From social determinants to biomarkers: understanding causal pathways

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LSHTM Centre for Statistical Methodology

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LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

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Recent developments from modern causal inference may be helpful

Outline of the talk

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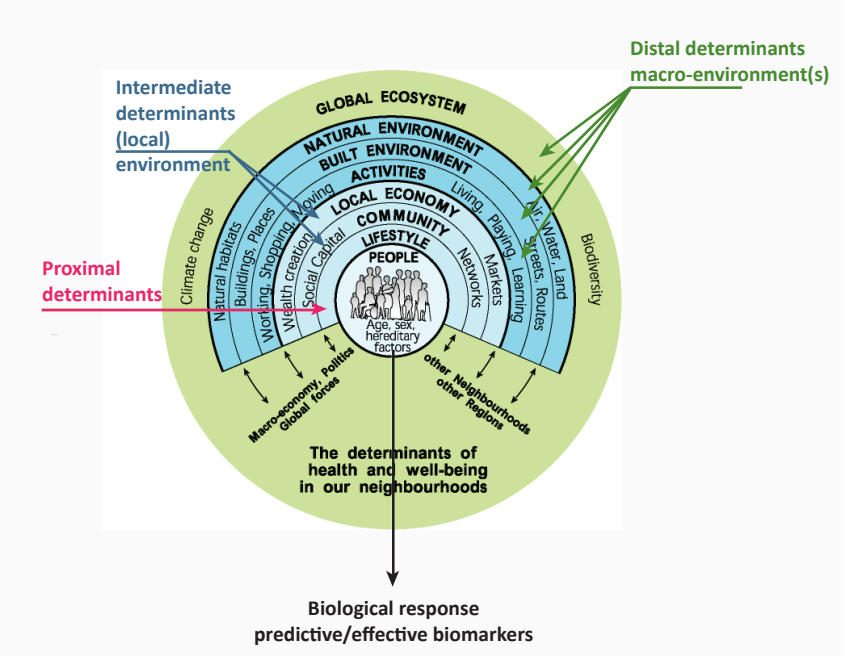
Inequalities in health

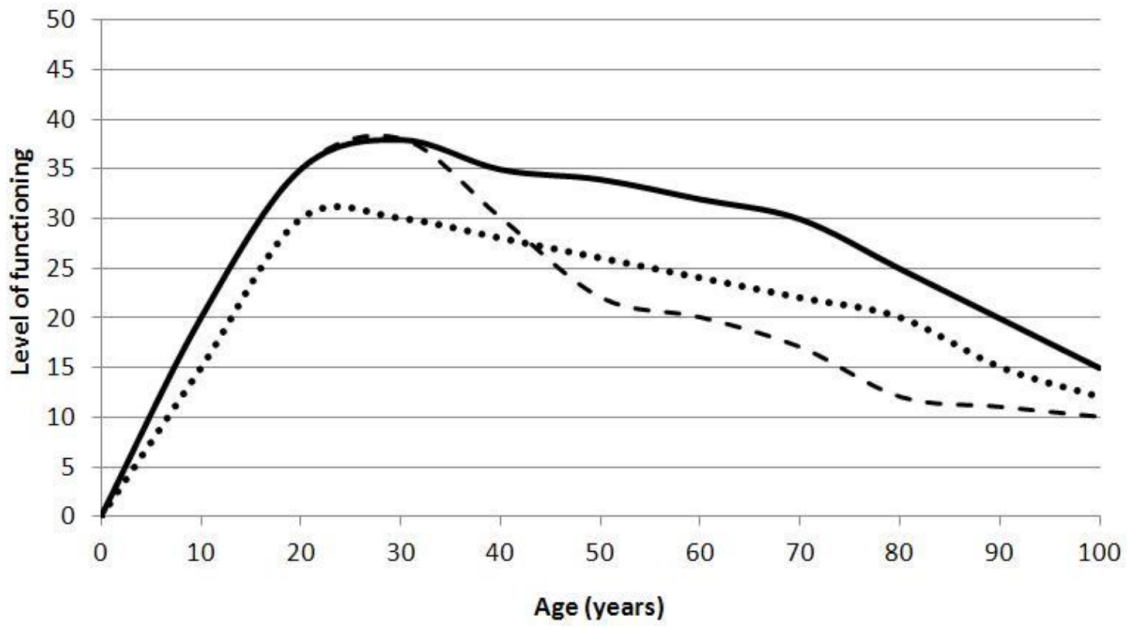
Biomarkers can be viewed as being influenced by exposures that are:

- distal (global environment)
- intermediate (socio-economic)
- proximal (behavioural)



Life course changes

Biomarkers change over the life course:



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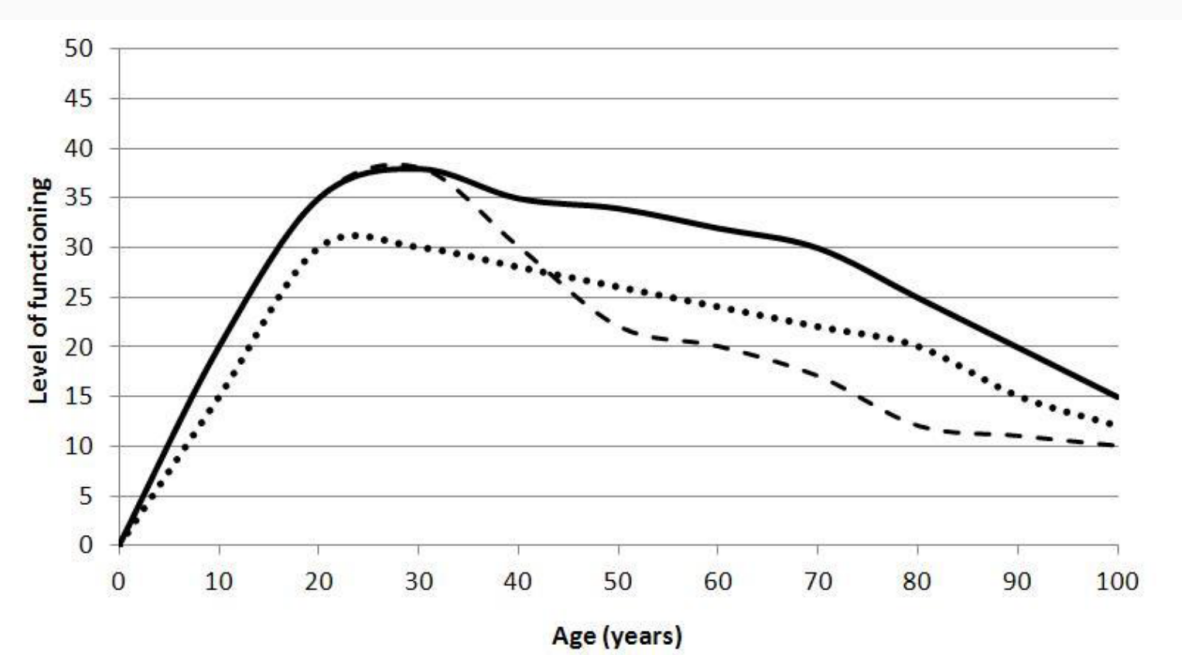

