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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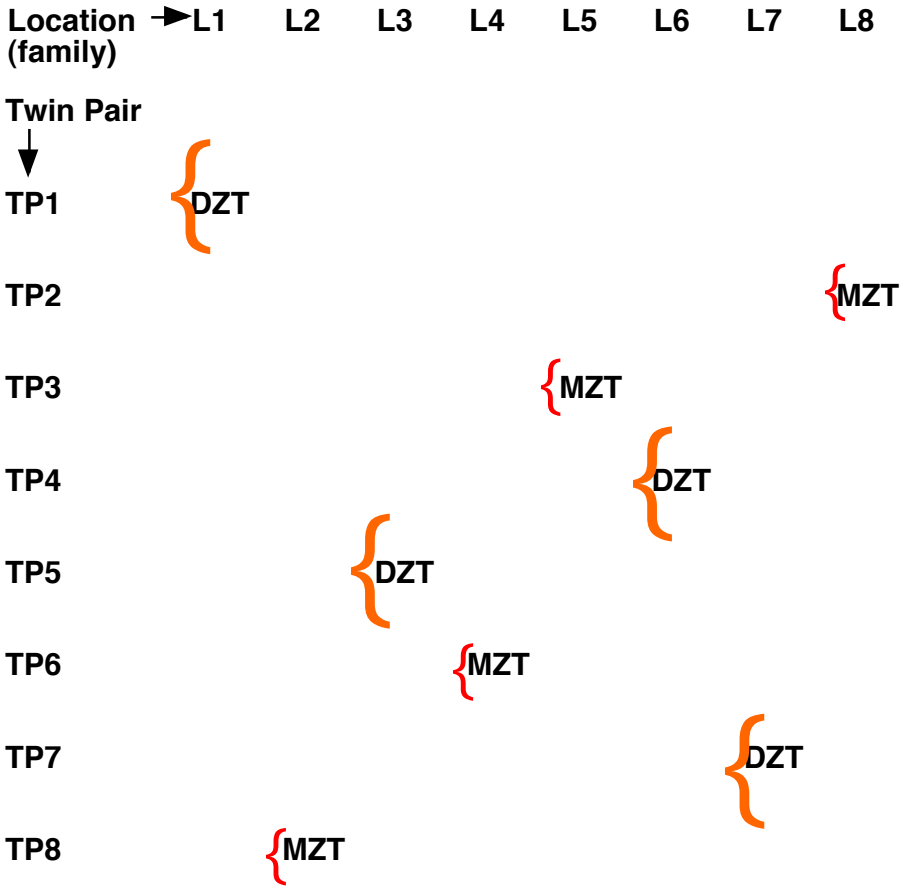
sources & follow-up: http://bit.ly/tayloroverlook

