What to do if we think that researchers have overlooked a significant issue for 100 years?
The case of quantitative genetics and underlying heterogeneity

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What to do if we think that researchers have overlooked a significant issue for 100 years?

1. In-principle question
2. Specific case
3. Some things I have done re: #2
1. In-principle question

What to do if we think that researchers have overlooked a significant issue for 100 years?
1. In-principle question

What to do if we think that researchers have overlooked a significant issue for 10 or 5 years?
U.S. philosophy of biology—last 30 years

Emphasis on conceptual systemization of biologists’ work
Conceptual structure of Chapters 1-4 of Darwin’s *On the Origin of Species*

IF

[#1 & 2] Variation among organisms in characters
& Inheritance (reproducibility) of characters
[# 3] Hyperfecundity

THEN

not all can survive
=> struggle for existence
=> differential representation of variant characters in lineages
   of organisms over time
= evolution (or "modification by descent")
Conceptual structure of Chapters 1-4 of Darwin’s *On the Origin of Species*

IF

[#1 & 2] Variation among organisms in characters & Inheritance (reproducibility) of characters

[# 3] Hyperfecundity

THEN

not all can survive

=> struggle for existence

=> differential representation of variant characters in lineages

Q: Which survive?

A: most fit to their environment

IF  [#4] Survival (& reproduction) of the fitter (=N.S.)

THEN  evolution will result in (local) improvement of adaptation to conditions of existence
Audiences for Conceptual Systemization?

Students:
Economical account (for didactic effect)

Other philosophers:
“My systematization is better than yours (b/c ...)”
Audiences for Conceptual Systemization?

Researchers:

“We make systematic and clear what you had not.” [Or more systematic and clearer.]

“We endorse researcher A over researcher B.”

“We can extend researcher A’s thinking.”

Systemization in philosophy of biology => philosophers want to show researchers some things they have overlooked
Aside:
Science = rational interpretation + *empirical discrimination*
Aside:
Science = rational interpretation + empirical discrimination

Q: What is needed to demonstrate that change and the resulting characters were produced by a process of natural selection?
What to do if we think that researchers have overlooked a significant issue?

“We” =

scientists

as well as

philosophers, sociologists & historians

of science
What to do if we think that researchers have overlooked a significant issue?

Audience participation:

Your response?

Example: Submit your ideas to science journals

Think -> pair -> share
What to do if we think that researchers have overlooked a significant issue?

Some answers:
1. Stay quiet
2. Submit ideas to science journals
3. Submit ideas to philosophy of science journals
4. Tease out hist., social., pol., cultural implications
5. Tease out the political implications
What to do if we think that researchers have overlooked a significant issue?

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Q: Case studies or systematic treatment of range of ways (direct -> backdoor) to influence scientific debates?
2. Specific Case: Quantitative Genetics and Underlying Heterogeneity
TRAIRT is height

DZT less similar on average than MZT

& MZT share all genes, while DZT do not

⇒ genetic similarity is associated with similarity in trait

(substantial heritability of height)
Twin Pair

TP1

TP2

TP3

TP4

TP5

TP6

TP7

TP8

Location: L1 L2 L3 L4 L5 L6 L7 L8

DZT

MZT

AAbbccDDee // FghiJ

MZT aabbCCDDEE // FgHiJ

DZT

MZT

DZT

MZT

DZT

MZT

DZT

MZT

DZT

MZT

DZT

sequence of environmental factors

genetic factors (pairs of alleles)
-> Qs: Implications?
Why overlooked?
Why overlooked?

