Finding Normality in Abnormality: Normal Function Ascription in Cancer Biology

Seth Goldwasser
University of Pittsburgh

Outline

1. Normal Function and Function Pluralism

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2. Two Desiderata

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> *An activity, **φ**, of a part, **p**, of a token system, **s**, is a **normal function**, F, iff items of p's type make contributions, **C**, to systems of s's type by φ-ing (cf. Weber 2017).*

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- *That said, different types of function are ascribed in different sub-disciplines of biology.*
- *Causal role or “minimal” functions are ascribed in cladistic systematics, while normal functions are ascribed in physiology.*
- *If an account of function aims to explicate the ascription of function in a sub-discipline then it aims to be descriptive.*
- *There are at least two desiderata on descriptive accounts of function*

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Two Desiderata

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- *Example: allowing the ascription of normal functions to solar systems (broad)*

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Accounts can be criticized for being too broad or too narrow:

- *Example: allowing the ascription of normal functions to solar systems (broad)*

OR

- *Example: assuming ecosystems don't have parts with normal functions (narrow).*

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Methodological Adequacy: *a descriptive account should provide conditions for ascription consistent with how a the relevant functions are ascribed in the relevant sub-discipline.*

Accounts can be criticized for entailing conditions on the ascription of function to which biologists do not adhere.

- *Example: Amundson and Lauder (1994) and Griffiths (1994, 2006) claim that cladists do not nor need to appeal to history when ascribing a function.*

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Cancer Biology

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***The standard classificatory scheme**: anatomical site and tissue type of origin, stage, and grade.*