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

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

0. Specific Case: Quantitative Genetics and Underlying Heterogeneity



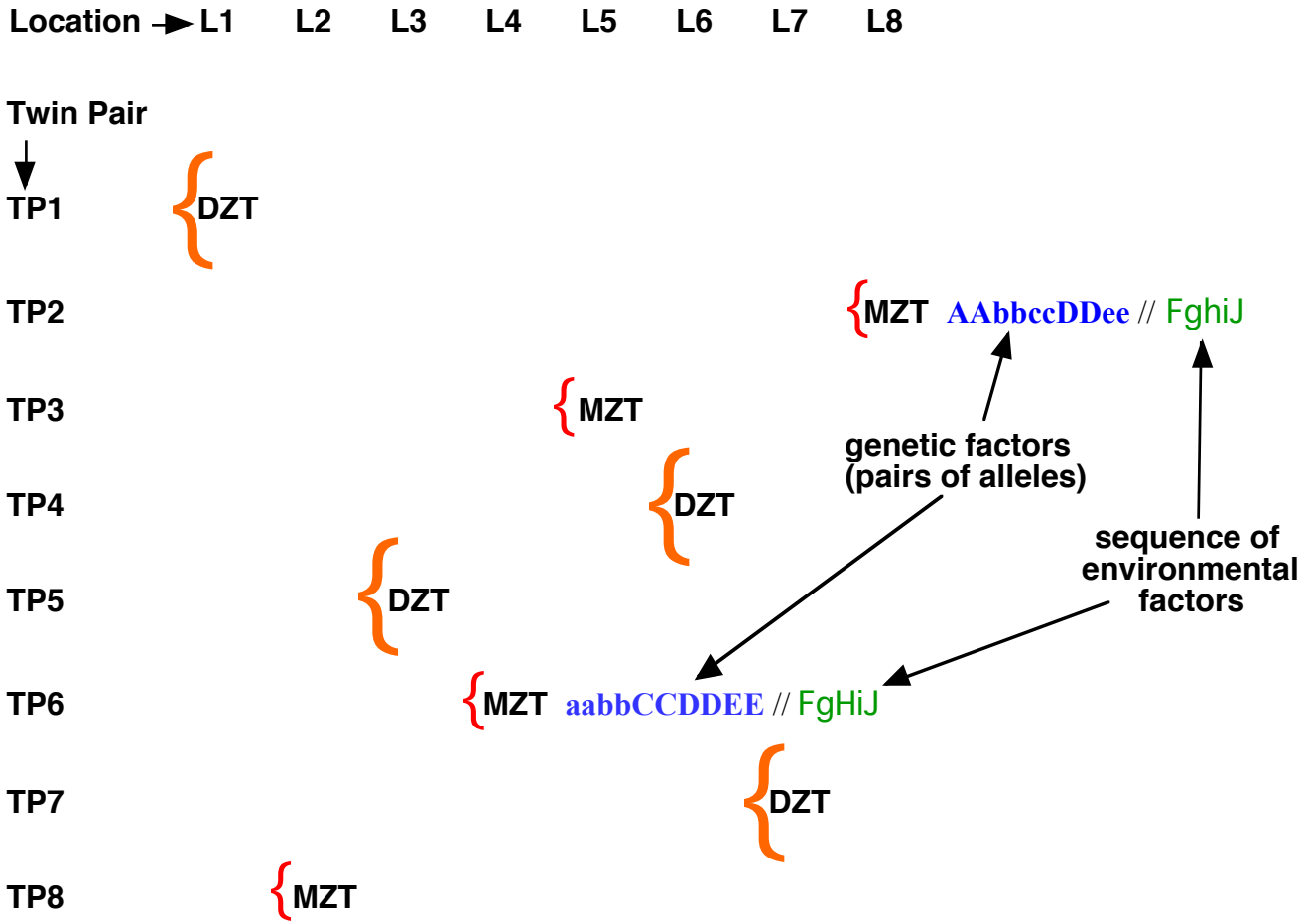
TRAIT is height

DZT less similar on average than MZT

& MZT share all genes, while DZT do not

=> genetic relatedness is associated with similarity in trait

(substantial heritability of height)


Location → L1 L2 L3 L4 L5 L6 L7 L8
Twin Pair
TP1
DZT
TP2
MZT AAbbccDDee // FghiJ
TP3
MZT
TP4
DZT
TP5
DZT
TP6
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TP7
DZT
TP8
MZT
genetic factors (pairs of alleles)
sequence of environmental factors

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

U.S. philosophy of biology-last 30 years

Emphasis on conceptual systemization of biologists' work

Notably: Theory of natural selection

Conceptual structure of Chapters 1-3 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*

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    [#1 & 2] Variation among organisms in characters
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    [# 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 most fitted (=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

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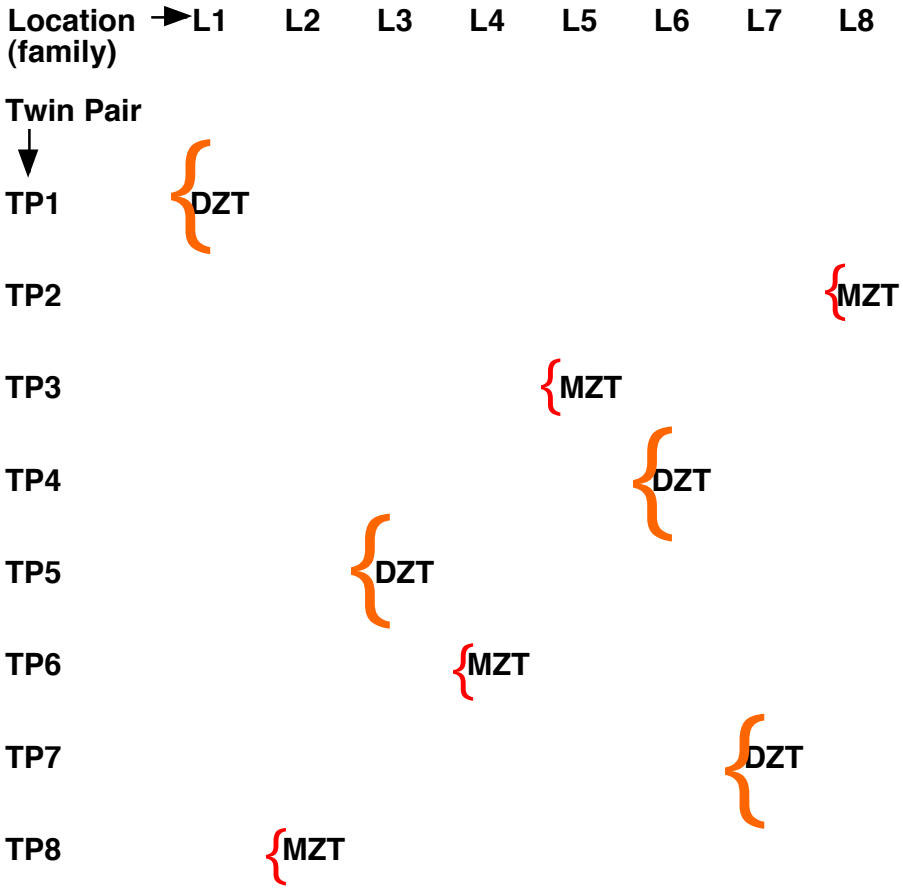
Q: Case studies or systematic treatment of range of ways *(direct -> backdoor)* to influence scientific debates?