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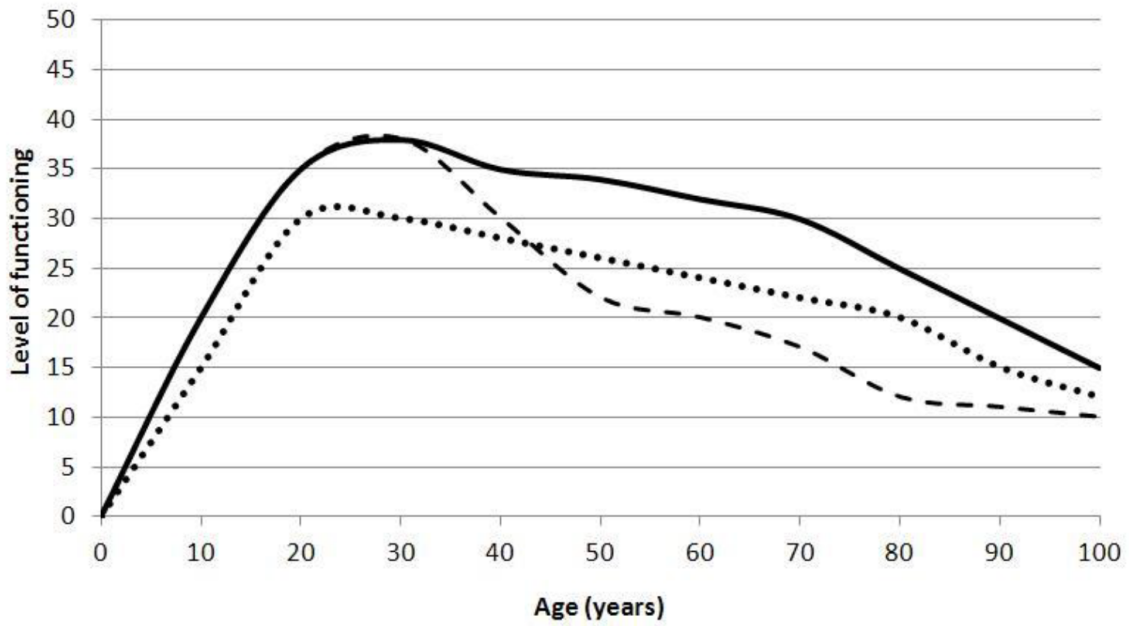

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[1] cumulatively: → *Cumulative exposure model*

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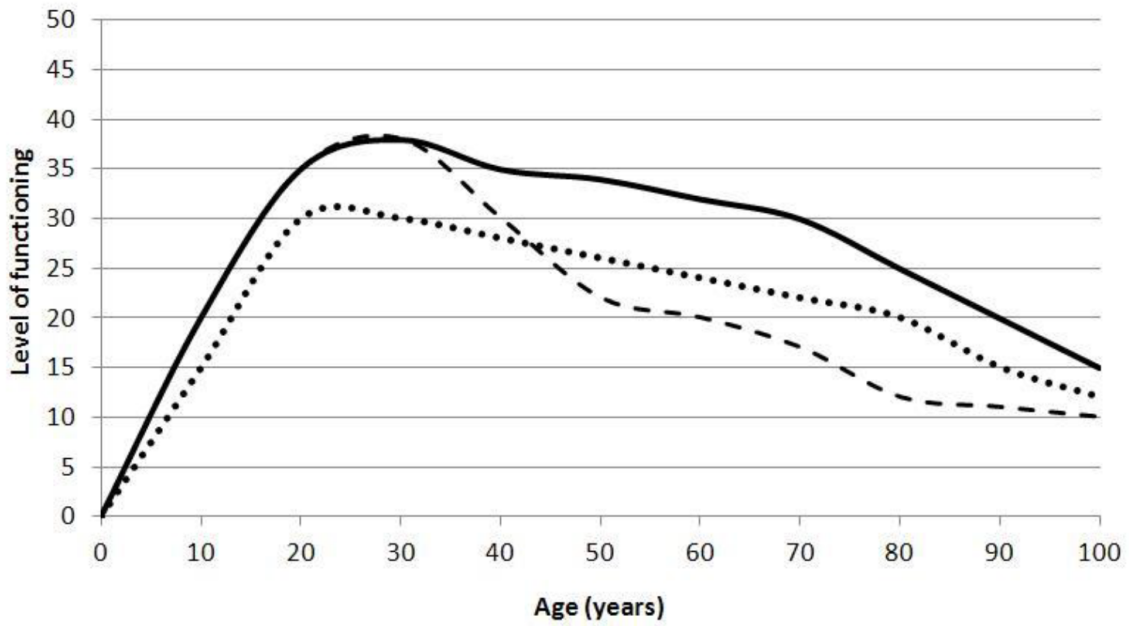

Their trajectories may be affected by exposures over the life course:

[2] only during specific periods: → *Critical period model*

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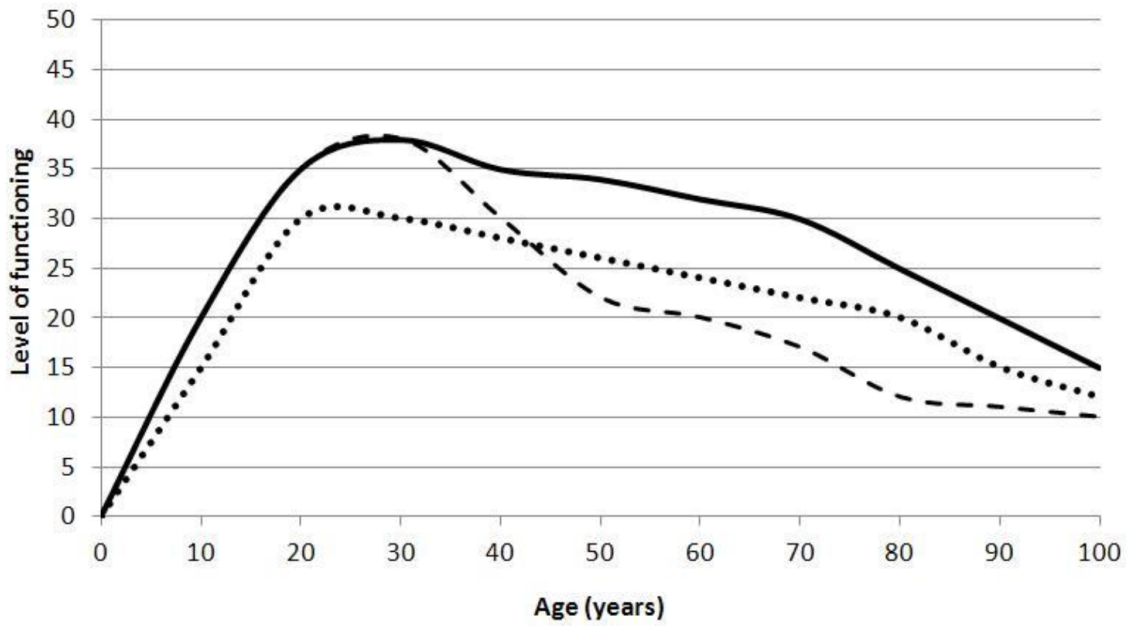

Their trajectories may be affected by exposures over the life course:

