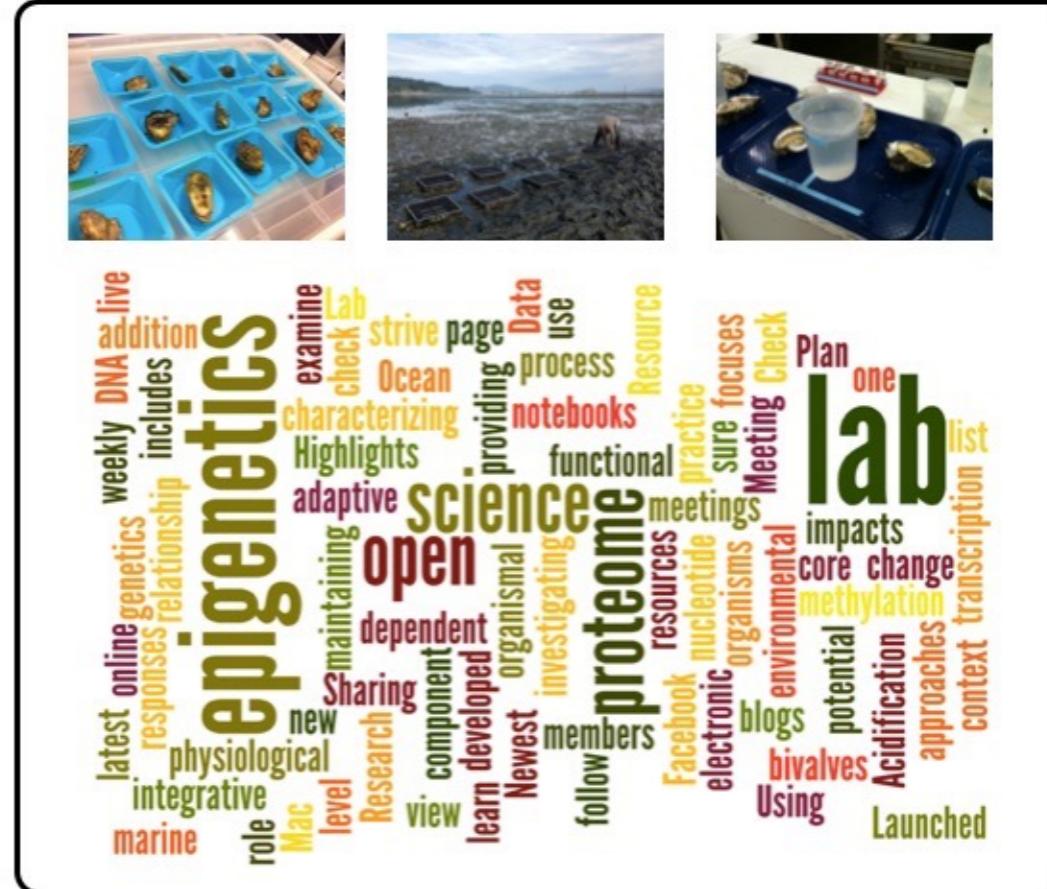


Does DNA Methylation Facilitate Genome Diversity and Phenotypic Plasticity in Marine Invertebrates?

Steven Roberts
Associate Professor
School of Aquatic and Fishery Sciences
robertslab.info
@sr320

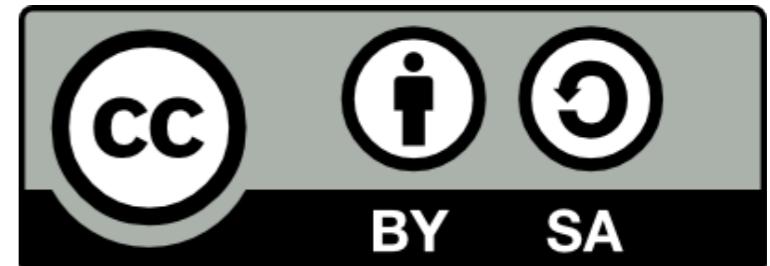


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IP[y]: IPython
Interactive Computing



OpenNotebookScience

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onsnetwork.org

- Data, Preprints, Proposals, Lab Meetings, Web Cams, Slidedecks available

These slides plus links @ robertslab.info

Background

disease resistance

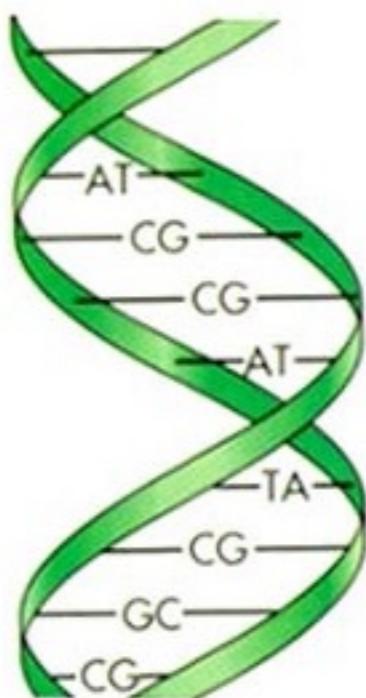


growth

color

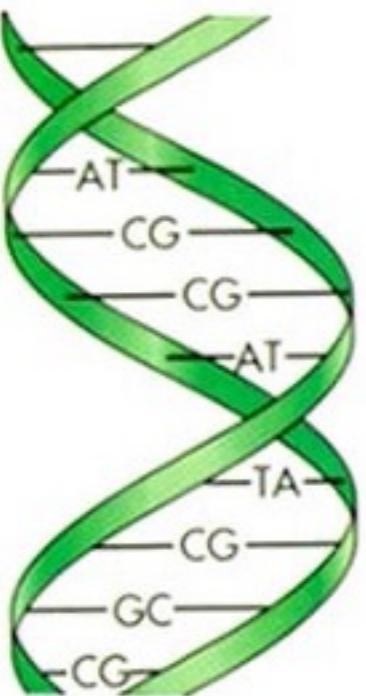
stress
tolerance

Traits



Background

Transcriptome



disease resistance



Traits

growth

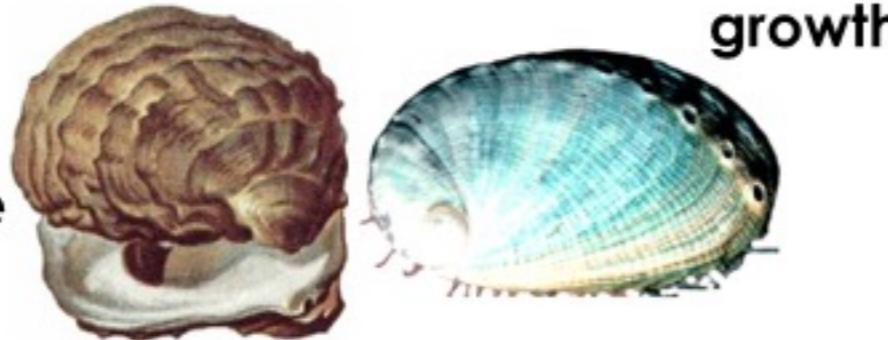
color

stress
tolerance



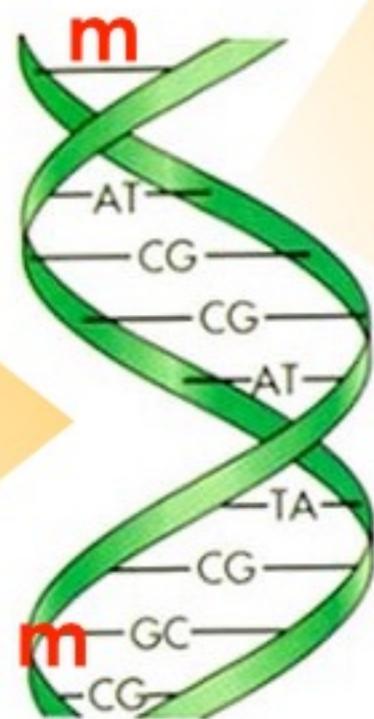
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disease resistance



