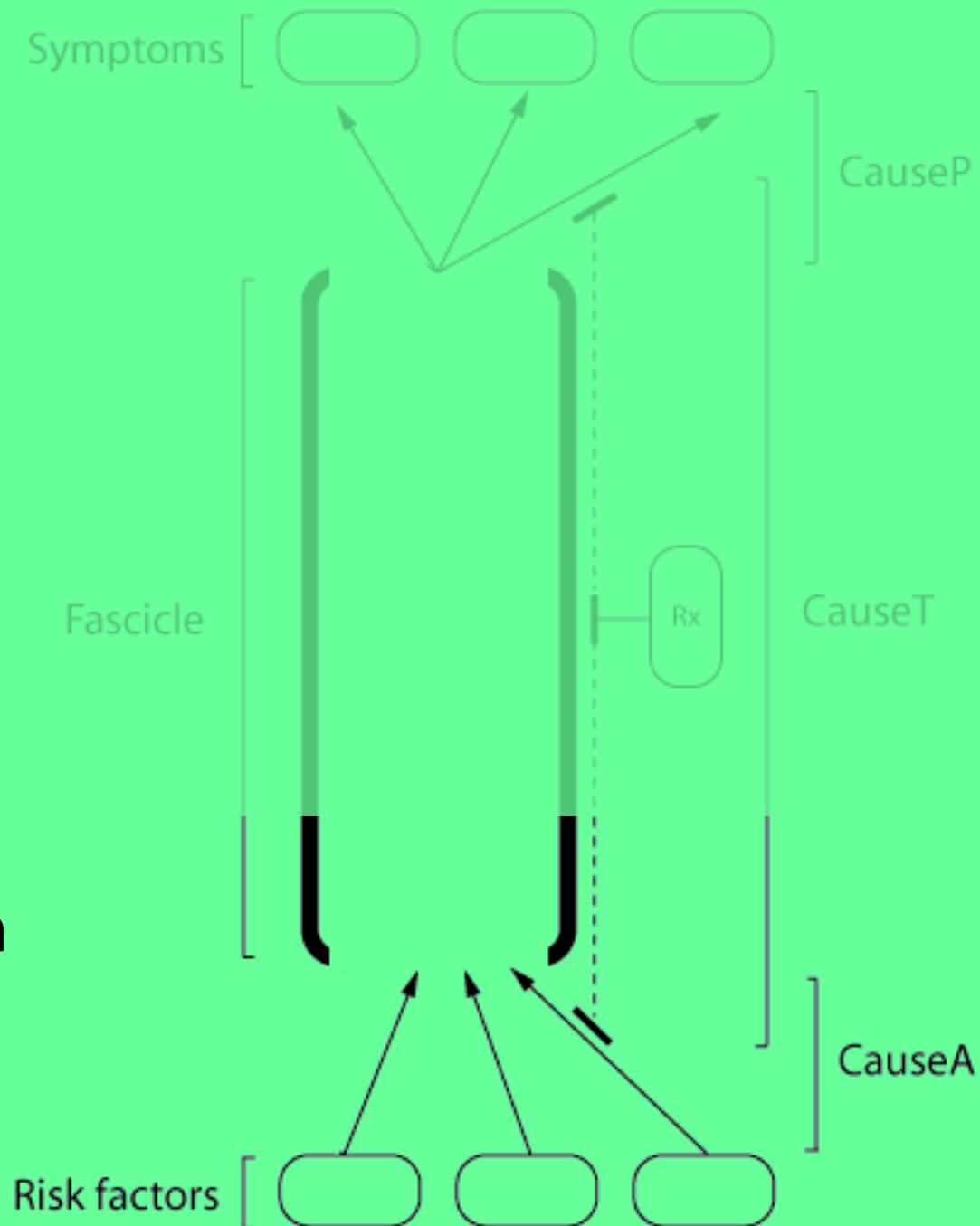
CauseP: a (presumptively causal) link between a specified pathogenic fascicle with some set of clinical features.

This is the *pathological* narrative that describes the development of some set of clinical features from a fascicle.