*The standard classificatory scheme is helpful **but not perfect**.*

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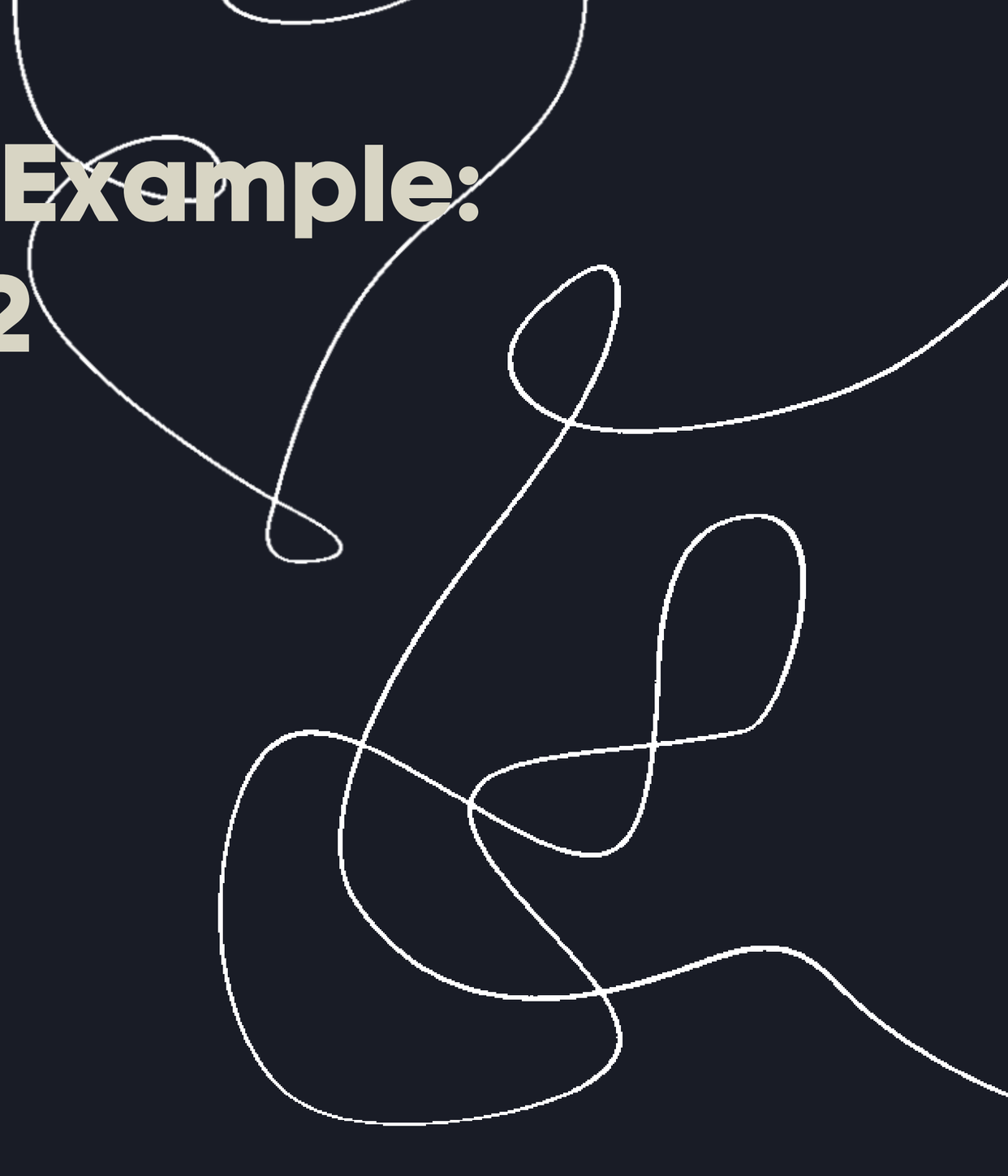
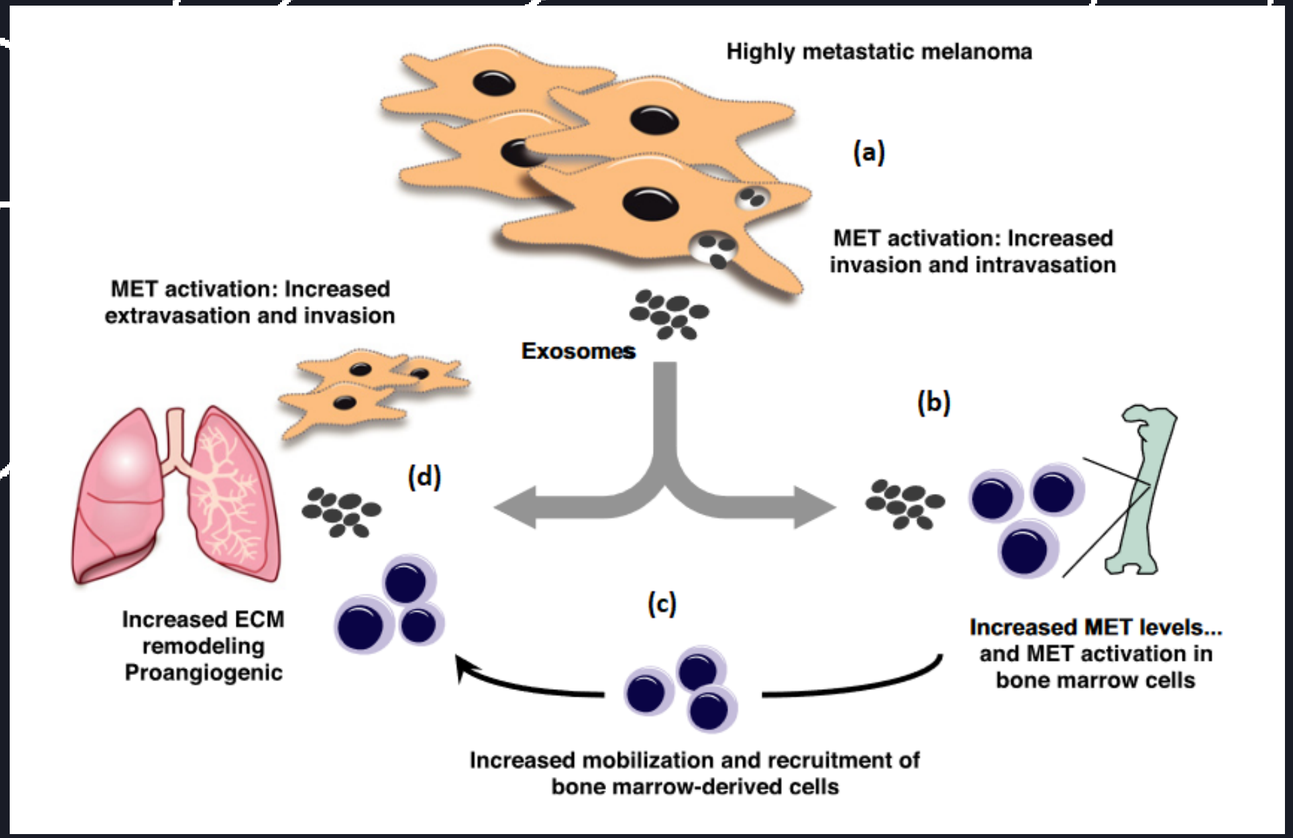
A Representative Example: Peinado et al. 2012