[3] especially during specific periods: → *Sensitive period model*

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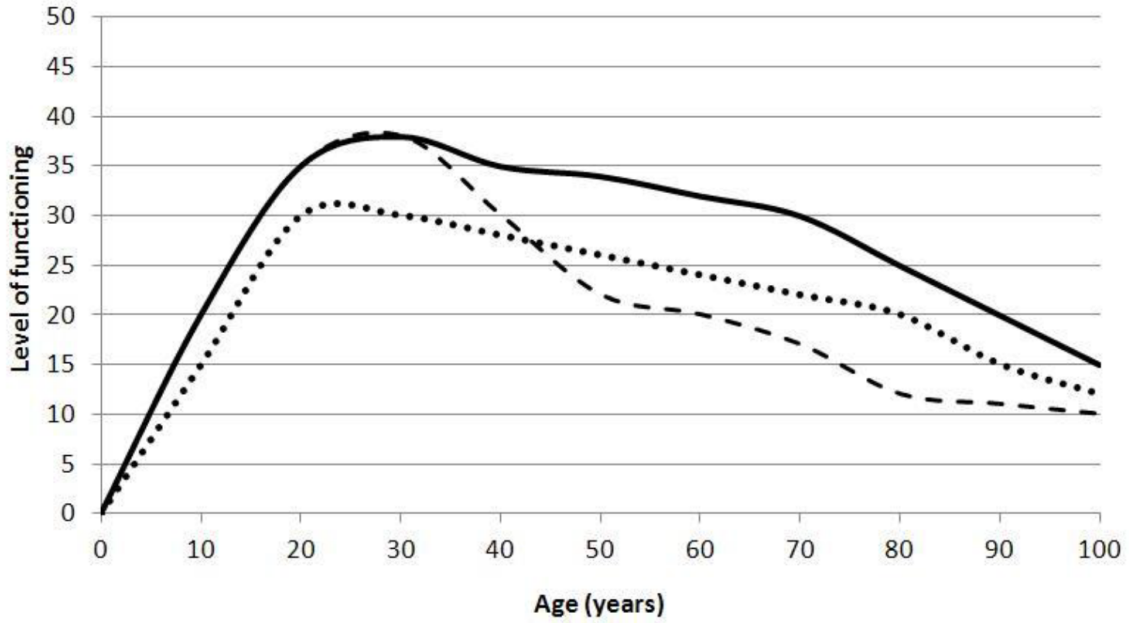
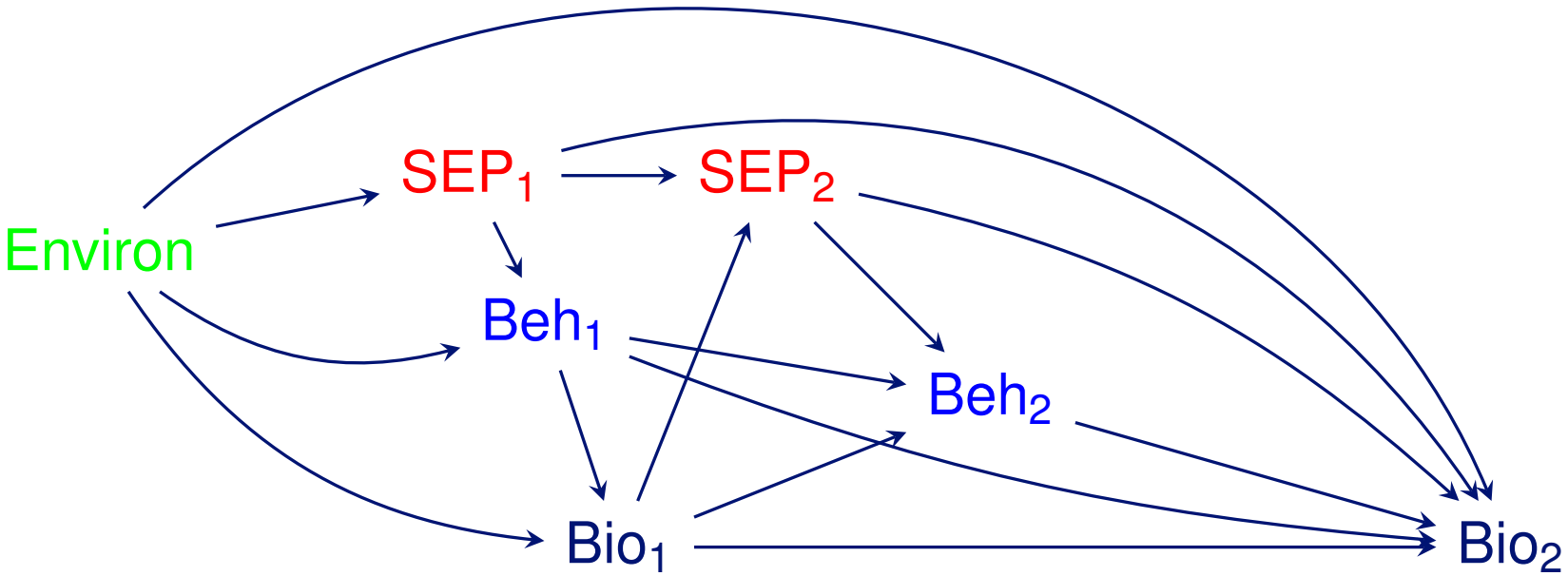


Their trajectories may be affected by exposures over the life course:

[4] synergistically: → *Pathways model*

The conceptual model

The conceptual model could be expanded to include the dimension of time:



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Will illustrate how certain causal questions can be formulated using this framework

Potential outcomes

Focussing on socio-economic disadvantage as the exposure of interest and Biomarker at time 2 the outcome, let:

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- Similarly for the potential outcome $Y(s_2)$
- $Y(s_1, s_2)$, the value that Y would take were we to intervene on both S_1 and S_2 and set them to s_1 and s_2

Total causal effect (TCE)

- The total causal effect of S_1 on Y can be expressed as a comparison of aspects of the mean (*i.e.* expectation(E)) of $Y(s_1)$ for different values of s_1,

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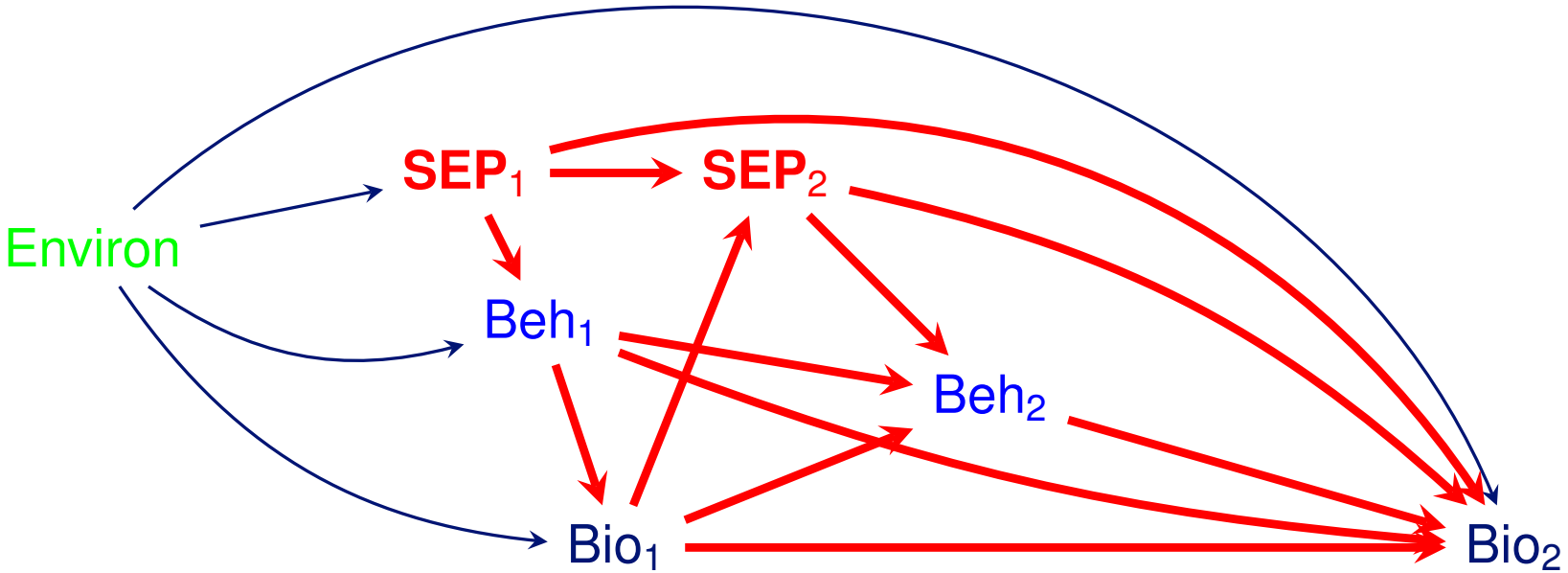