Symptoms

CauseP

Fascicle

Rx

CauseT

CauseA

Risk factors
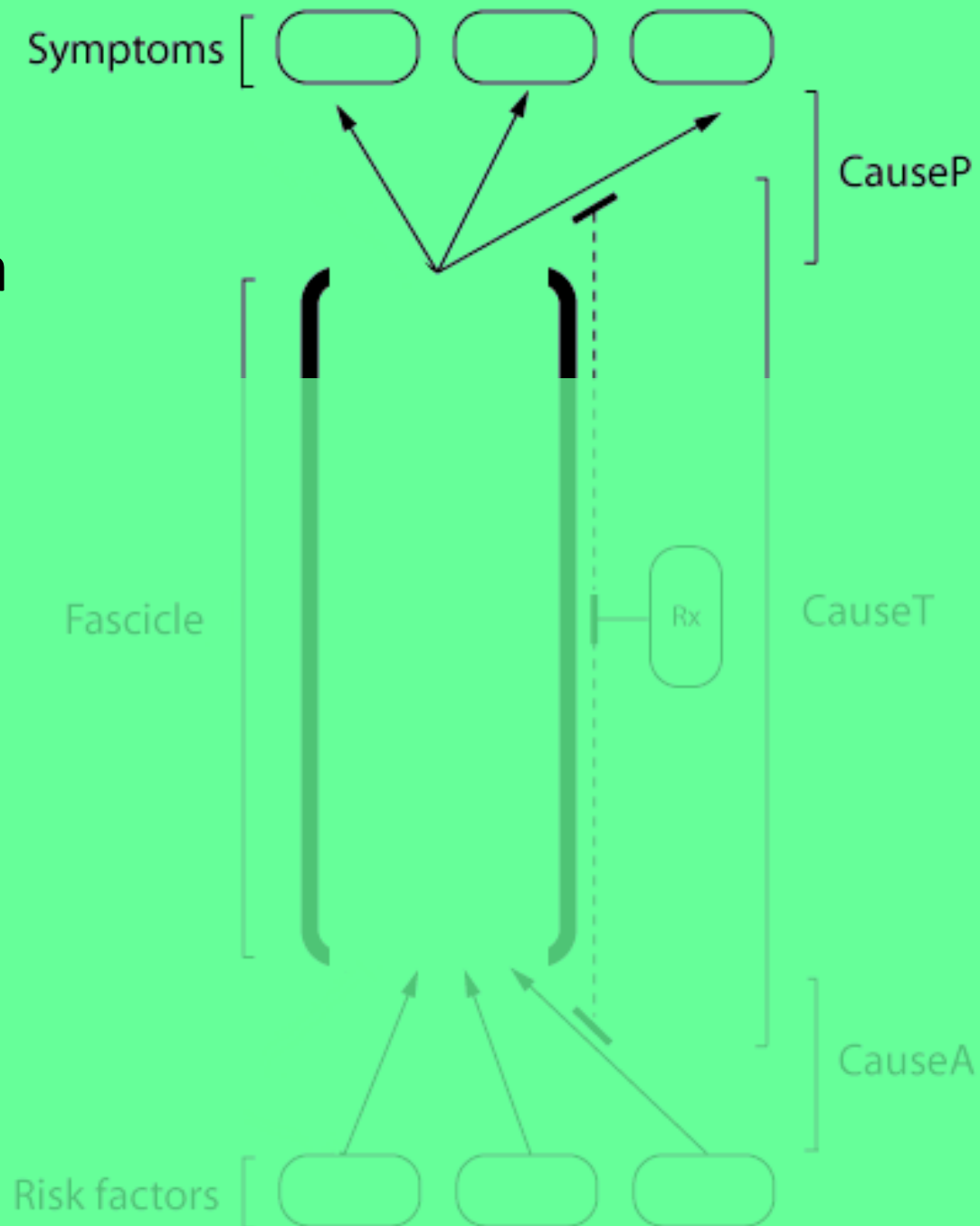
CauseT: a link between a specified *treatment* and a fascicle.