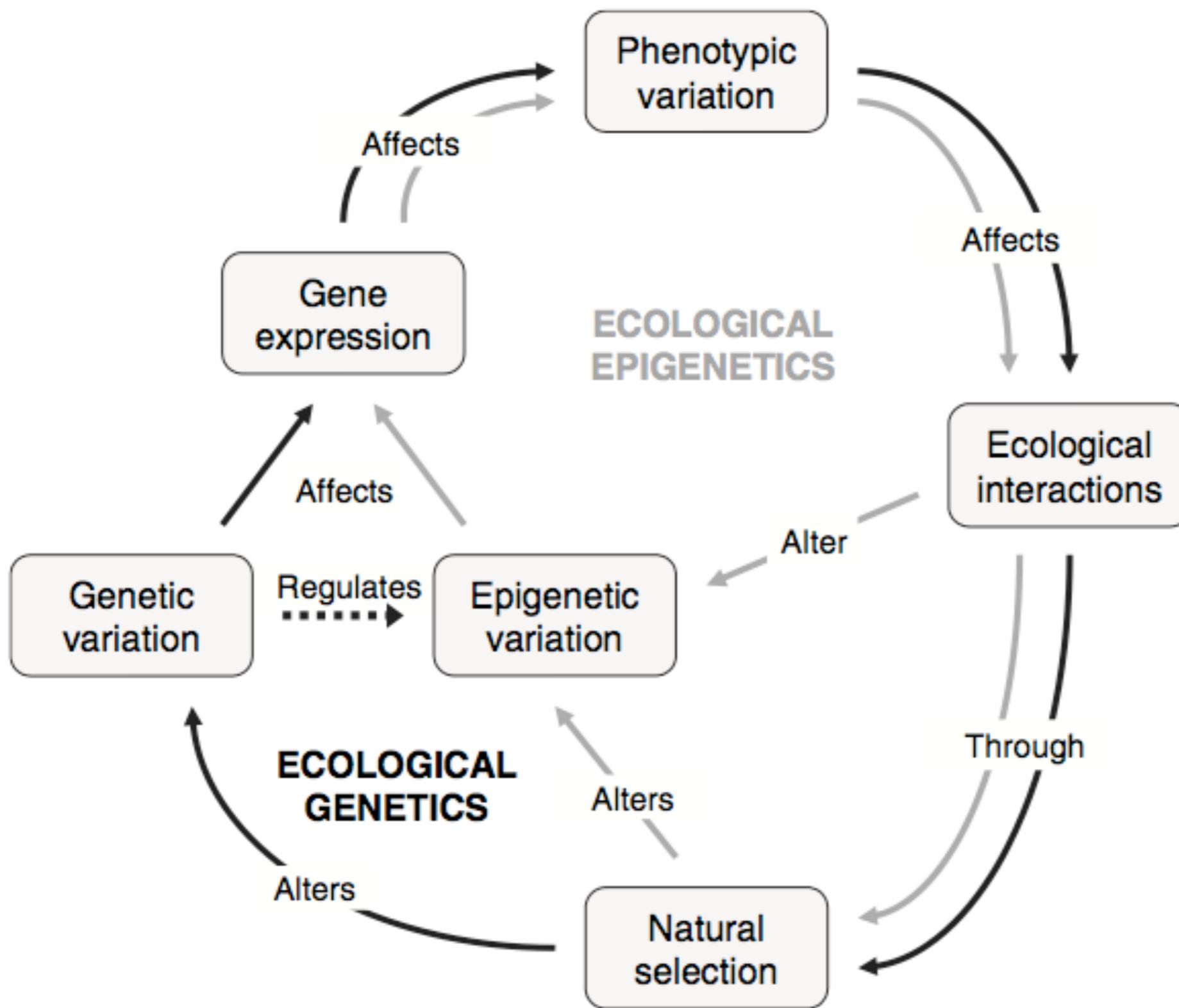
growth

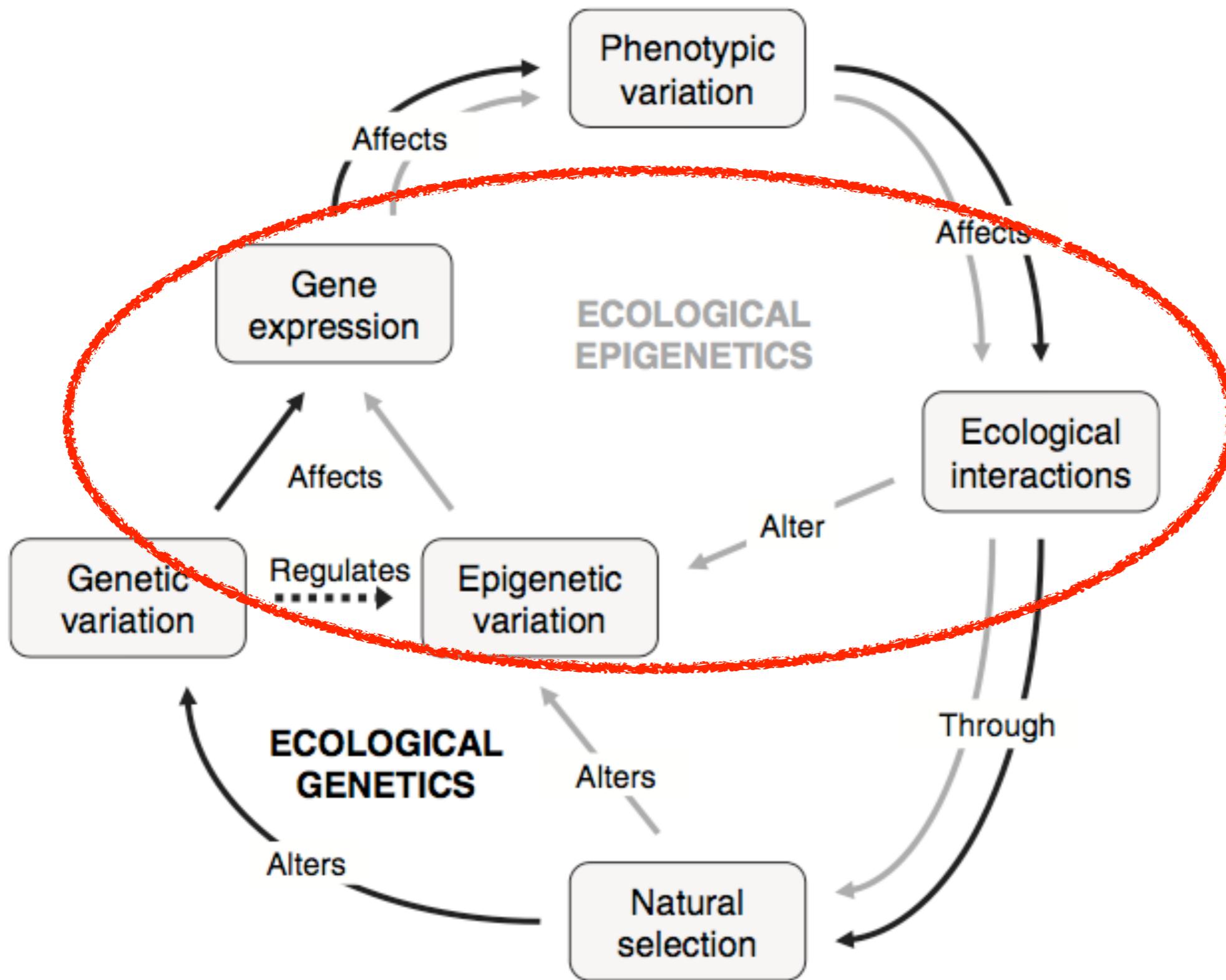
Traits

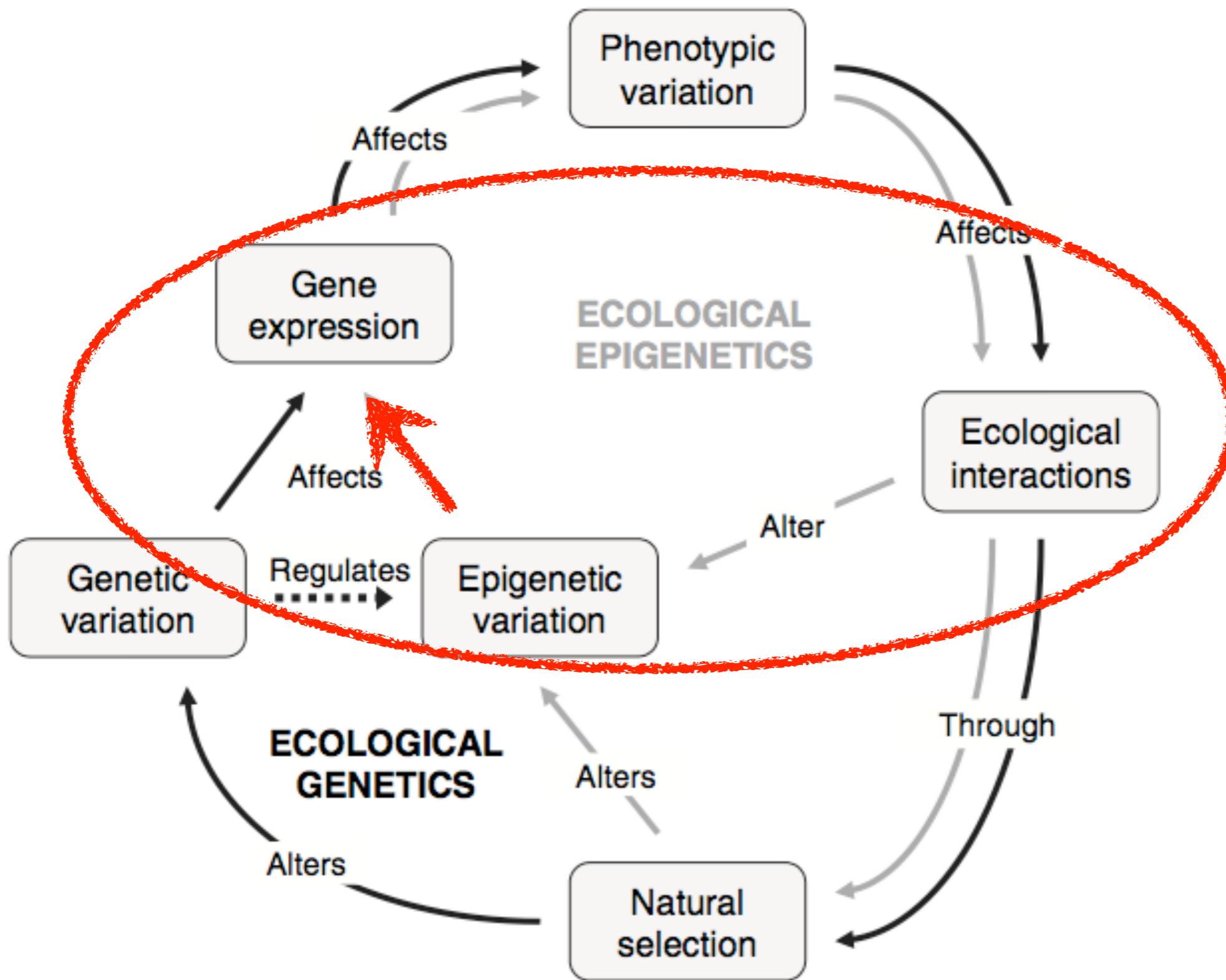


Epigenetics

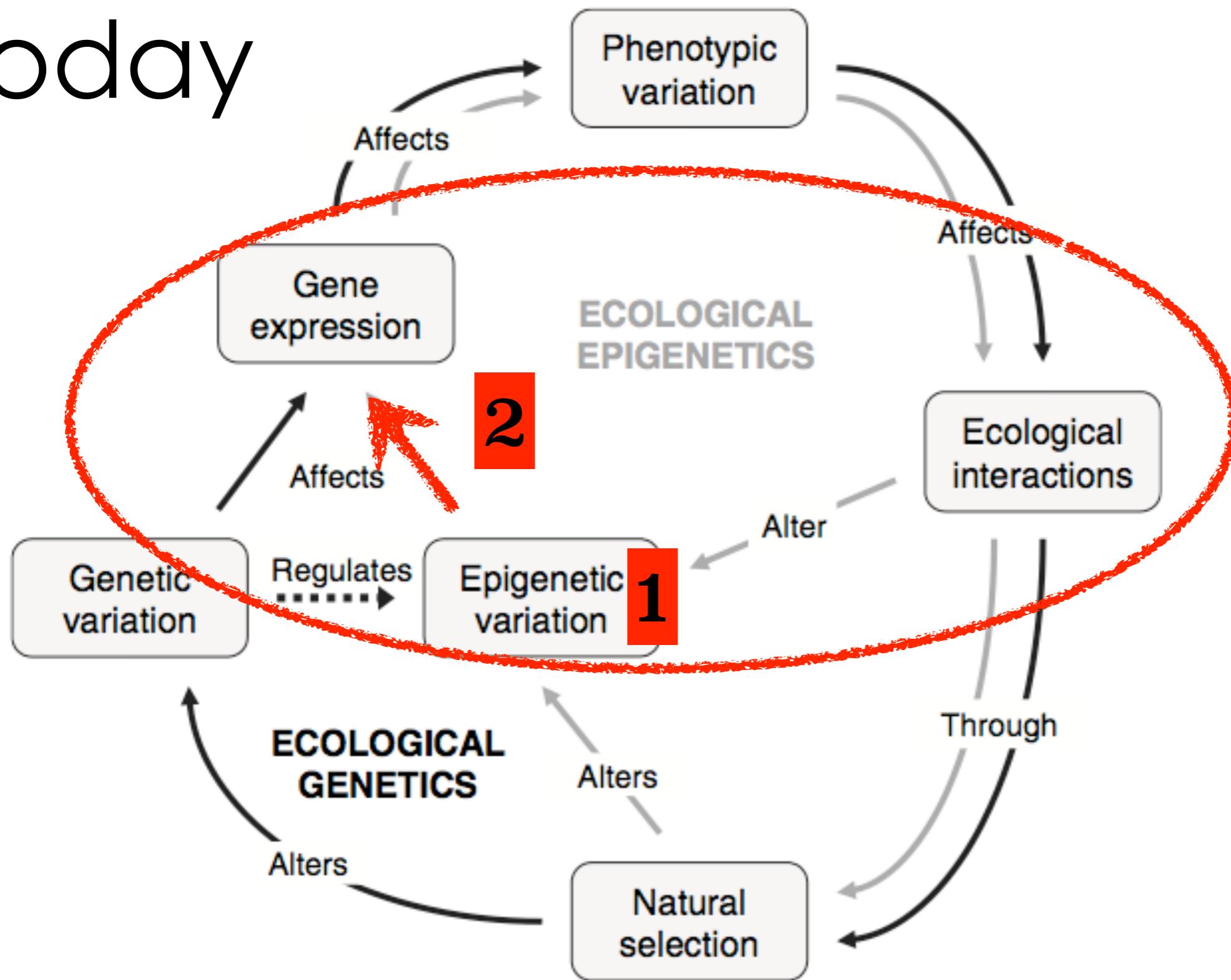








Today



Ecology Letters, (2008) 11: 106–115

doi: 10.1111/j.1461-0248.2007.01130.x

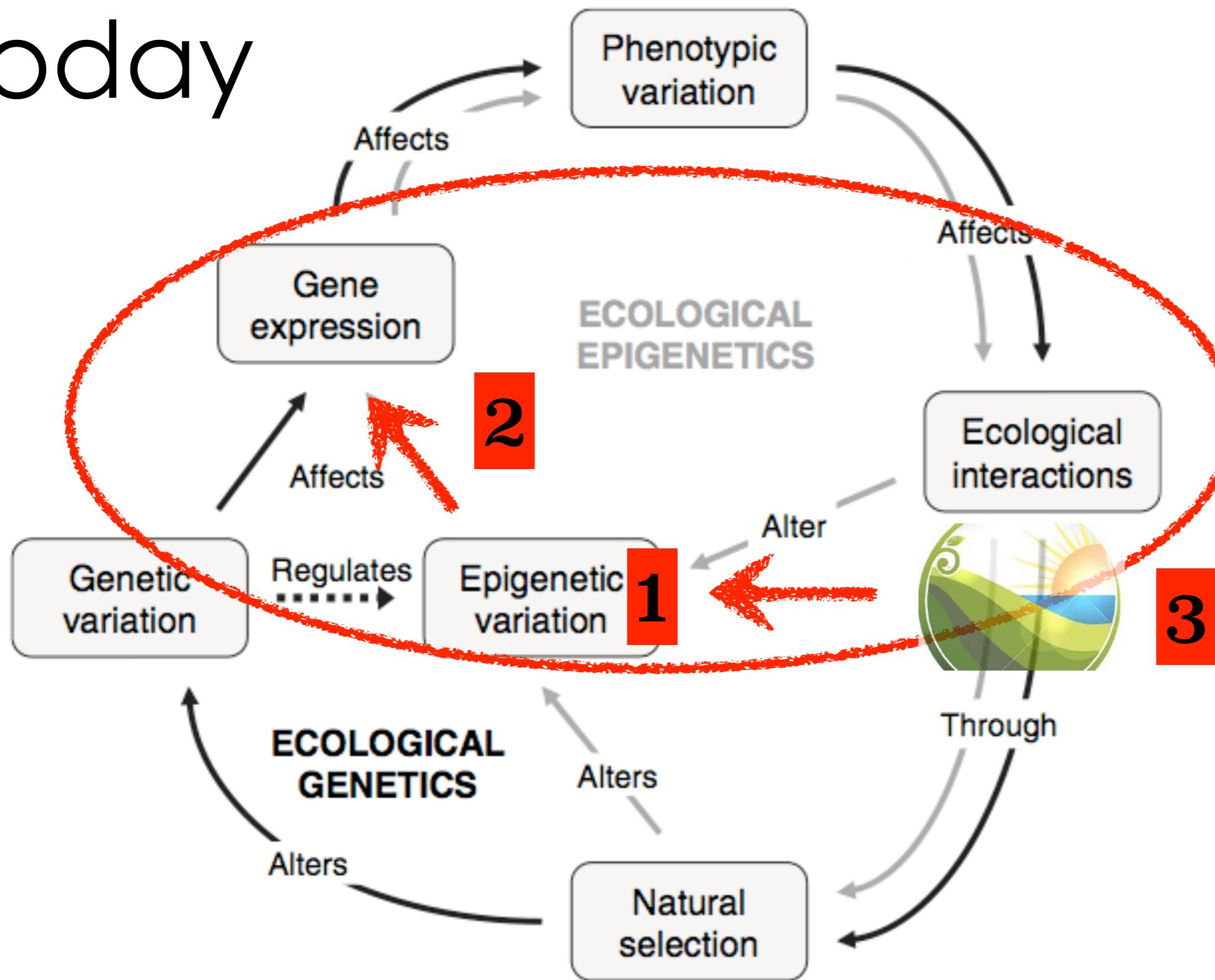
modified from

IDEA AND
PERSPECTIVE

Epigenetics for ecologists

Oliver Bossdorf,^{1,*} Christina L.
Richards² and Massimo Pigliucci³

Today



Ecology Letters, (2008) 11: 106–115