Peinado et al. (2012) features the ascription of a normal function to part of melanoma.




Highly metastatic melanoma
(a)
MET activation: Increased invasion and intravasation
MET activation: Increased extravasation and invasion
Exosomes
(b)
(d)
(c)
Increased ECM remodeling Proangiogenic
Increased MET levels... and MET activation in bone marrow cells
Increased mobilization and recruitment of bone marrow-derived cells

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The experiments they ran were designed to figure out how sEV contribute to premetastatic niche construction.

The ascription tells us how sEV normally so contribute. That is, the function ascription identifies a ***standard*** *for sEV activity, disposition, and structure.*

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Selected effects accounts claim that an activity of a part is a normal functions if and only if that part ***is selected for performing that activity****.*

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1. *The system(s) has to exhibit **heritable variants** of the trait or trait-type.*
2. *The **fit** between system(s) and environment has to **favor some traits over others**.*
3. *The selected trait has to be **retained over variants**.*

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At the cellular level, parts of cancers that are ascribed normal functions are often the product of drift or genetic hitchhiking without being co-opted.

At the tumor level, these parts are often neither heritable or recapitulated in metastases nor the product of competition between tumors.

In which case, at least some parts of cancers have normal functions despite not being subject to selection

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Another type of normality that's thought to be scientifically respectable is ***conditional statistical typical ity***.

The normal function of a part then becomes what that part does to contribute to the (inclusive) fitness of an individual system which, conditional on that part's so contributing, is typical for systems of the type.

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One could try to stipulate a reference class for a type of cancer ad hoc.

But doing so threatens to undermine the normal function (pun intended) of ascribing normal functions, namely, identifying stan dards of the activities, dispositions, and structural features of biological systems.

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Talk of “the (novel) function” by Peinado and Colleagues is an unfortunately loose way of speaking.

Moreover, cancer biologists reserve talk of “normal functioning” to describe the healthy variants of the disease processes they study.

In response, if we understand normal functioning as a part's activity embodying a standard then cancer biologists are engaged in the practice of ascribing those functions.

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The reason for the practice is clinical: if there are normal ways that a disease progresses then understanding that standard aids undermining it.

A Reply

In response, if we understand normal functioning as a part's activity embodying a standard then cancer biologists are, in fact, engaged in the practice of ascribing those functions.

The reason for the practice is clinical: if there are normal ways that a disease progresses then understanding that standard aids undermining it.

The ascription of these functions is helpful here because cancers are so variable.

A Reply

Summary

1. Different types of function are ascribed in across biology.

2. Descriptive accounts of function must satisfy class adequacy and explanatory adequacy.

3. Cancer biology features the ascription of normal /abnormality inclusive functions.

4. Selected-effects Accounts and Fitness Contribution Accounts struggle to account for this.

Thank you!