Stanford (2006) *Exceeding Our Grasp: Science, History, and the Problem of Unconceived Alternatives*

Chang (2013) “Putting science back into the history of science” (video)

Other?

2. Specific Case: Quantitative Genetics and Underlying Heterogeneity



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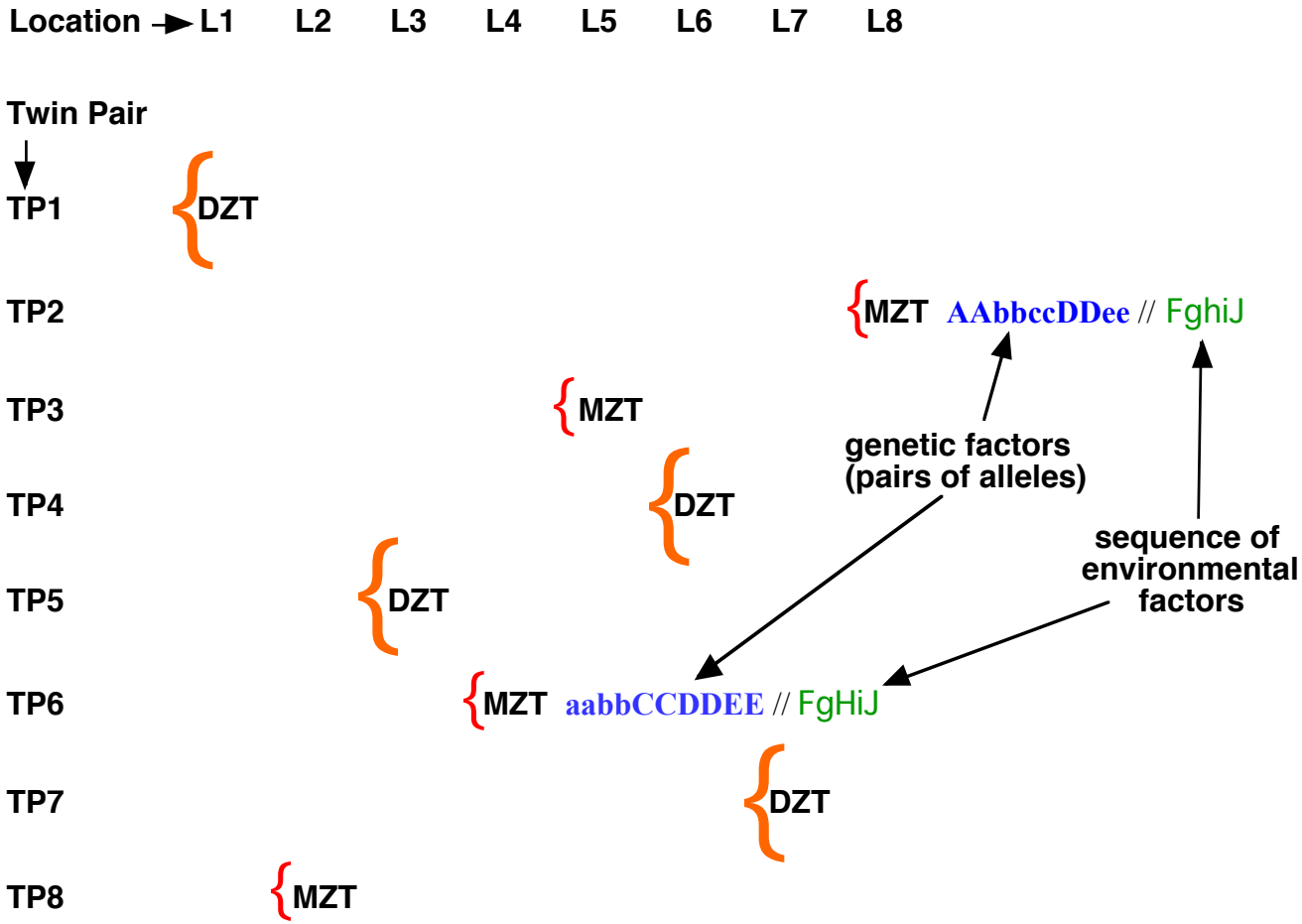
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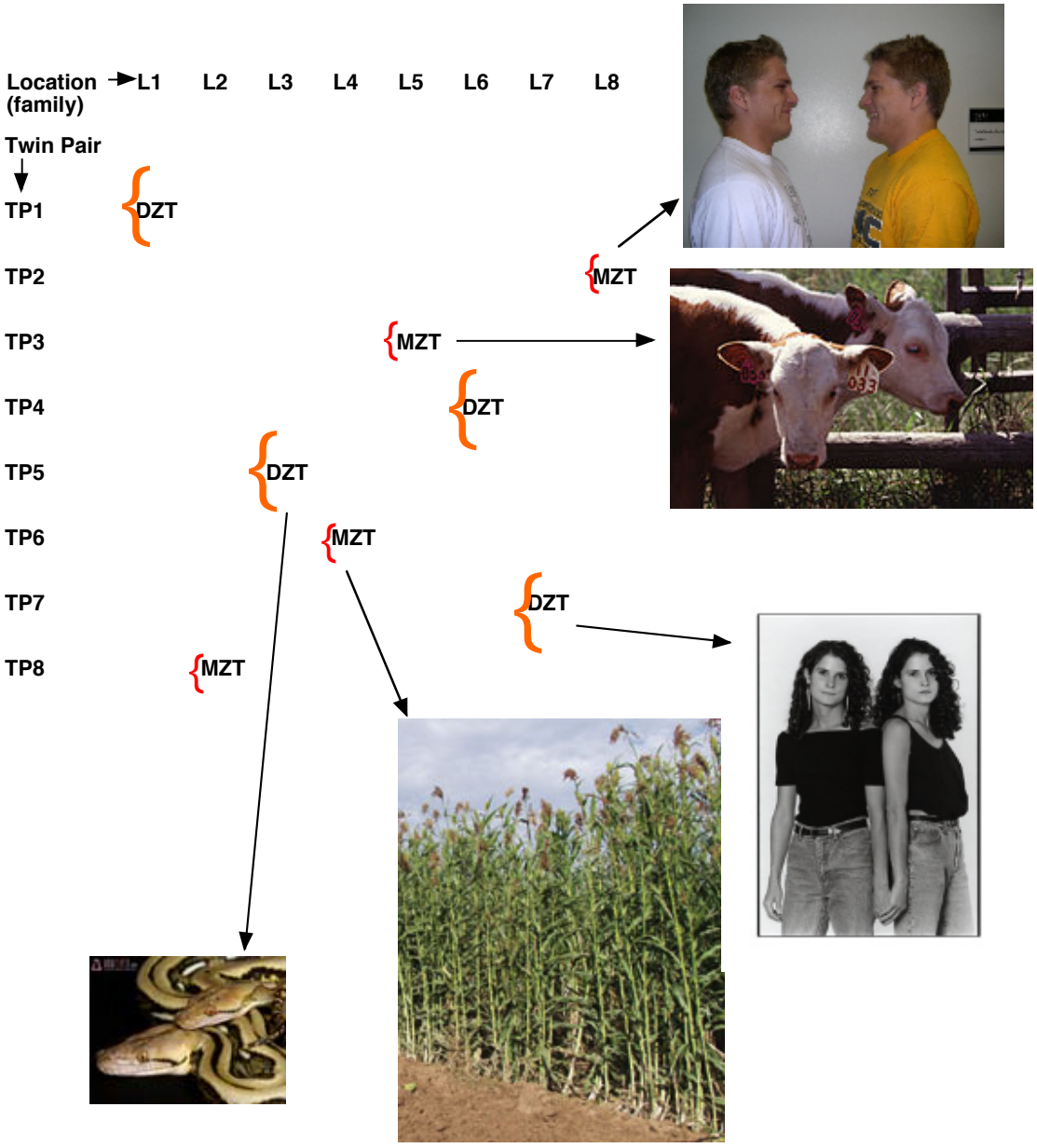
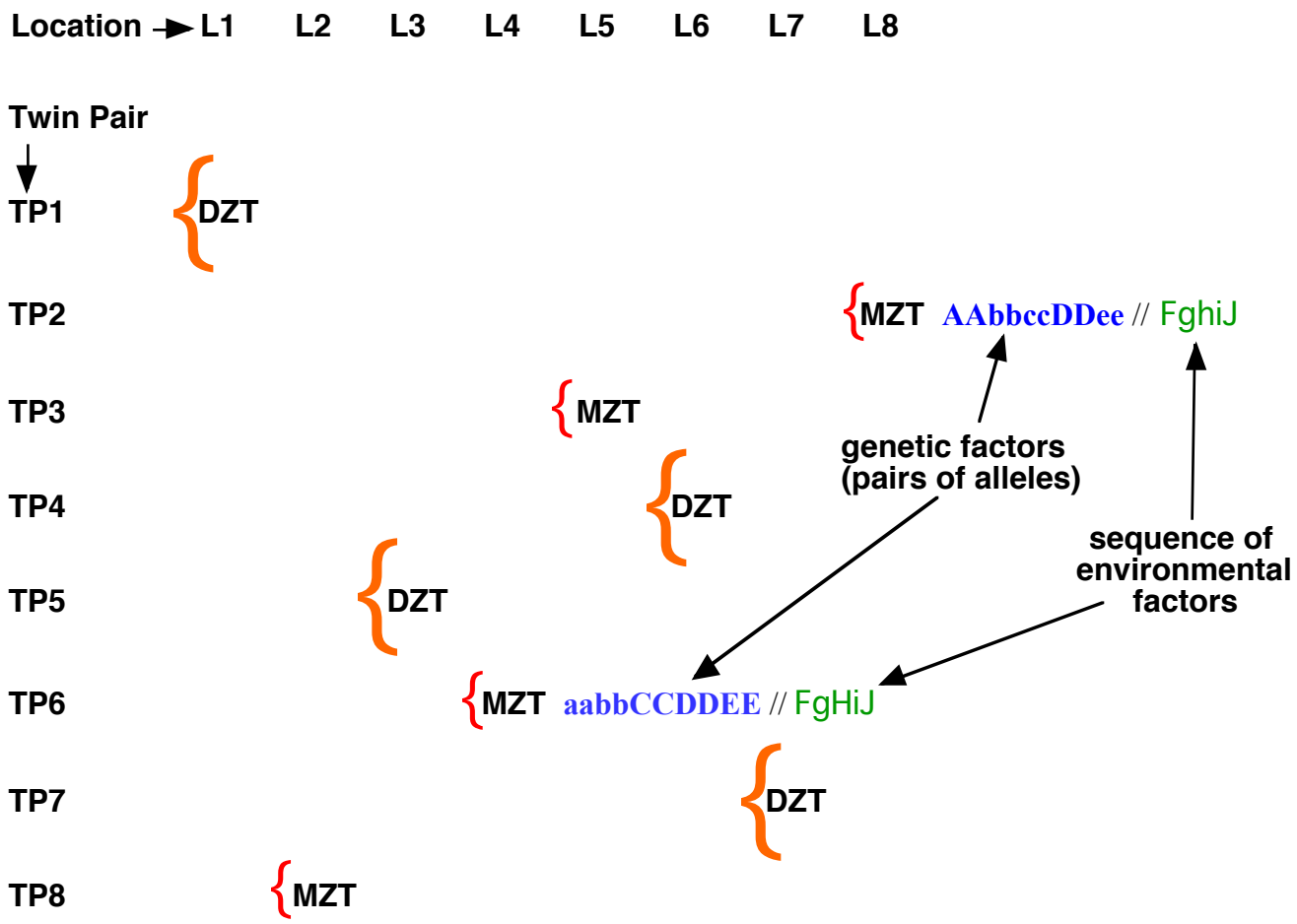