This narrative describes how, whatever the exact target of the treatment within the fascicle, it is considered essentially equivalent to any other, as both sever the presumptively causal narrative link from A to S.
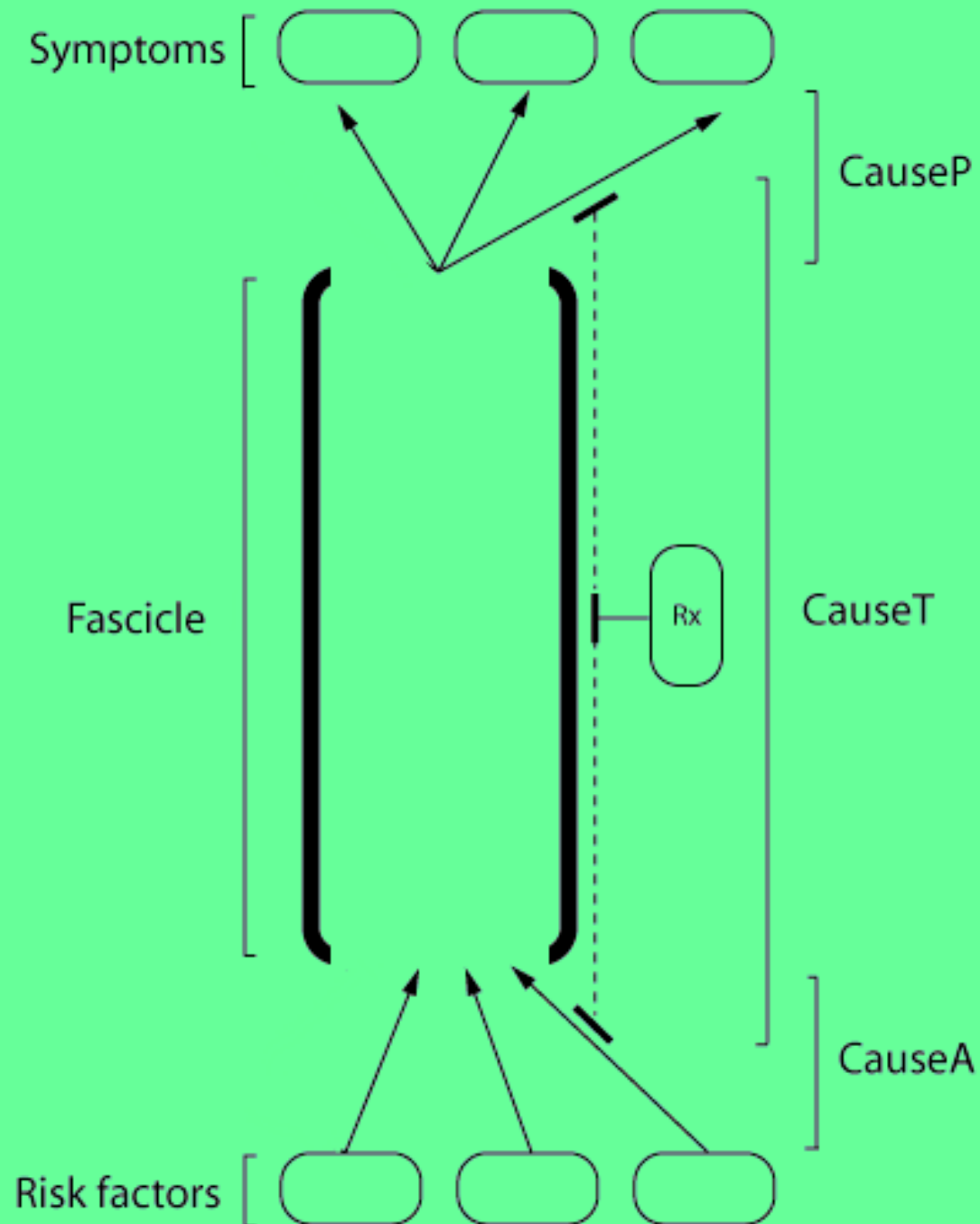
Toy example: lung cancer