doi: 10.1111/j.1461-0248.2007.01130.x

modified from

IDEA AND
PERSPECTIVE

Epigenetics for ecologists

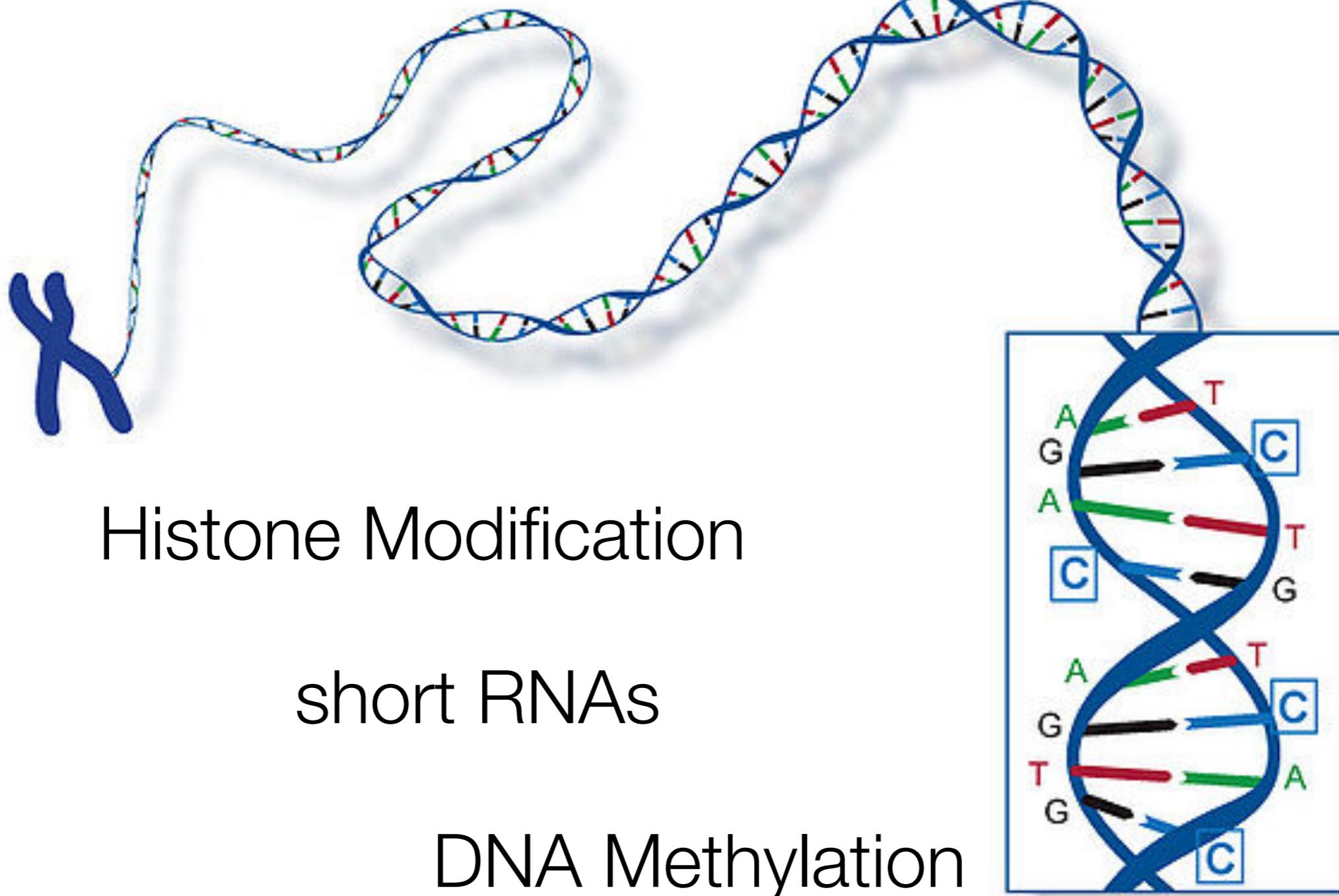
Oliver Bossdorf,^{1,*} Christina L.
Richards² and Massimo Pigliucci³



Genome Resources



Epigenetics



Epigenetics



Photo credit: Flickr, Creative Commons, he-boden



Epigenetics



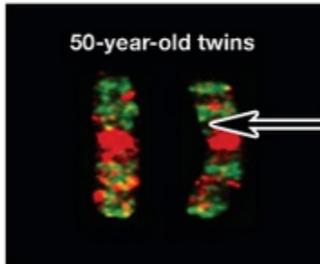
Nature AND Nurture

Chromosome 3 Pairs

3-year old twins vs. 50-year-old twins