Location (family)
L1
L2
L3
L4
L5
L6
L7
L8
Twin Pair
TP1
DZT
TP2
MZT
TP3
MZT
TP4
DZT
TP5
DZT
TP6
MZT
TP7
DZT
TP8
MZT



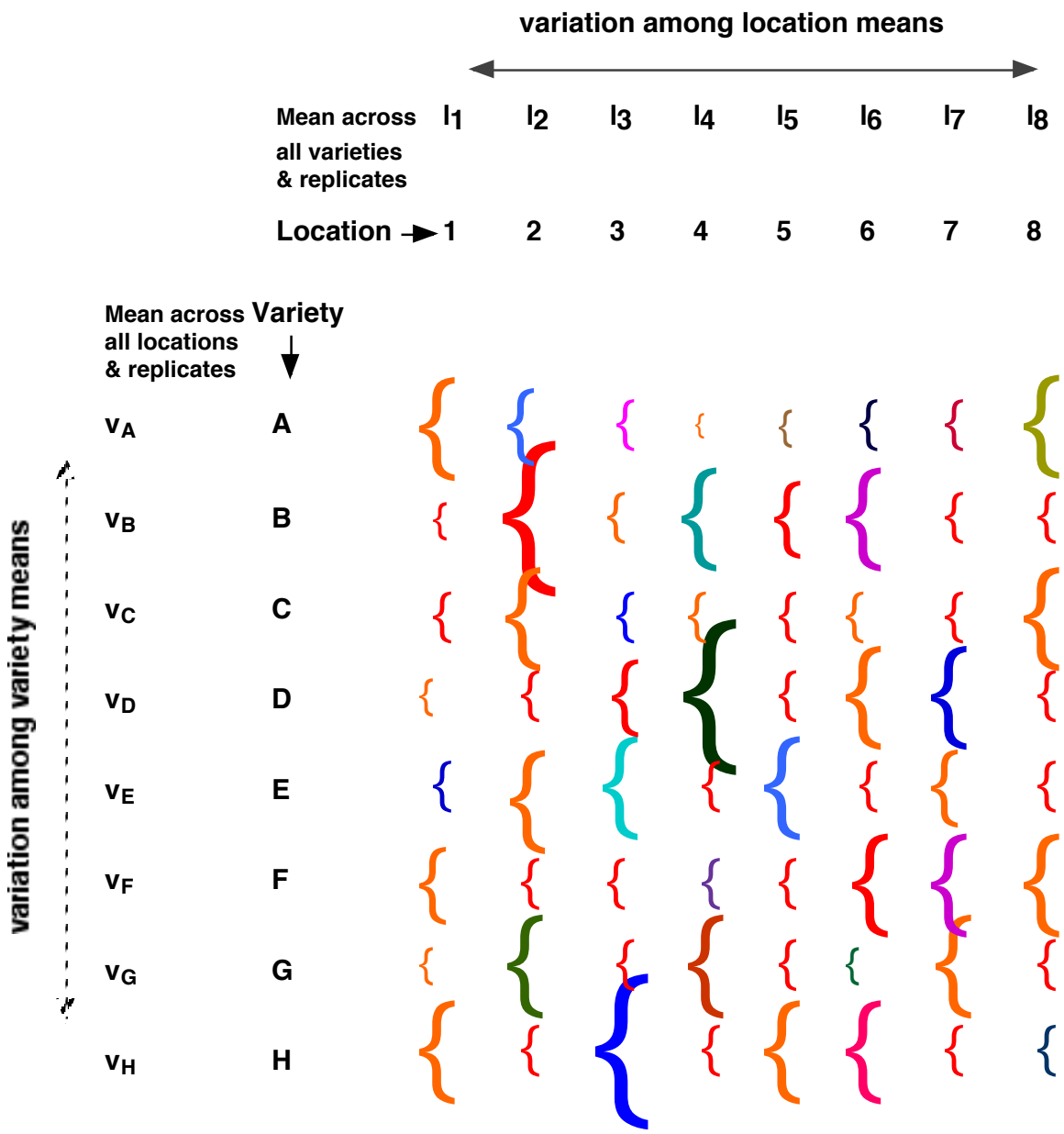
-> Qs: Implications?

Why overlooked?

Why overlooked?