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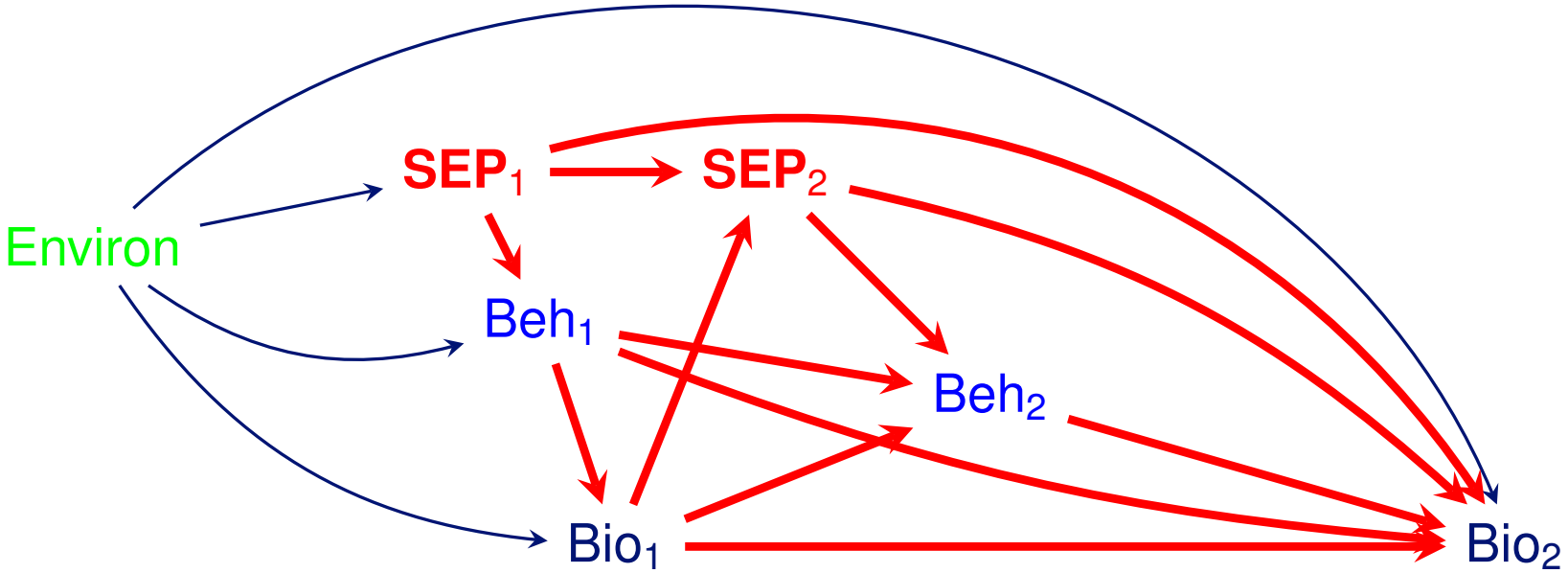
- TCE_1 would be of interest to assess the impact of (hypothetically) intervening on SEP_1 and changing its value



Total causal effect (TCE) (cont'd)

- The total causal effect of S_2 on Y can be expressed as a comparison of the mean of $Y(s_2)$ for different values of s_2,

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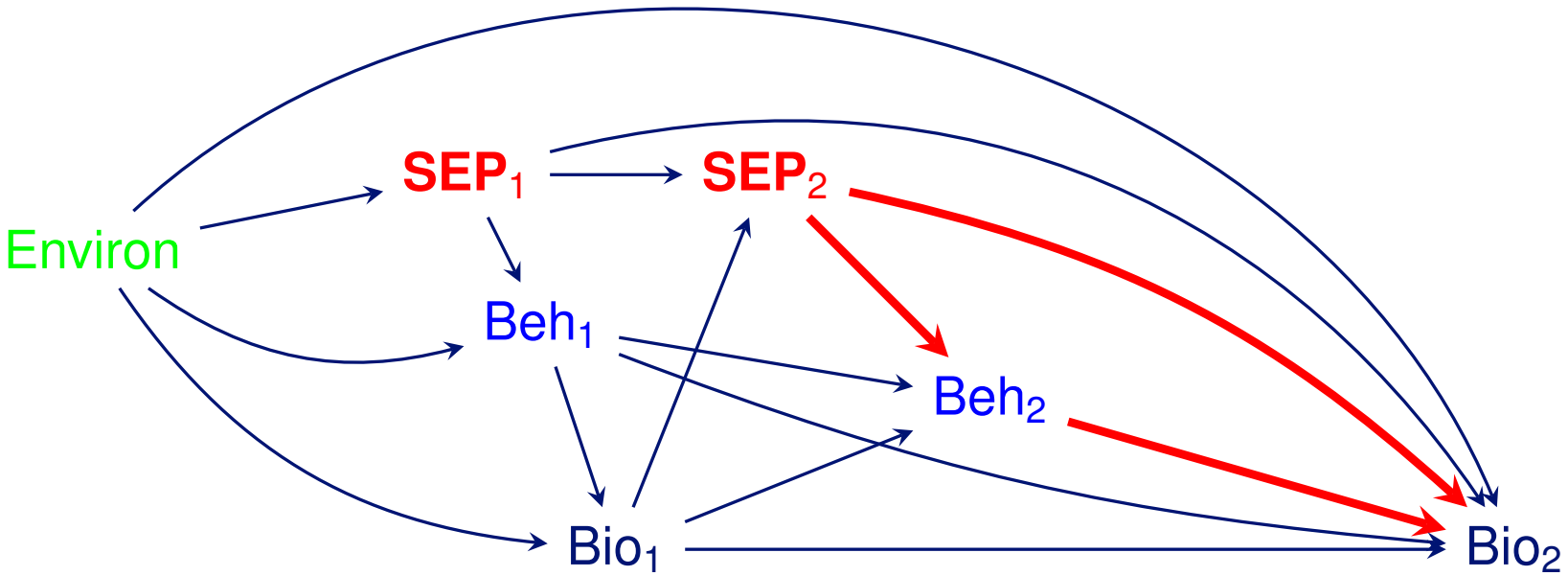

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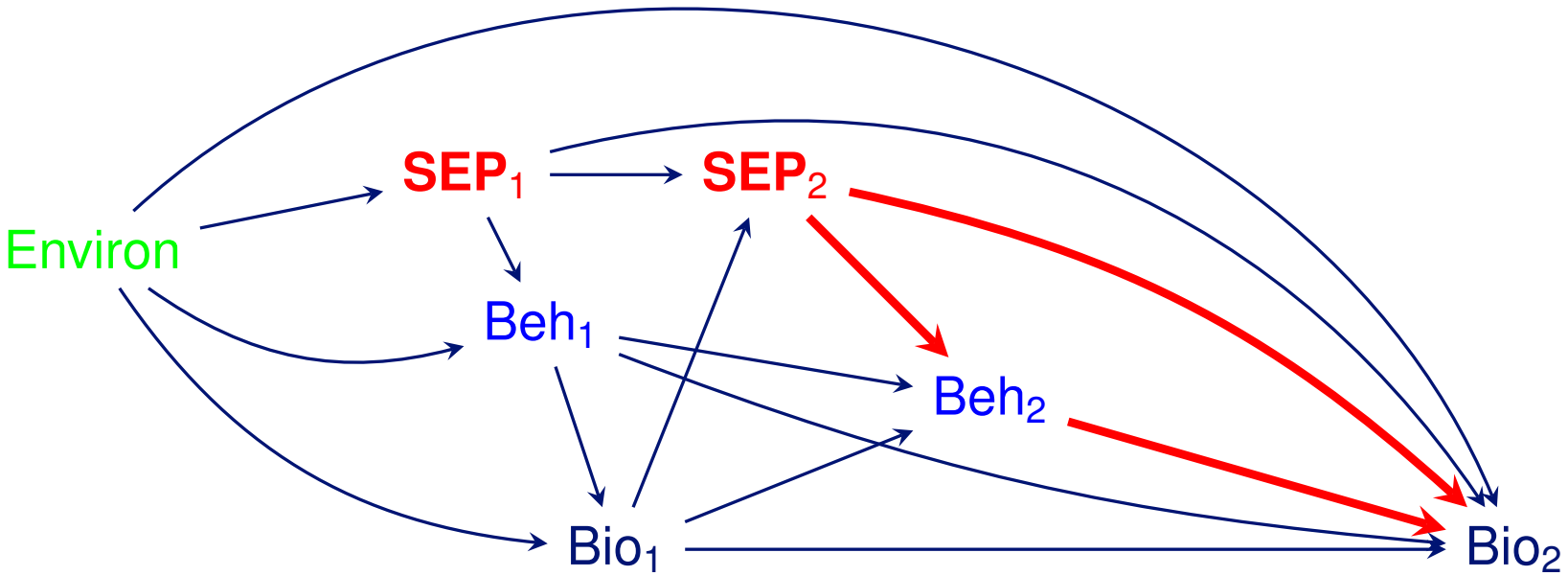