Yellow shows where the twins have epigenetic tags in the same place.



Red and green show where the twins have epigenetic tags in different places.

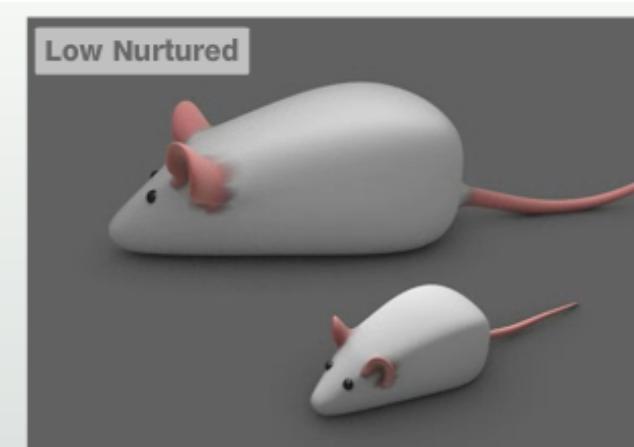
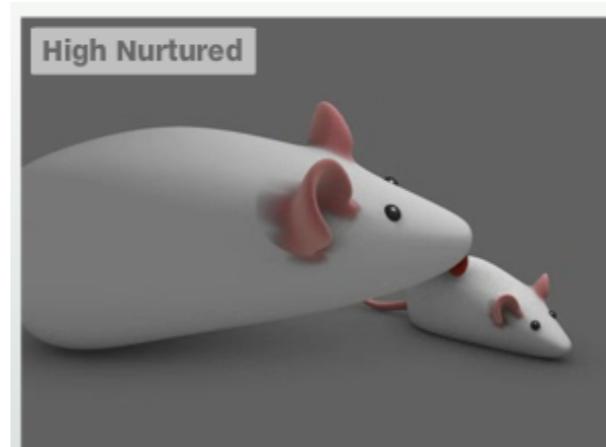
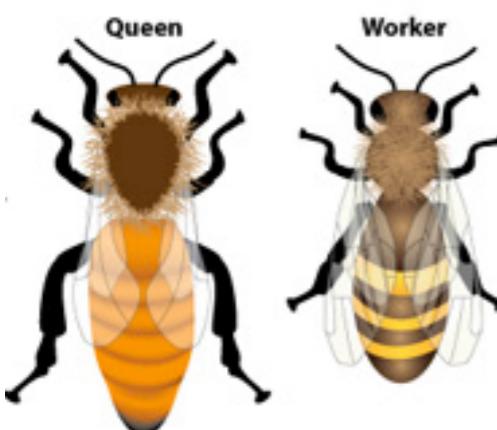
While pregnant, both of their mothers were fed Bisphenol A (BPA) but DIFFERENT DIETS:

The mother of this mouse received a **normal mouse diet**

The mother of this mouse received a diet **supplemented** with choline, folic acid, betaine and vitamin B12