Terminology

genetic$_1$	quantitative genetics	trait	variance of trait, partitioned (AnOVa)
genetic$_2$	relatedness	variable part of genome	fraction of variable part of genome shared
genetic$_3$	genetics	site(s) on genome	heterozygosity at site(s)


variation among location means
Mean across all varieties & replicates
l1 l2 l3 l4 l5 l6 l7 l8
Location → 1 2 3 4 5 6 7 8
Mean across all locations & replicates
Variety
vA A
vB B
vC C
vD D
vE E
vF F
vG G
vH H
variation among variety means

Heritability

=

variance

among

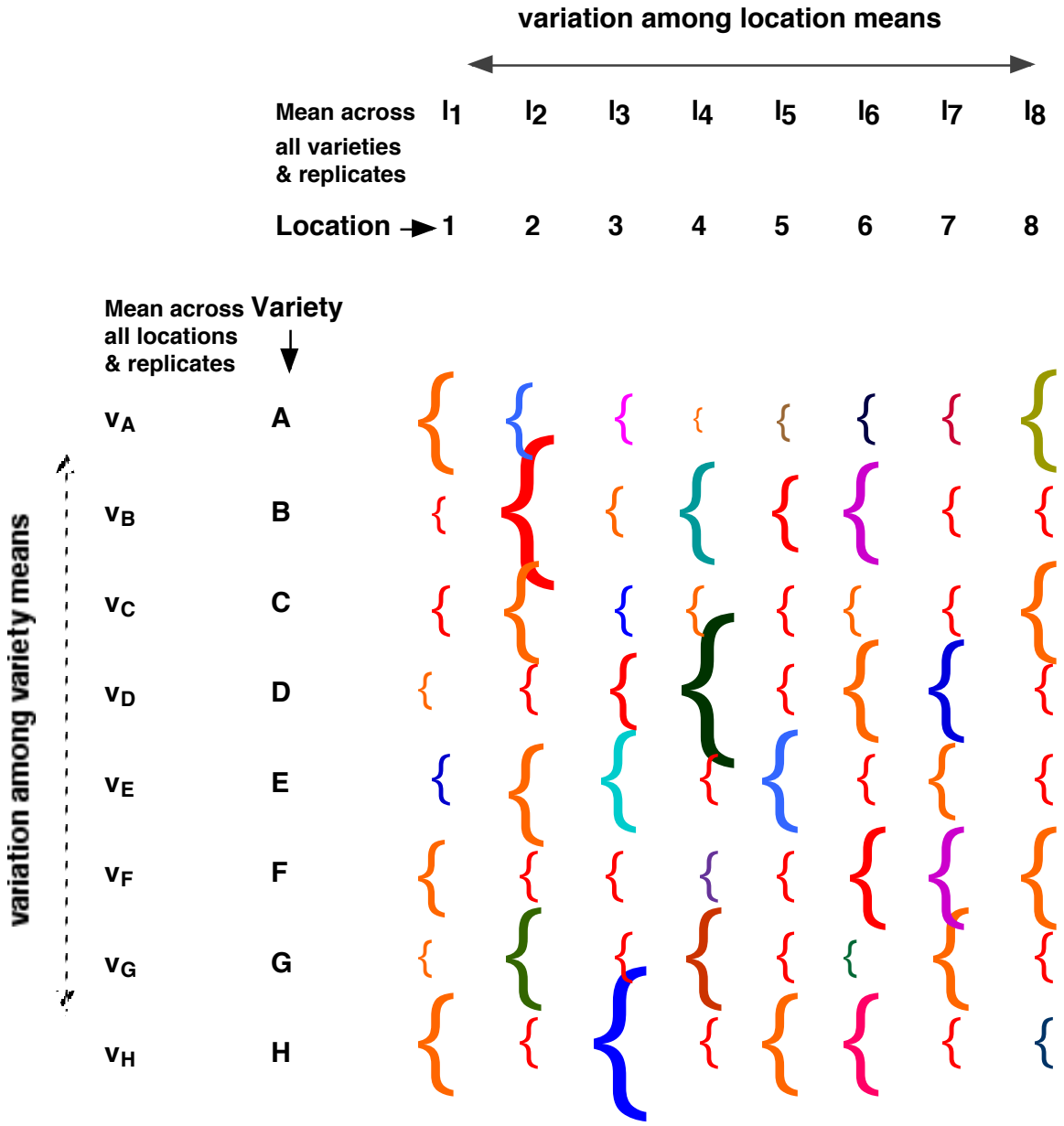
variety means

for the trait

/ total

variance for

the trait



Why overlooked?