Risk factors: smoking, asbestos exposure

CauseA: DNA mutations

Fascicle: lung cancer

CauseA disruption of lung architecture

Symptoms: coughing, haemoptysis

CauseT: chemotherapy, surgery
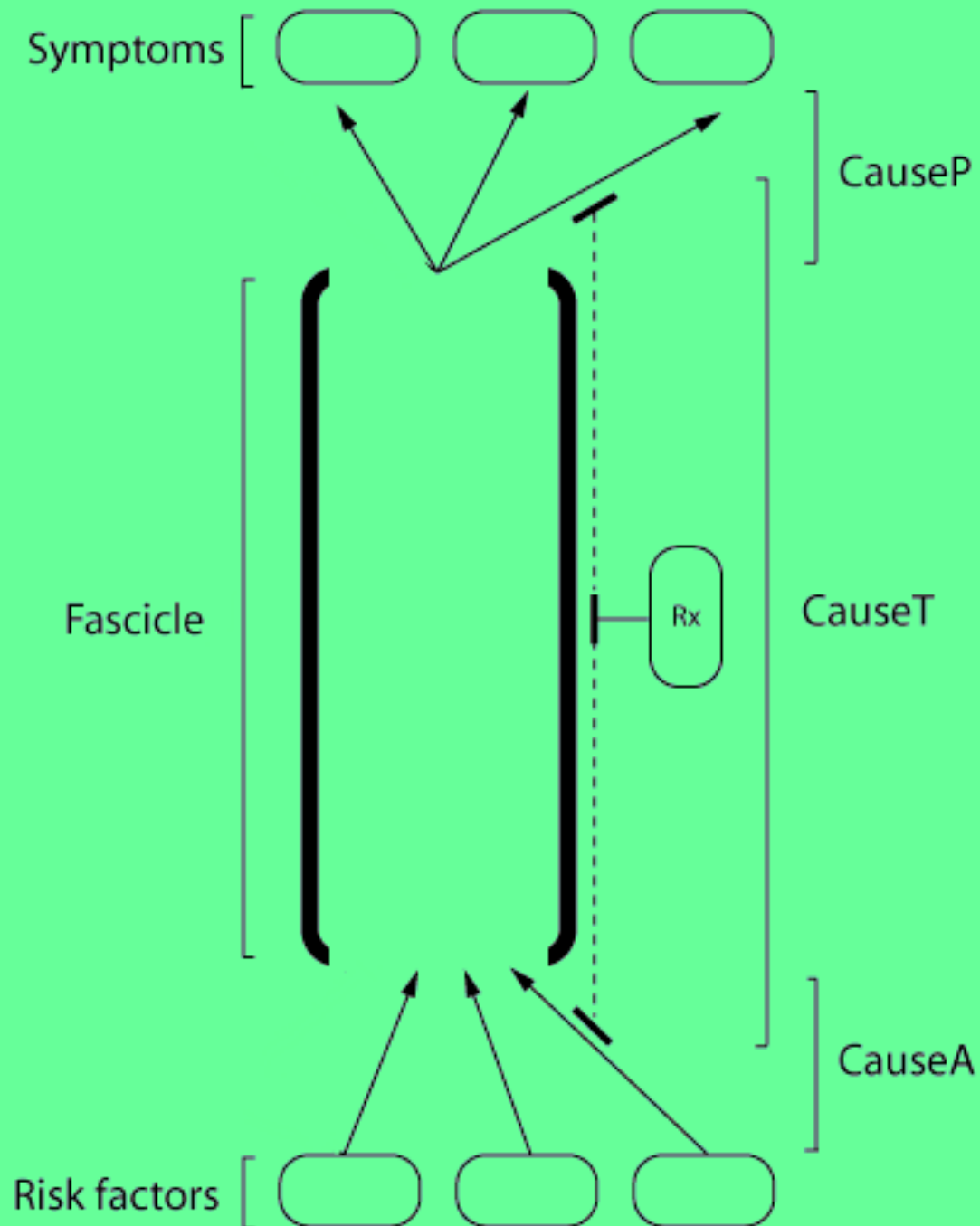
Better example: acute anterior uveitis

Risk factors: HLA-B27 status

CauseA: ?possibly mediated by HPA-B27 (e.g. by molecular mimicry)