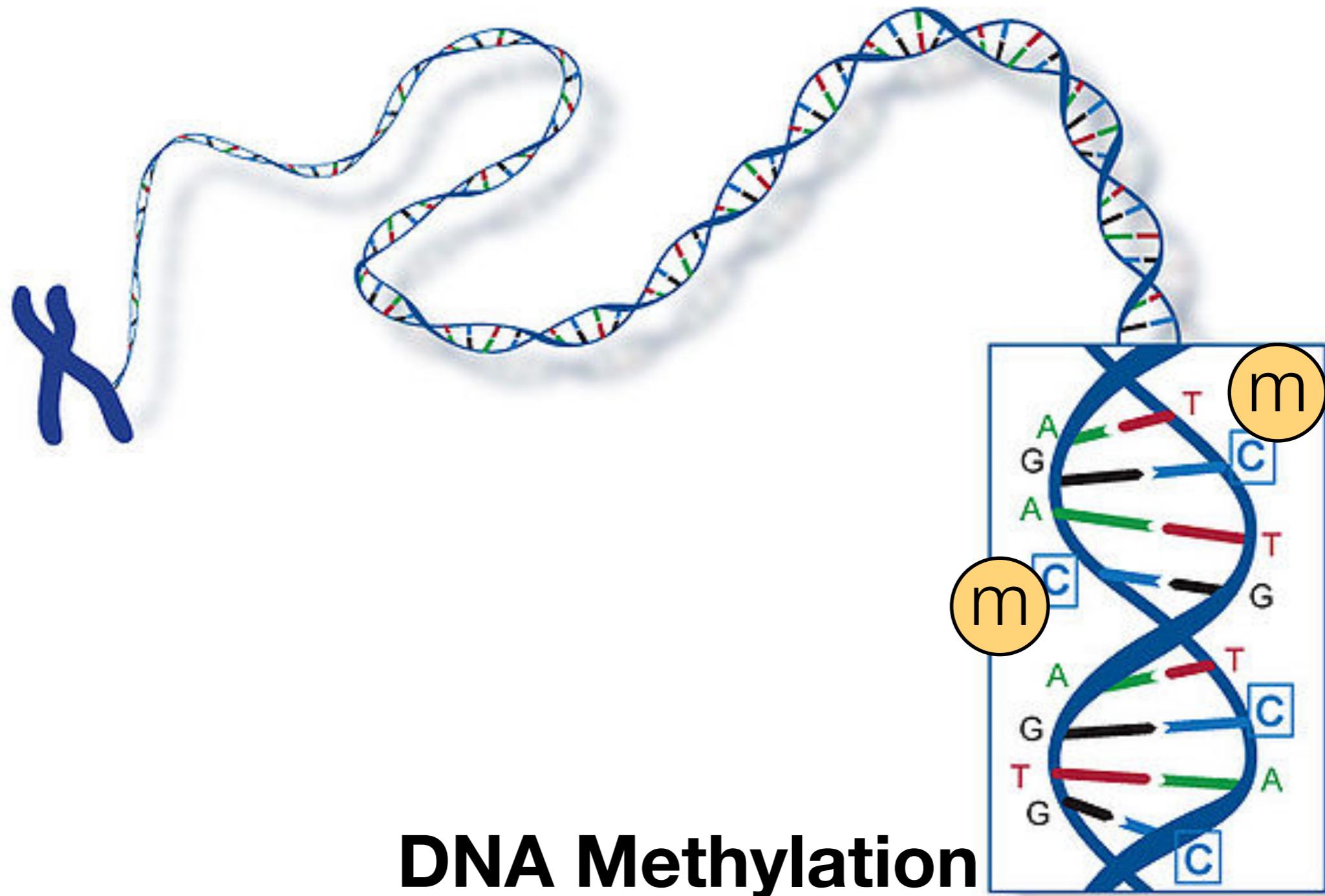


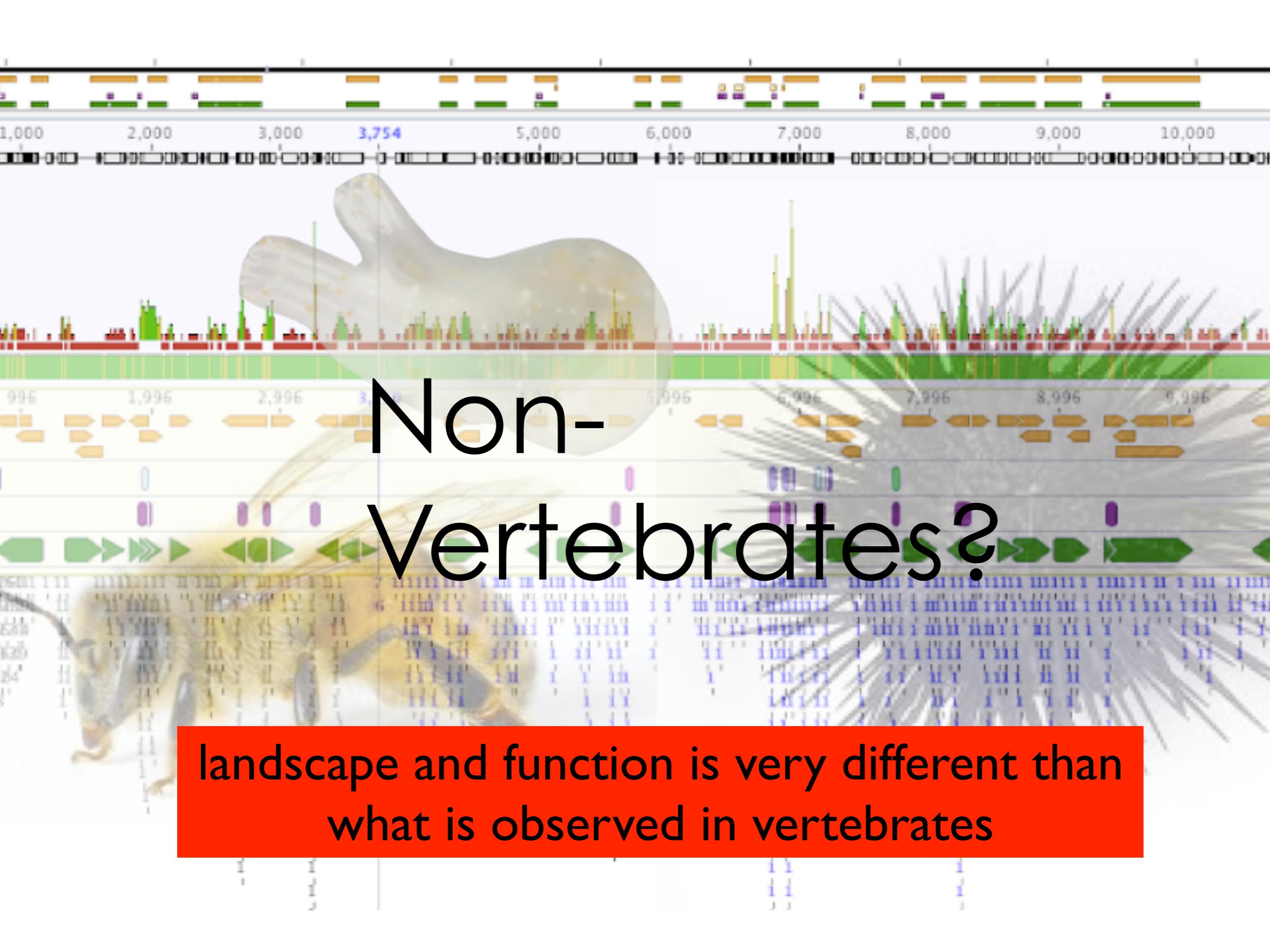
Queen Bee Larvae: Queens are raised in specially constructed cells called "queen cups," which are filled with royal jelly.



These mothers come from a long line of inbred rats, so their genomes are highly similar. But they care for their pups very differently.