Terminology

"contribution of genetic differences to observed differences among individuals"

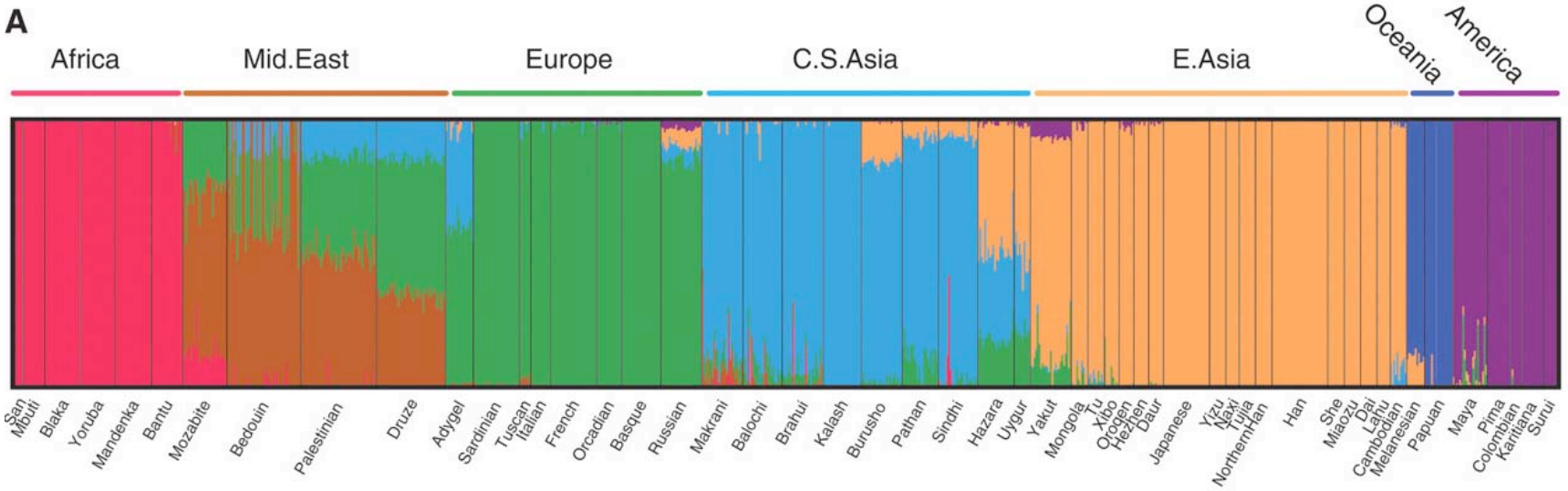
(Plomin et al. 1997, 83)

"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

Why overlooked? (additional angle)

Terminology <-> Convenient conflations

Nature-Nurture Sciences

partition variation in observable traits

partition variation associated with measurable factors

trait established by n.s. for trait in the past

factors associated with between-group averages

fixity vs flexibility of development of individual

Implications?

Q: Application of human heritability

if underlying heterogeneity is possible?

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- Undertake research w/o reference to trait's heritability

(heterogeneity, not polygenic, as explanation of GWA results)

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- Restrict attention to variation within a set of relatives
- Focus on heritability as a fraction of the variation (useful in ag. & lab. breeding)
- 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”

Historical Origins -> Unconceived alternative

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 (GxE) interaction variance subsumed in augmented "Variety" variance (h^2)

=> Human heritability estimates unreliable—usually overestimates

=> Acknowledge alternative assumptions & implications

3. Some things I have done re: specific case

1. Stay quiet	Almost quiet
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 Wrote book to move on (back to epidemiology) (*Nature-Nurture? No, 2014*)
4. Tease out the historical, sociological, political, cultural implications	Session at joint meetings of STS societies, Vancouver 2006; ISHPSSB 2015 Visiting fellowship at KLI near Vienna 2008 & 2010 ~~Planned blog of manuscripts and reviews~~ New sci. studies book in the works Blog: 50 whys to look for genes Puzzling: convenient conflation of 5 nature-nurture sciences and 2^{+} GxE interactions
5. Tease out the political implications	Genetic Studies Working Group Long interview with reporter for *Science*

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1. In-principle question

   Q: Case studies or systematic treatment of influencing research re-direction

2. Specific case

   Terminology. Implications. Origins & alternative. Implications.

3. Some things I have done re: #2

   Range from direct -> backdoor/indirect ways to influence scientific debate

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Latest installment: Give this talk today -> discussion??

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