Fascicle: Inappropriate immune system activation in the eye

CauseP: Protein deposition in anterior chamber of the eye

Symptoms: Flare, cells, keratitic precipitates develop

CauseT: steroid eye-drops, preventing the development of inflammation

Symptoms

CauseP

Fascicle

Rx

CauseT

CauseA
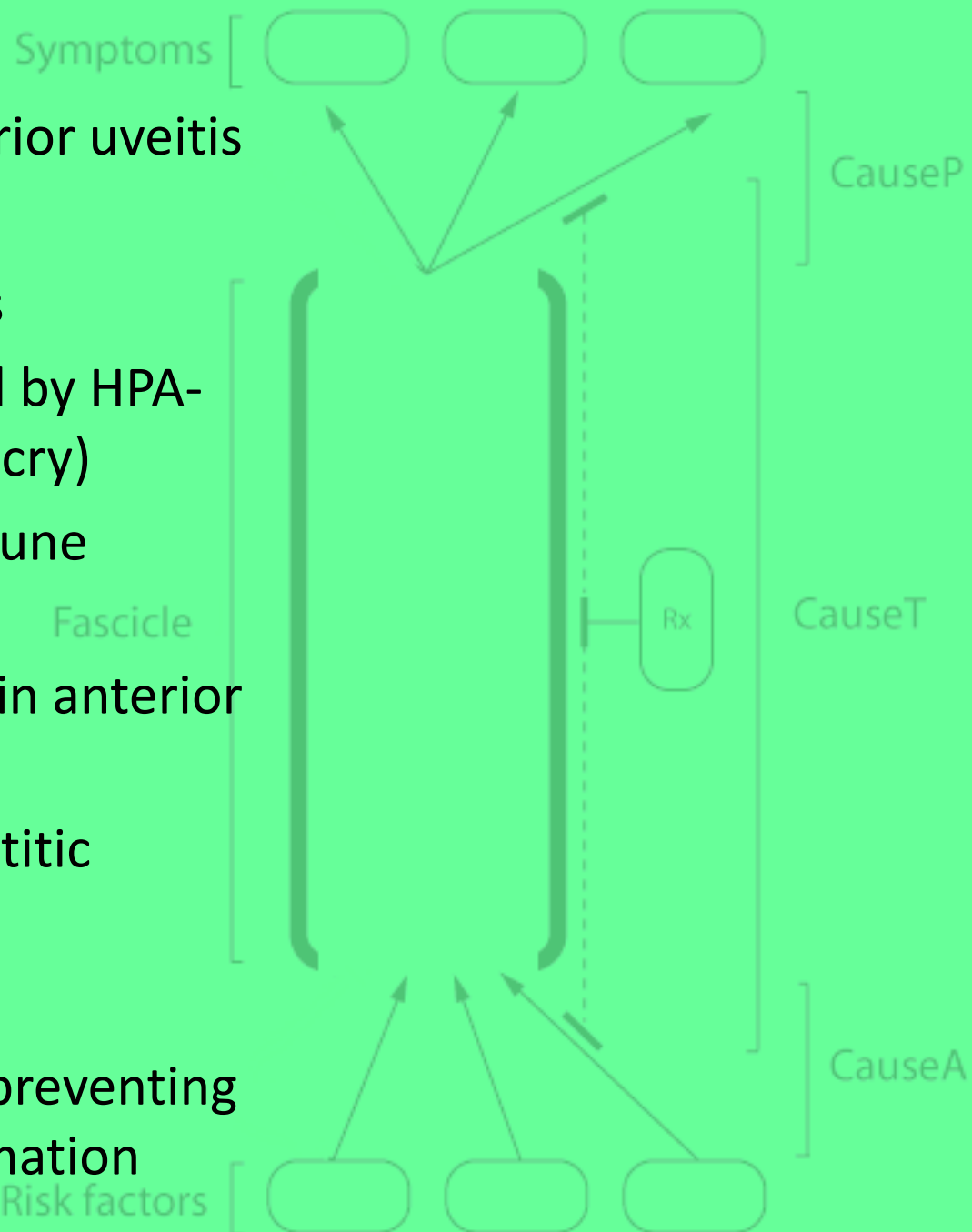
Risk factors

2b: fascicles

	Infectious abdominal pain	Neoplastic abdominal pain
Clinical findings	Sudden onset Diarrhoea and vomiting	Change in bowel habit Gradual onset Weight loss Anaemia
Risk factors	History of travel Altered immune status	Smoking Age
Treatment	Rapid response to antibiotics Response to supportive therapy	Surgical pathology
…	…	…