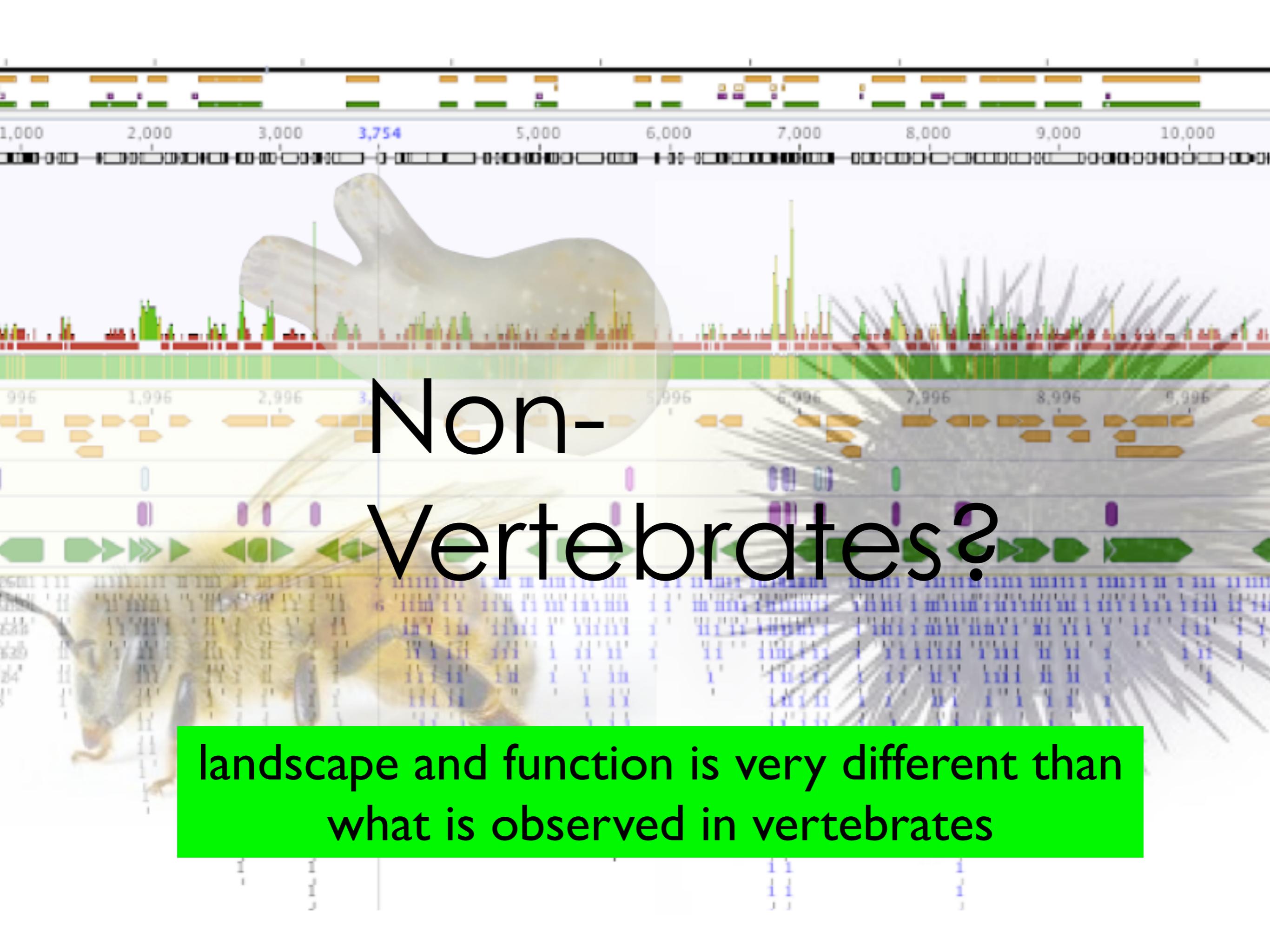
AUDIO





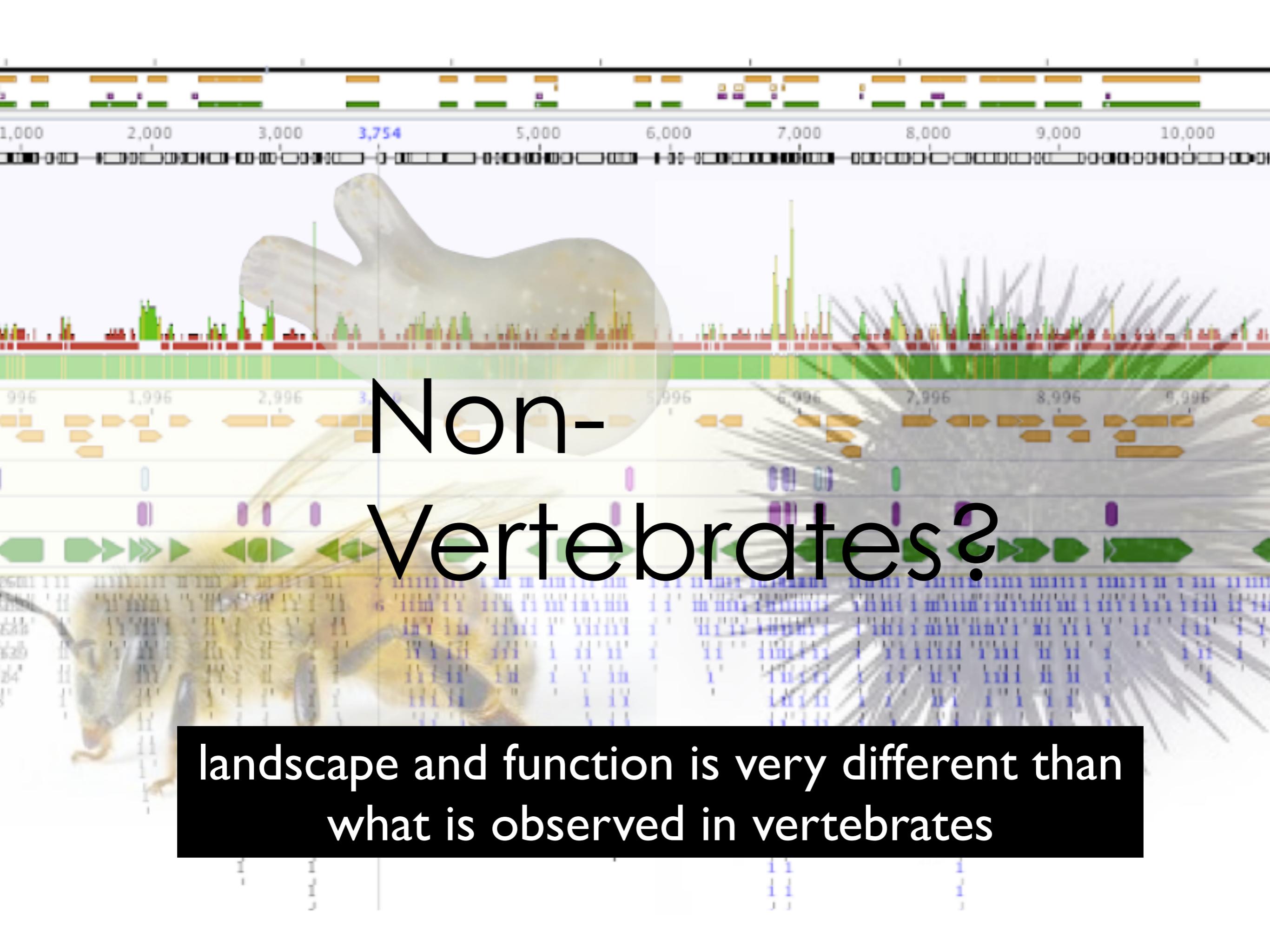
Non- Vertebrates?

landscape and function is very different than
what is observed in vertebrates



Non- Vertebrates?

landscape and function is very different than
what is observed in vertebrates



Non- Vertebrates?

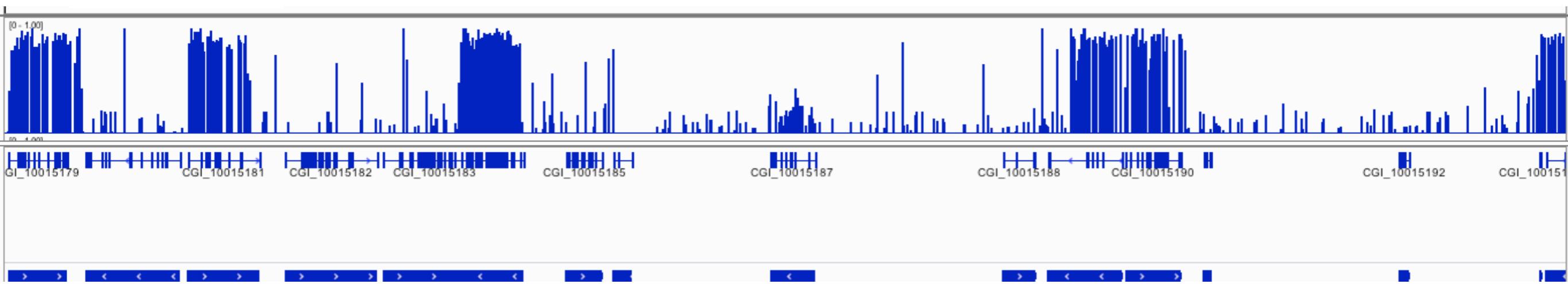
landscape and function is very different than
what is observed in vertebrates

*Absent in
several
model
organisms*



Oysters?