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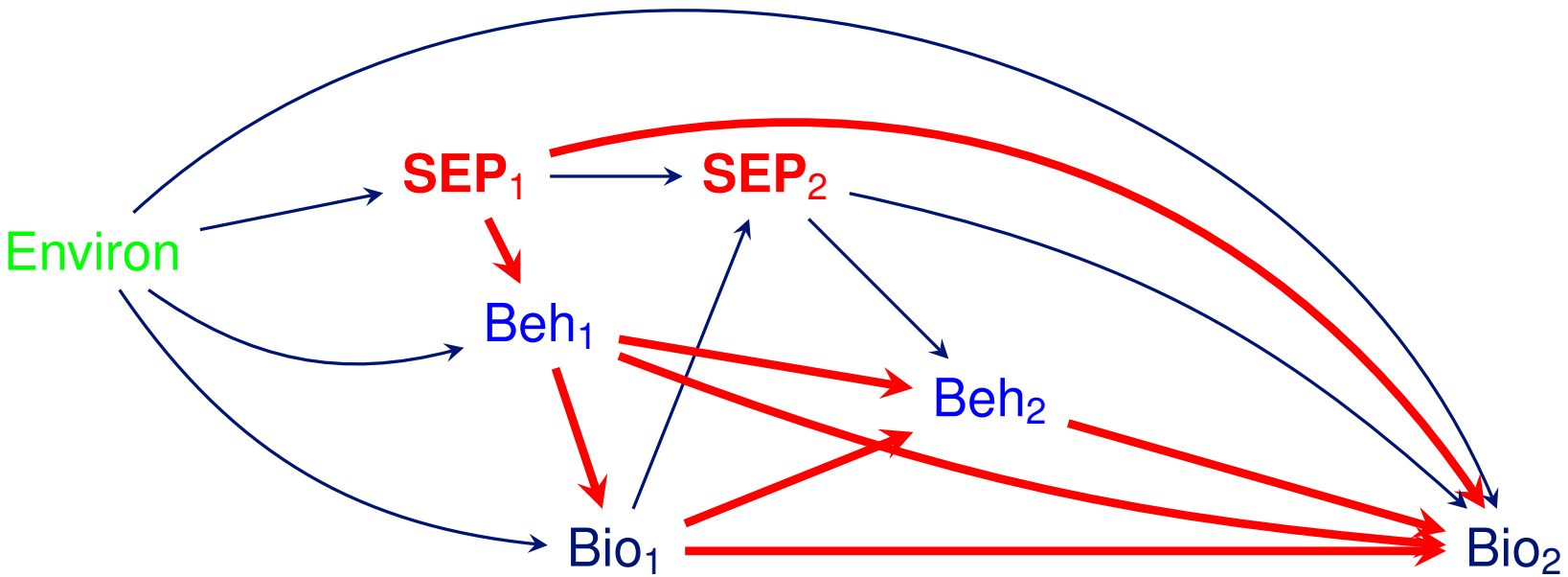

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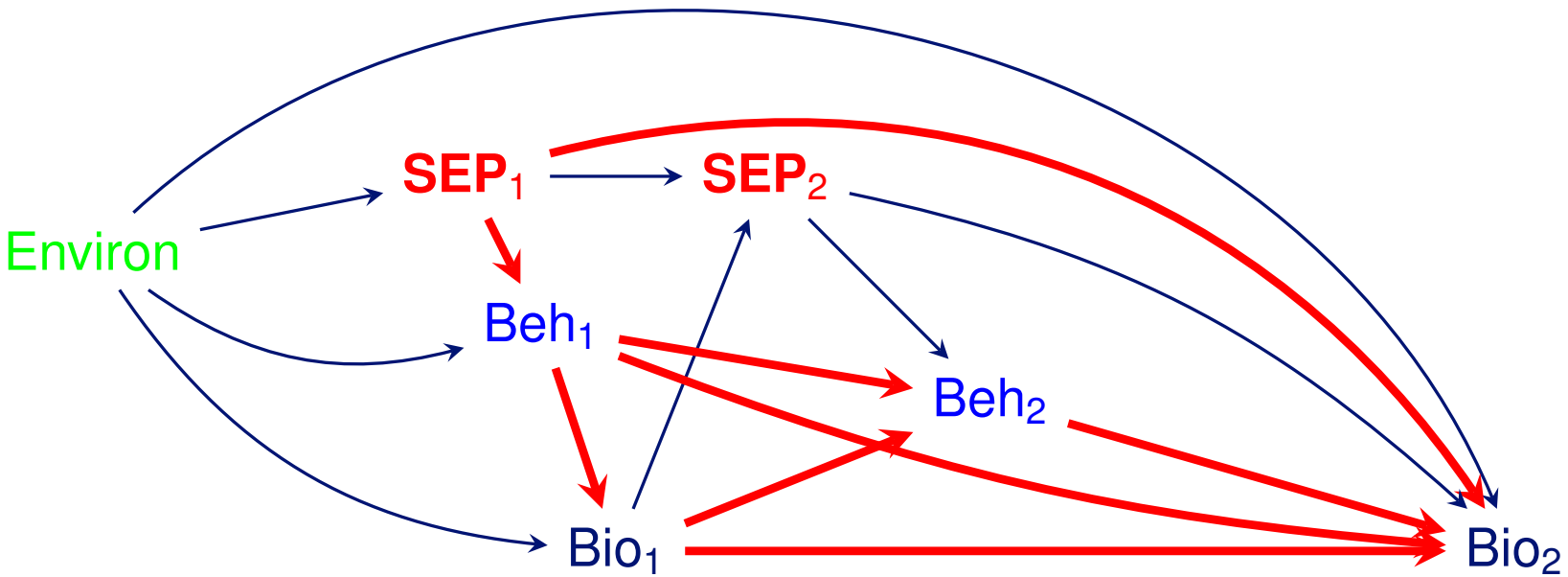
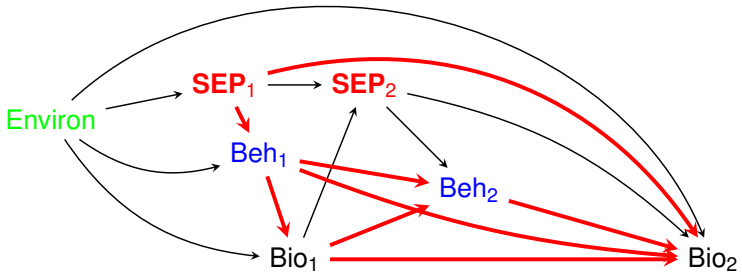
- It represents the direct effect of S_1 that is not mediated by S_2



Comparing effects



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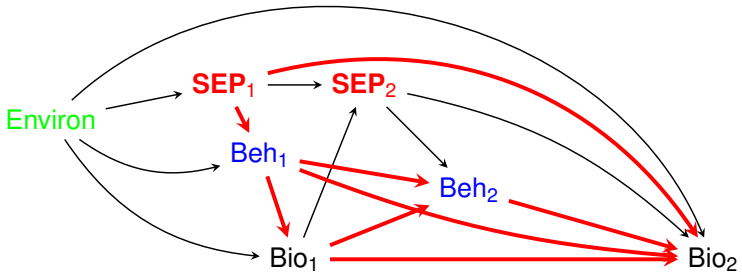