2c: DEM vs mechanisms

DEM	Mechanisms
No detailed account of entities and activities	Activities and entities, obvs.
No real productive continuity	Productive continuity
Tractable	Exhaustive
Concentrates on functionally important causes and effects	More holistic
Impression or abstraction of causal knowledge	(Jonathan Fuller's talk made this harder)

3. -omics

A type of model where states are described comparatively by an exhaustive list of biological variables, without any regard to whether they are causes or effects, nor to any chain of causation, nor to any traditional diagnostic class.

3a: signatures

-omic disease signature: an exhaustive list of biological variables describing a state of a diseased organism, whether the disease is identified or not, whether the list is common to many organisms or idiosyncratic.

-omic treatment signature: an exhaustive list of biological variables describing a state of an organism submitted to a given treatment.

C-map
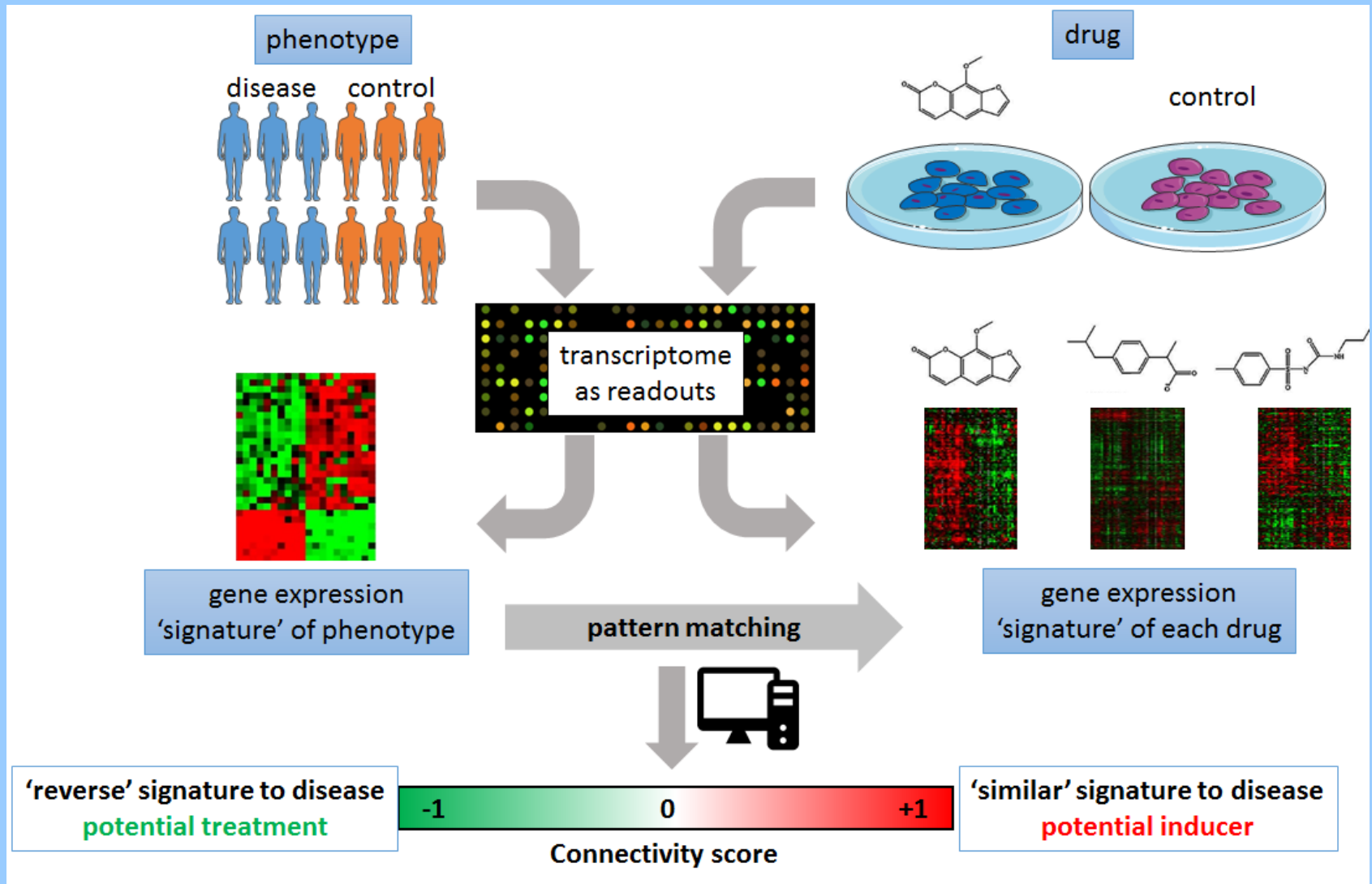
3c: DEM vs -omics

DEM	-omics
Clear distinction between risk factors, symptoms, and so on	Symmetry between signs, mechanisms, causes – everything is just a biomarker
Depends on a diagnosis – selecting a fascicle	Theranostic – no diagnosis required
All about disease entities!	Disease entities not required for confirmation/practice (but might be for discovery)

3c: mechanisms vs -omics

Mechanisms	-omics
Clear distinction between different parts of the mechanism – Ca causes Cb causes Cc…	Symmetry between signs, mechanisms, causes – everything is just a biomarker
Causation	Association
Linked to biomedical theories (Elena)	Theoretical neutrality (apparently)
Depends on a diagnosis – selecting a mechanism, or classifying a new mechanism	Theranostic – no diagnosis required

4a: DEM vs mechanisms vs -omics

DEM	Mechanisms	-omics
No detailed account of entities and activities	Activities and entities, obvs.	Signatures
No real productive continuity	Productive continuity	No causation
Tractable	[crowdsourced]	Exhaustive
Concentrates on functionally important causes and effects	More holistic	Exhaustive
Impression or abstraction of causal knowledge	(Jonathan Fuller's talk made this harder)	Not about causes at all
All about disease entities!	All about disease entities – for refining/changing/challenging existing ideas about disease.	Disease entities not required for confirmation/practice (but might be for discovery)