Epigenetic variation **1**



mosaic

associated with gene bodies

Epigenetic variation **1**

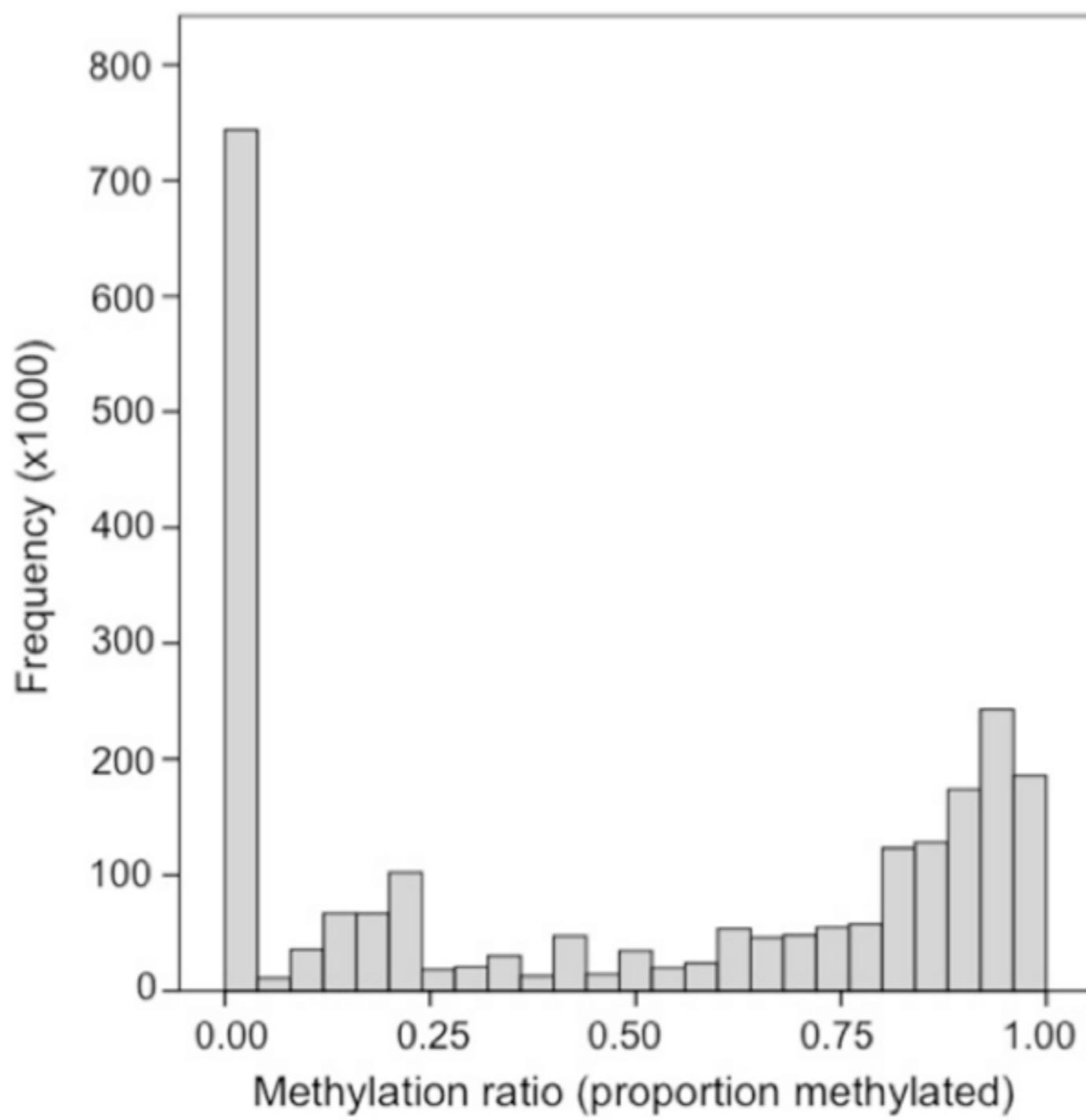
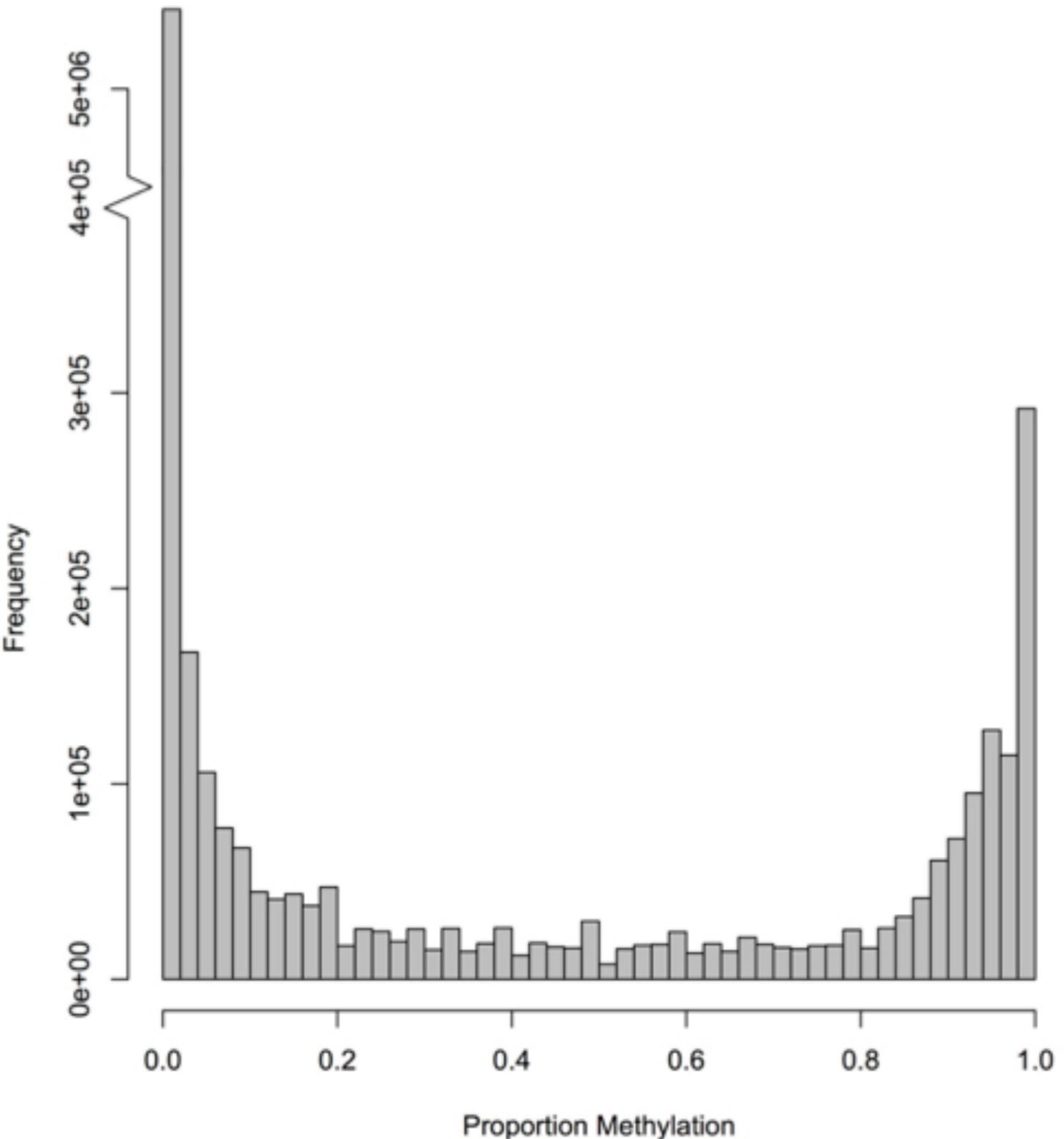
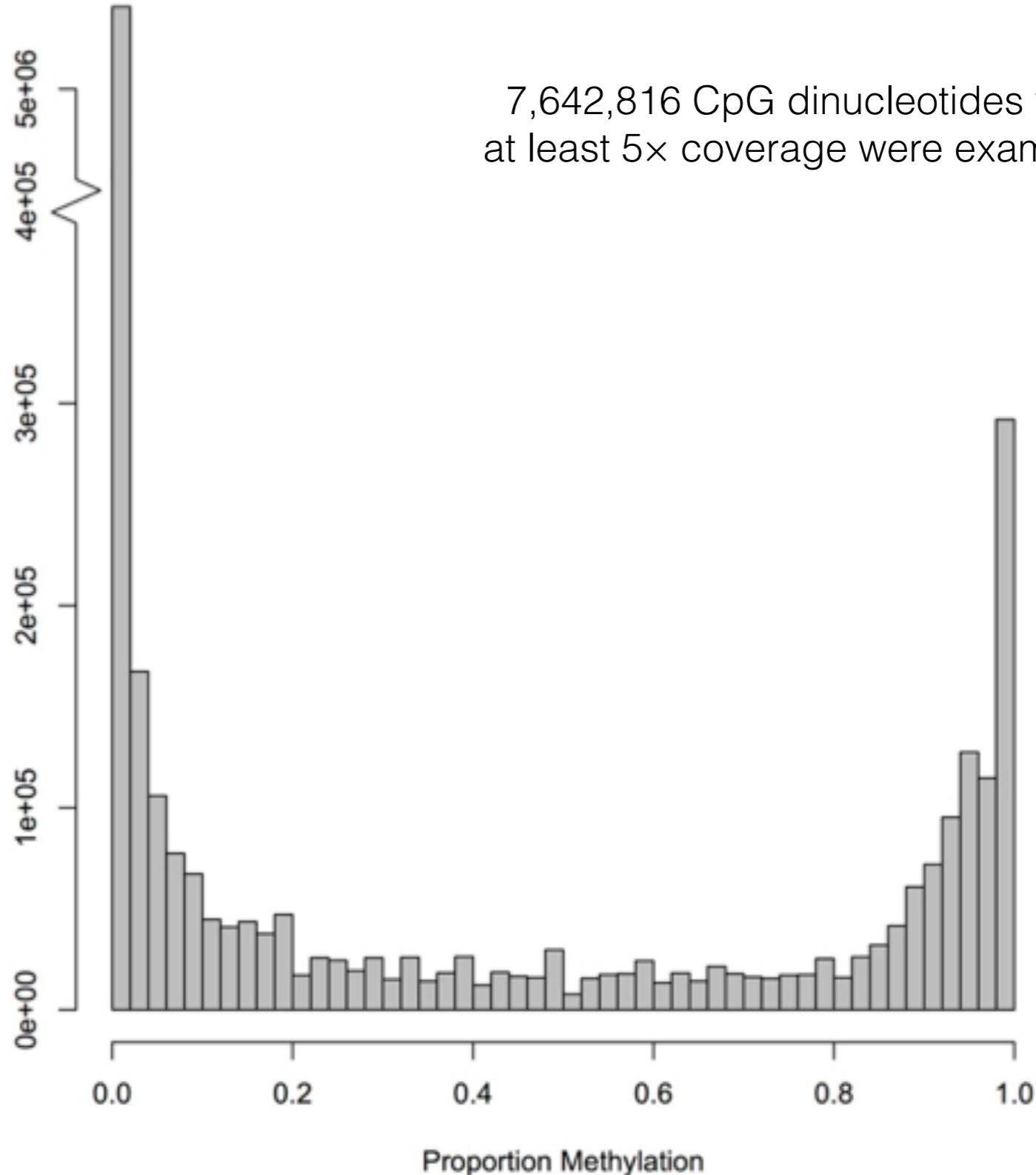
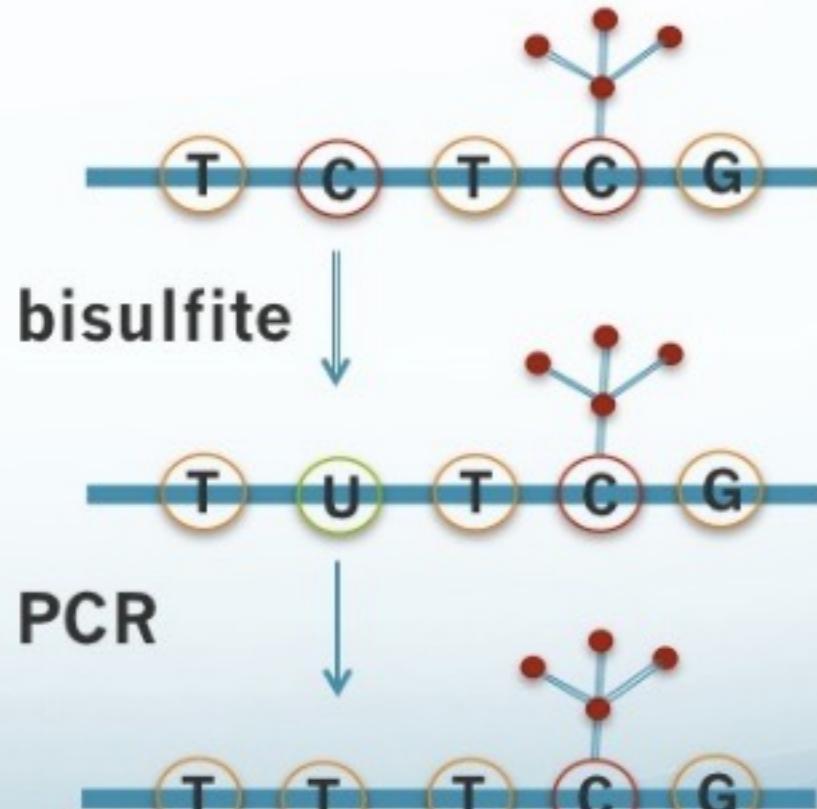


Figure 1 Frequency distribution of methylation ratios for CpG dinucleotides in oyster gill tissue. A total of 2,625,745 CpG dinucleotides with $\geq 5 \times$ coverage are represented.