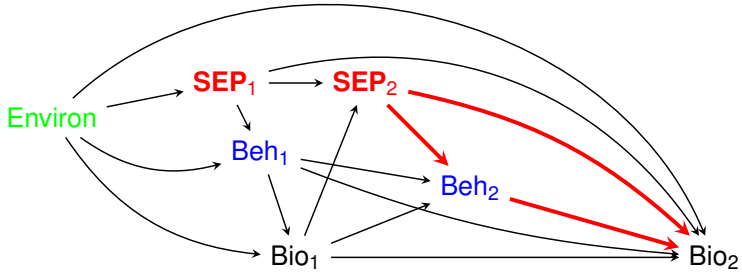

- If $CDE_1(s_2)$ varies with s_2 there would be support for the pathways model
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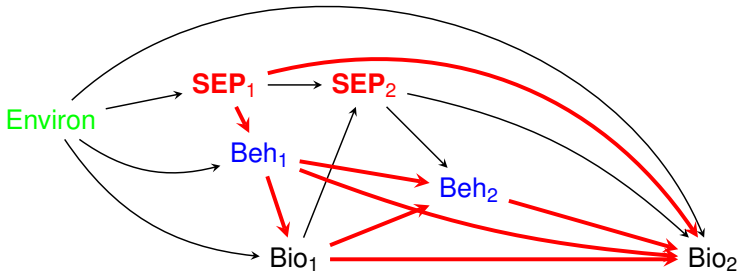

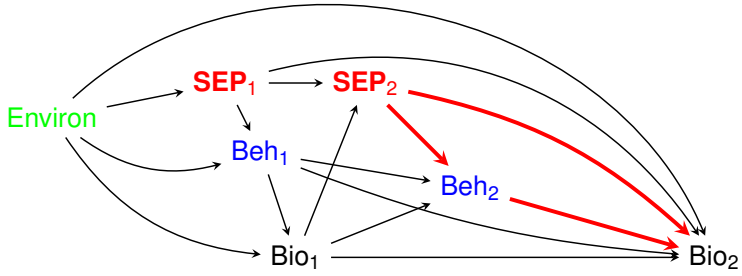

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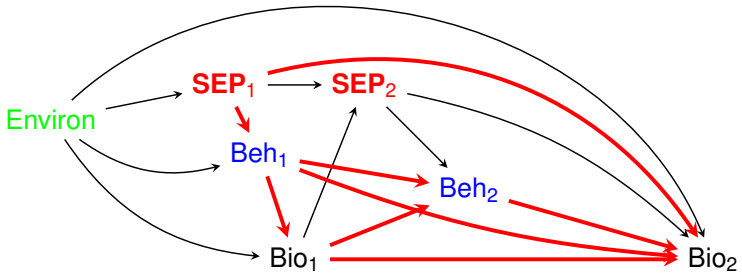

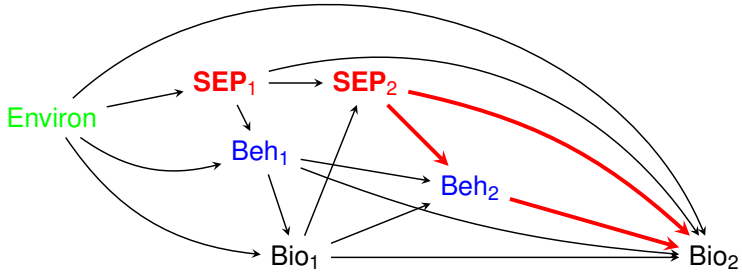

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- If $CDE_1 \ll TCE_2$ (or $CDE_1 \gg TCE_2$) there would be support for the sensitive period model
- If $CDE_1=0$ or $TCE_2=0$ there would be support for the critical period model

Effect decomposition

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Only in very simple settings this decomposition can be achieved by comparing TCE_1 and TCE_2

Comments

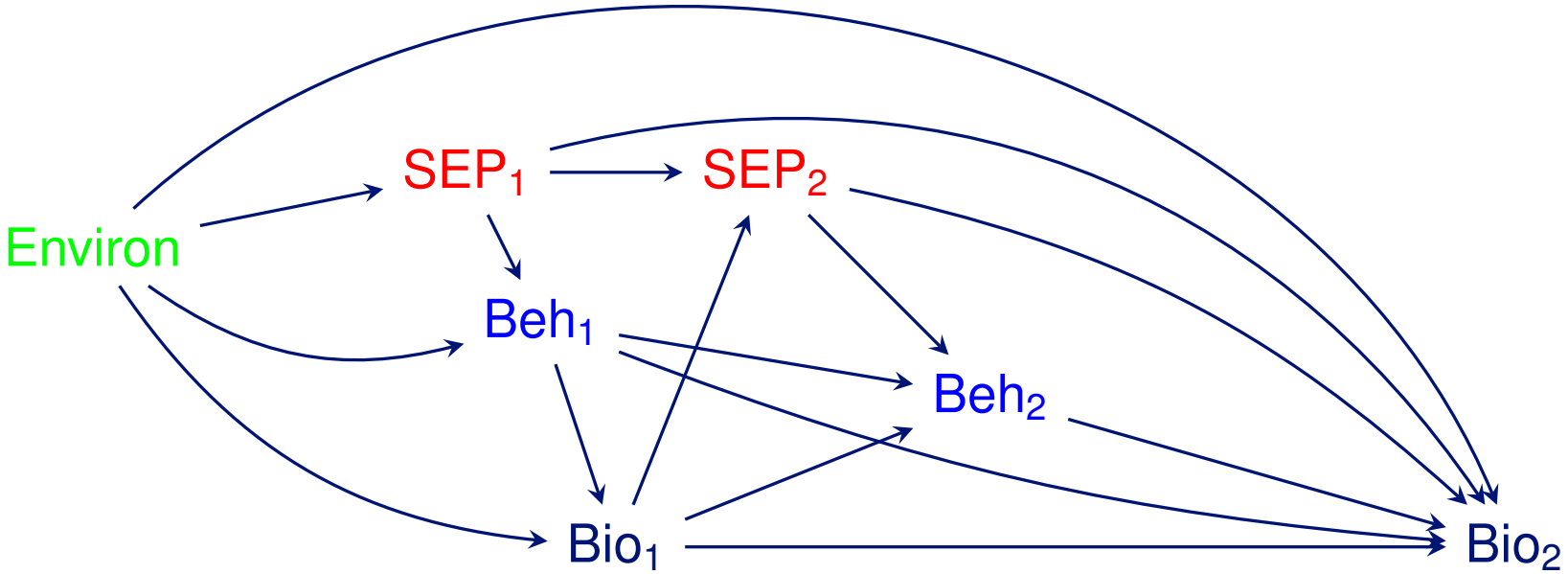
- This is not an exhaustive list of possible causal questions, nor of possible causal parameters
- Given here to illustrate the advantages of adopting the potential outcome framework in order to clarify the question(s) one wishes to address
- Importantly, the chosen question guides the choice of causal parameters to estimate from the data

Outline of the talk

Answering the question

- Given the question, consider assumptions required to estimate the chosen parameter(s) from the data
- Causal DAGs (directed acyclic diagrams) can aid this step
- Unlike the earlier conceptual diagram, causal DAGs are mathematical objects that must obey certain rules
- In particular that any common causes of variables in the diagram must be included, even if unmeasured