Weak links to theory	Explicitly linked to biomedical theories (Elena)	Theoretical neutrality (apparently)
All about diagnosis!	Depends on a diagnosis – selecting a mechanism, or classifying a new mechanism	Theranostic – no diagnosis required

4b: broader HPS literature

How/where are the different models used?

- Miriam Solomon's "untidy pluralism"
- John Pickstone's (2000) historical "ways of knowing"
- Lara Keuck's "epistemic hubs"

4c: an open question about ordering

Need to organise stuff (knowledge – facts – whatever) before epistemology happens

Diseases are epistemic meta-entities

Diagnostic kinds are epistemic meta-entities

'Mechanism of X' is an epistemic meta-entity

Signatures are epistemic meta-entity

4d: pending research questions

- Are the last two models really not derived from the mechanistic model?

- How and when is any of these models more relevant than any other?

- What happens when the three models do not overlap or contradict one another?

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Spare bits for Q&A

Introduction: the nature of disease

"Instead of beginning with diseases as such, we can begin simply with those entities actually of interest to medicine, i.e., the various diagnoses that are made. Our question will then be, to what do these diagnosis names refer and what is the nature of these referents? When a doctor says that a patient has X, where X is lung cancer or cystic fibrosis, etc., what is the nature of that X? The word "disease" does not enter in at all."

(Simon 2011)

Introduction: a bit on the medical model

Engel's 1977 tripartite characterisation :

1. The "old medical model" - disease as deviation from normal, mediated by natural causes
2. The "biomedical model" – a "scientific model; that is, it involved a shared set of assumptions and rules of conduct based on the scientific method and constituted a blueprint for research."
3. the "biopsychosocial model" (p.132) – Engel's own (normative) account of a medical model

Introduction: a bit more on the medical model

"We propose that the 'medical model' is a process whereby, informed by the best available evidence, doctors advise on, coordinate or deliver interventions for health improvement. It can be summarily stated as 'does it work?'"

(Shah and Mountain 2007: 375)

Is this just a foil…

Murphy (2013): chimerical and procrustean