Terminology

<table>
<thead>
<tr>
<th>genetic&lt;sub&gt;1&lt;/sub&gt;</th>
<th>quantitative genetics</th>
<th>trait</th>
<th>variance of trait, partitioned (AnOVa)</th>
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</thead>
<tbody>
<tr>
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<td>relatedness</td>
<td>variable part of genome</td>
<td>fraction of variable part of genome shared</td>
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<tr>
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<td>genetics</td>
<td>site(s) on genome</td>
<td>heterozygosity at site(s)</td>
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<tr>
<td></td>
<td>Location 1</td>
<td>Location 2</td>
<td>Location 3</td>
</tr>
<tr>
<td>---</td>
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</tr>
<tr>
<td>Variety</td>
<td>Mean across all locations &amp; replicates</td>
<td>Mean across all locations &amp; replicates</td>
<td>Mean across all locations &amp; replicates</td>
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Heritability
=
variance among variety means for the trait / total variance for the trait
Why overlooked?

Terminology

"contribution of genetic differences to observed differences among individuals"

(Plomin et al. 1997, 83)

"fraction of the variance of a phenotypic trait in a given population caused by (or attributable to) genetic differences"

(Layzer 1974, 1259).
Genetic gradient:
Not shown by QG, but plausible

Li, J. et al. (2008) Science 319: 1100-1104
Implications?
Q: Application of human heritability if underlying heterogeneity is possible?
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- Undertake research \textit{w/o reference to trait’s heritability}
  (heterogeneity, not polygenic, as explanation of GWA results)
Q: Application of human heritability if underlying heterogeneity is possible?

- Undertake research \textit{w/o reference to trait’s heritability}
- Use high heritability $\Rightarrow$ trait is potentially worthwhile candidate for molecular research
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- Restrict attention to variation \textit{within a set of relatives}
Q: Application of human heritability if underlying heterogeneity is possible?

- Undertake research w/o reference to trait’s heritability
- Use high heritability => trait is potentially worthwhile candidate for molecular research
- Restrict attention to variation within a set of relatives
- Focus on heritability as a fraction of the variation (useful in ag. & lab. breeding)
Q: Application of human heritability if underlying heterogeneity is possible?

- Undertake research \textit{w/o reference to trait’s heritability}
- Use high heritability $\Rightarrow$ trait is potentially worthwhile candidate for molecular research
- Restrict attention to variation \textit{within a set of relatives}
- Focus on heritability \textit{as a fraction of the variation} (useful in ag. & lab. breeding)
- \textit{Restrict range of varieties or locations}
Why overlooked? —Historical Origins

Mendelian model at base of classical quantitative genetics

single locus + dominance,
duplicated over many loci
+ noise + variance across locations of the average value of the trait in each location = “polygenic”
Gene-free model

Must be possible

Instead of assumption

All other things being equal, similarity in traits for relatives is proportional to the fraction shared by the relatives of all the genes that vary in the population

Resemblance among relatives -> empirically determined parameter
Gene-free model

1. Simulations => Assumption is not reliable

2. VxL interaction variance subsumed in augmented “Variety” variance

=> Human heritability estimates unreliable—usually overestimates

=> Acknowledge alternative assumptions & implications
### 3. Some things I have done re: specific case

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<tbody>
<tr>
<td><strong>1. Stay quiet</strong></td>
<td>Almost quiet</td>
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</table>
| **3. Submit ideas to philosophy of science journals** | Most effort here.  
No errors identified yet.  
NSF SGER. |
| **2. Submit ideas to science journals** | Progressively stripped back.  
NSF-funded visits with researchers.  
Unpublished mss.  
Write book & move on. |
| **4. Tease out the historical, sociological, political, cultural implications** | Session at joint meetings of STS societies, Vancouver 2006.  
Visiting fellowship at KLI near Vienna 2008 & 2010.  
Planned blog of manuscripts and reviews.  
New book in the works. |
| **5. Tease out the political implications** | Genetic Studies Working Group.  
Long interview with reporter for *Science*. |
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   Q: Case studies or systematic treatment of influencing research re-direction

2. Specific case

3. Some things I have done re: #2
   Range from direct -> backdoor/indirect ways to influence scientific debate
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*Latest installment: Come to IU -> discussion??*