Conceptual and causal diagrams



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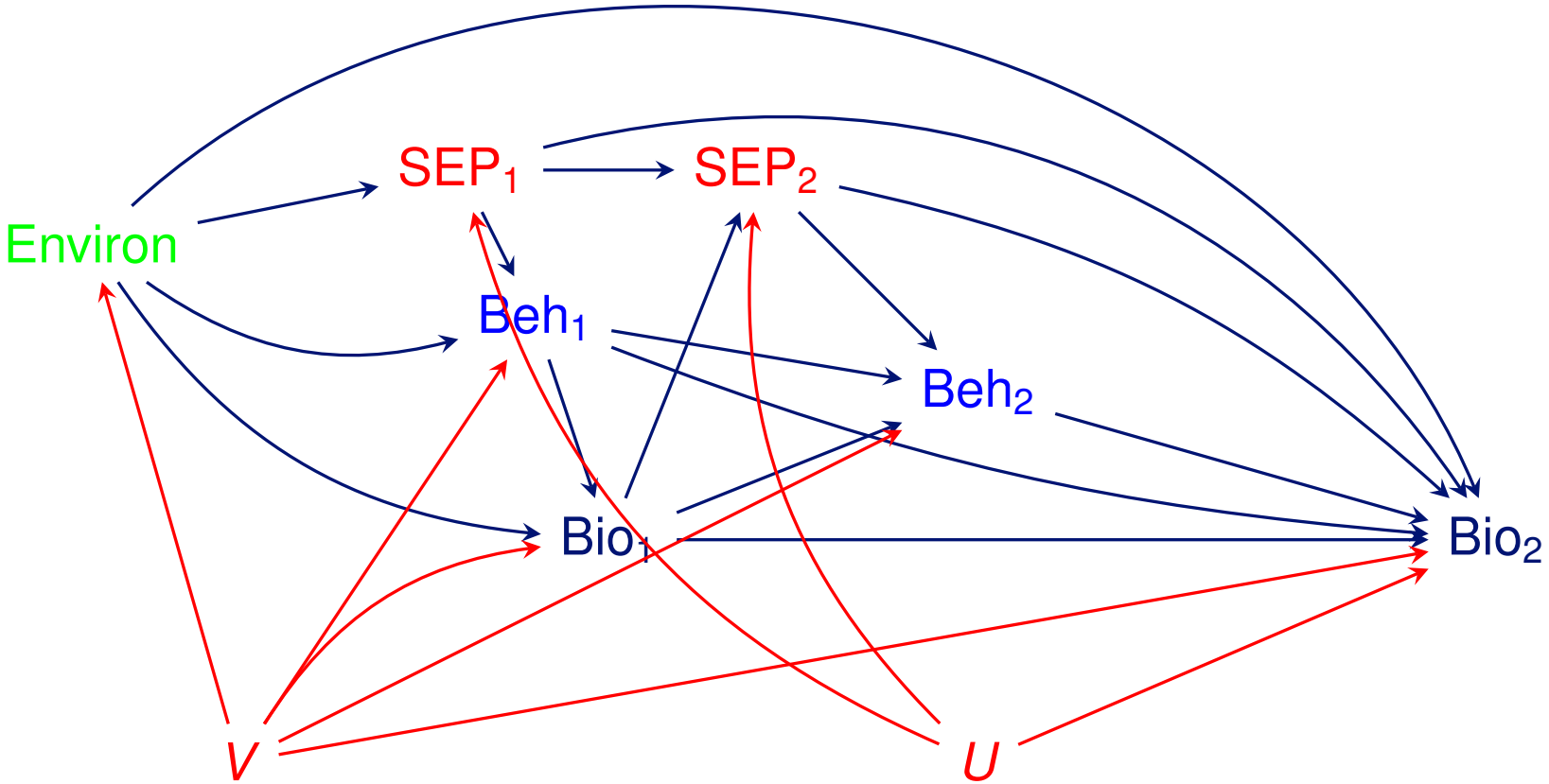

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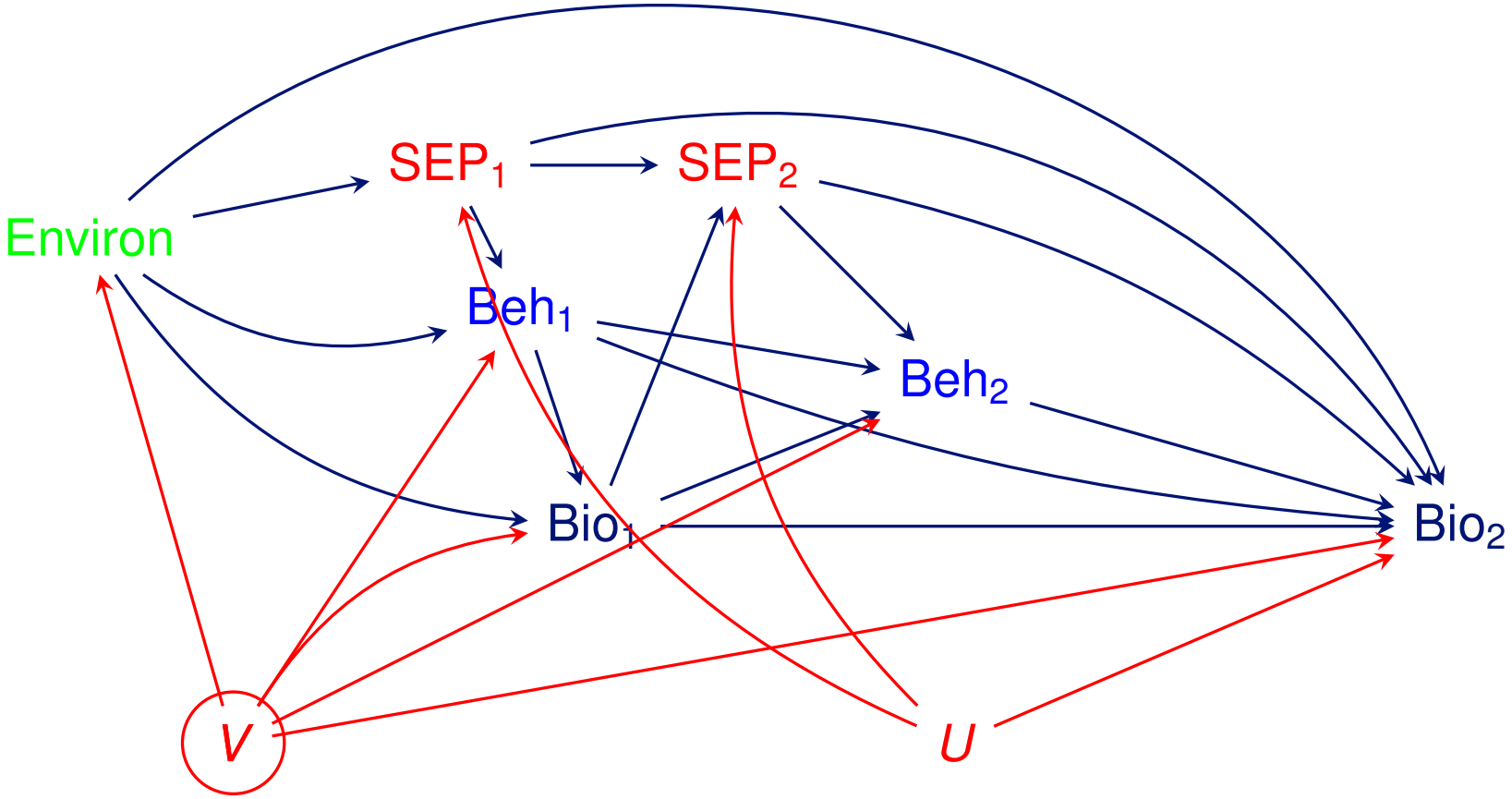

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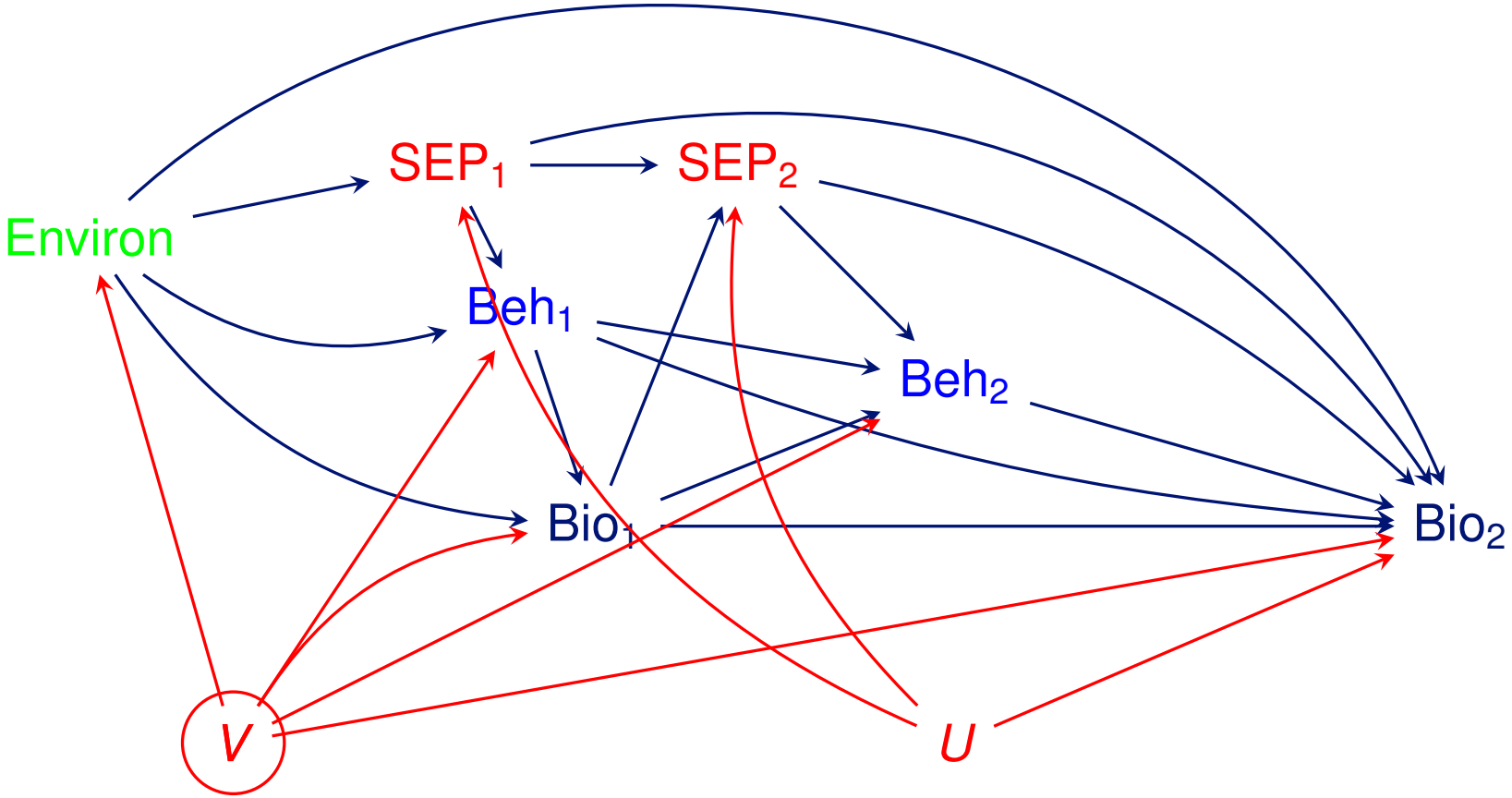

The DAG can be interrogated to find out whether the chosen parameter can be estimated from the available data and also whether traditional regression methods would suffice.

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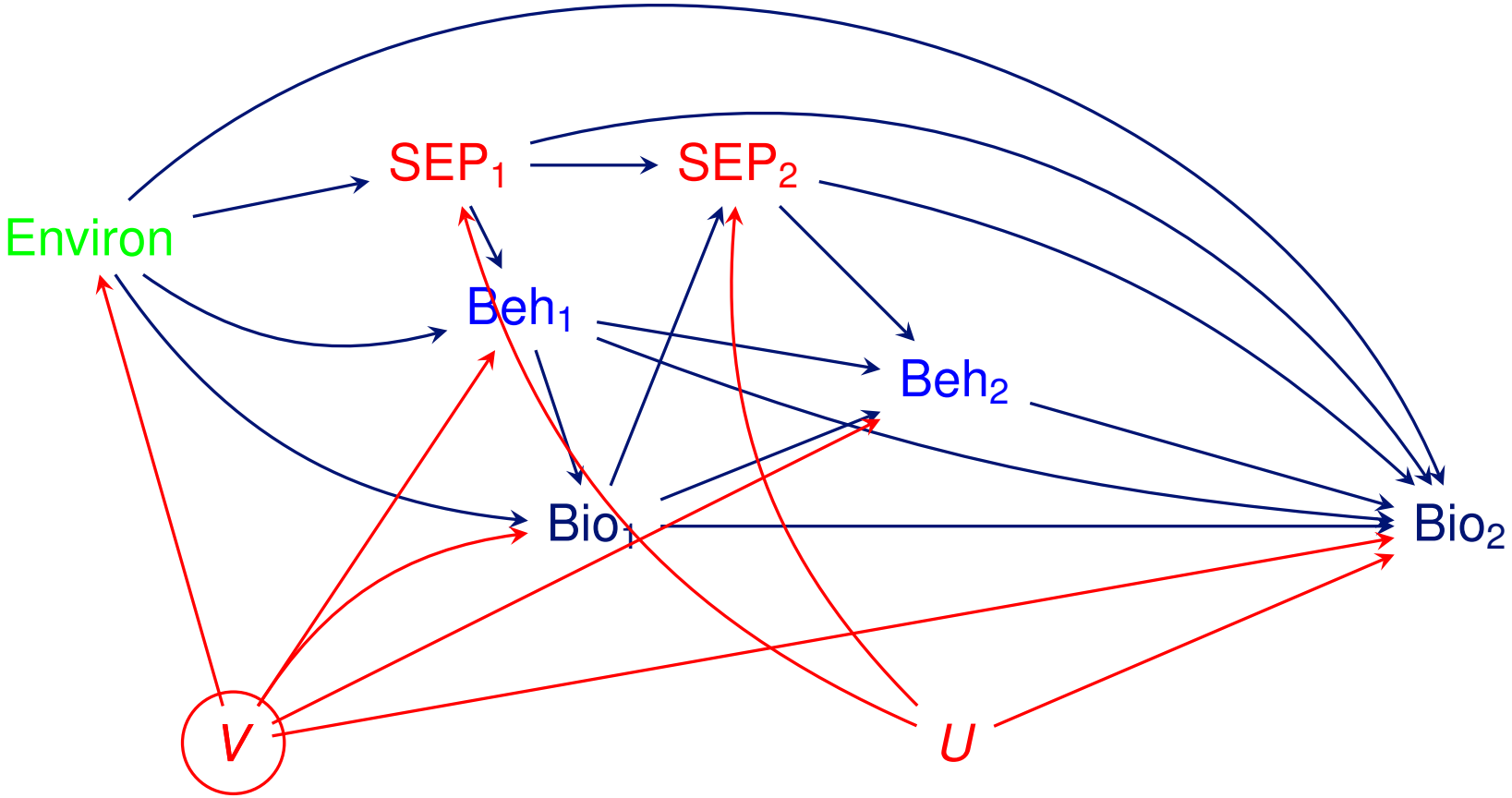

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- Concepts (and methods) from the field of causal inference can be useful to formalise the questions in a clear and unambiguous manner
- They are also extremely useful for identifying the appropriate estimation methods

Reference

De Stavola BL and Daniel R
"Commentary: Incorporating concepts and methods from causal inference into life course epidemiology"
Int J Epi, 2016 (in press)