Epigenetic variation **1**

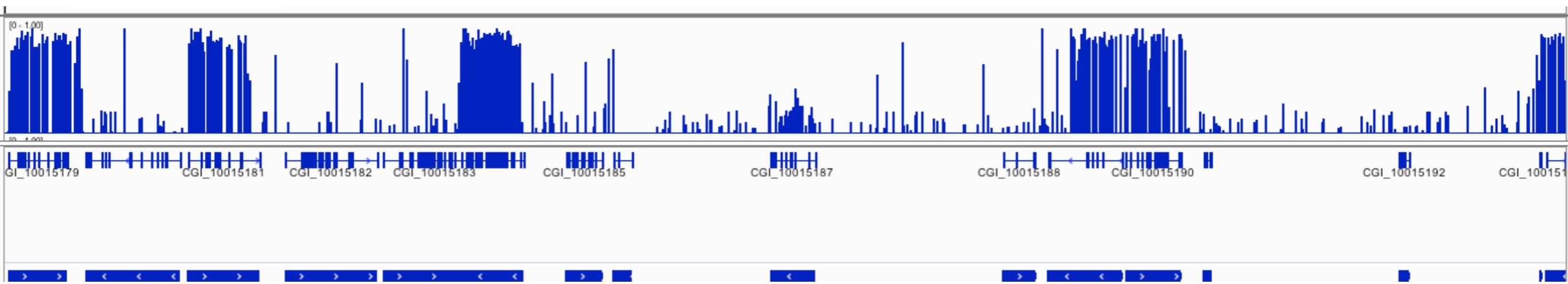
– Bisulfite conversion



7,642,816 CpG dinucleotides with at least 5x coverage were examined



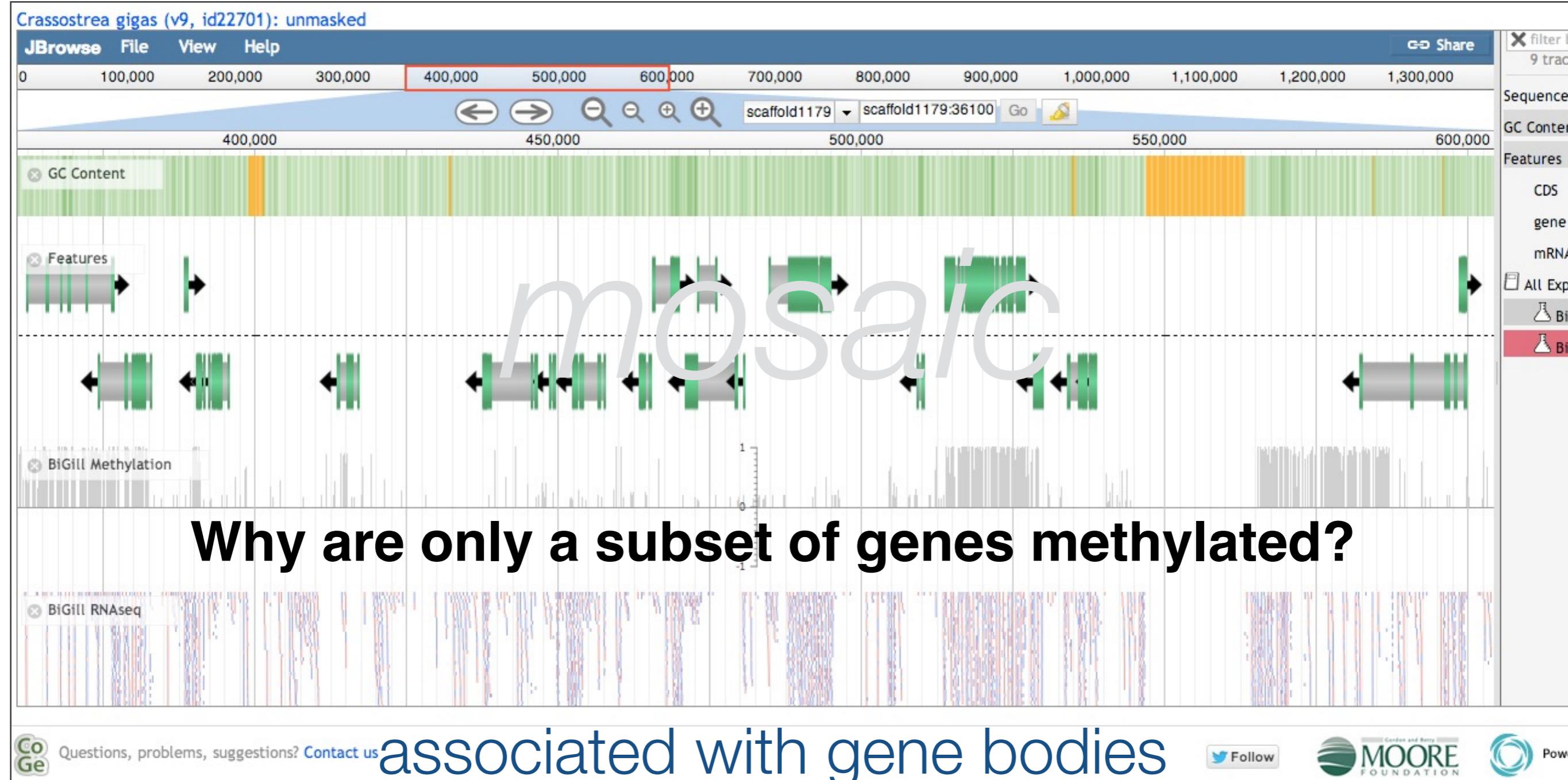
Epigenetic variation **1**



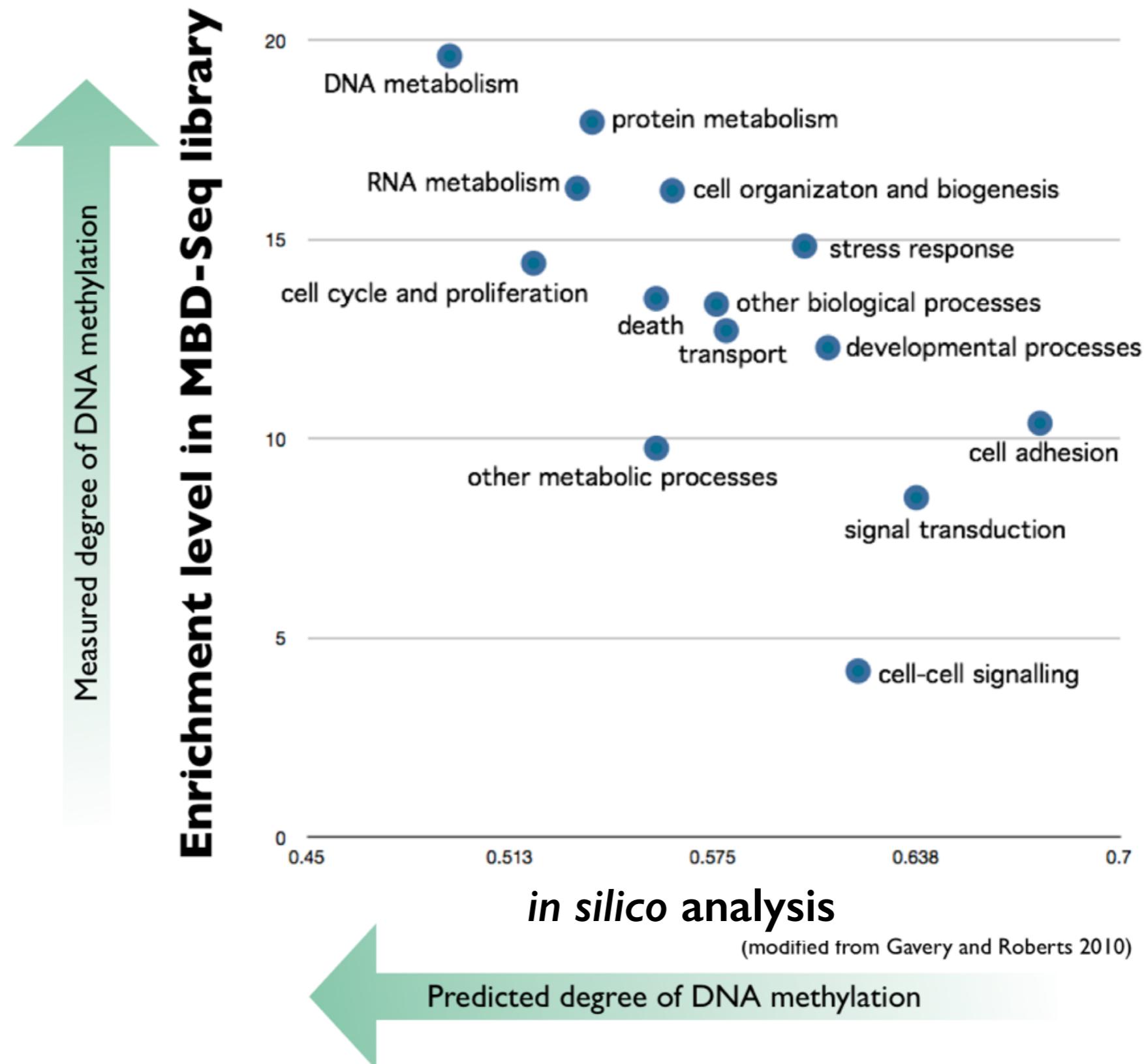
mosaic

associated with gene bodies

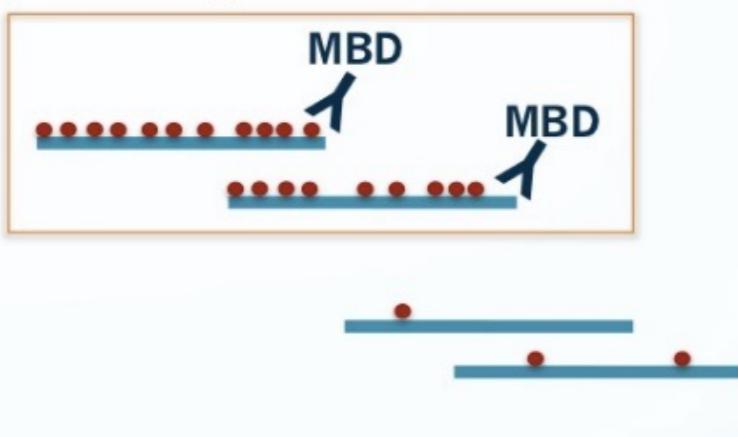




Epigenetic variation **1**

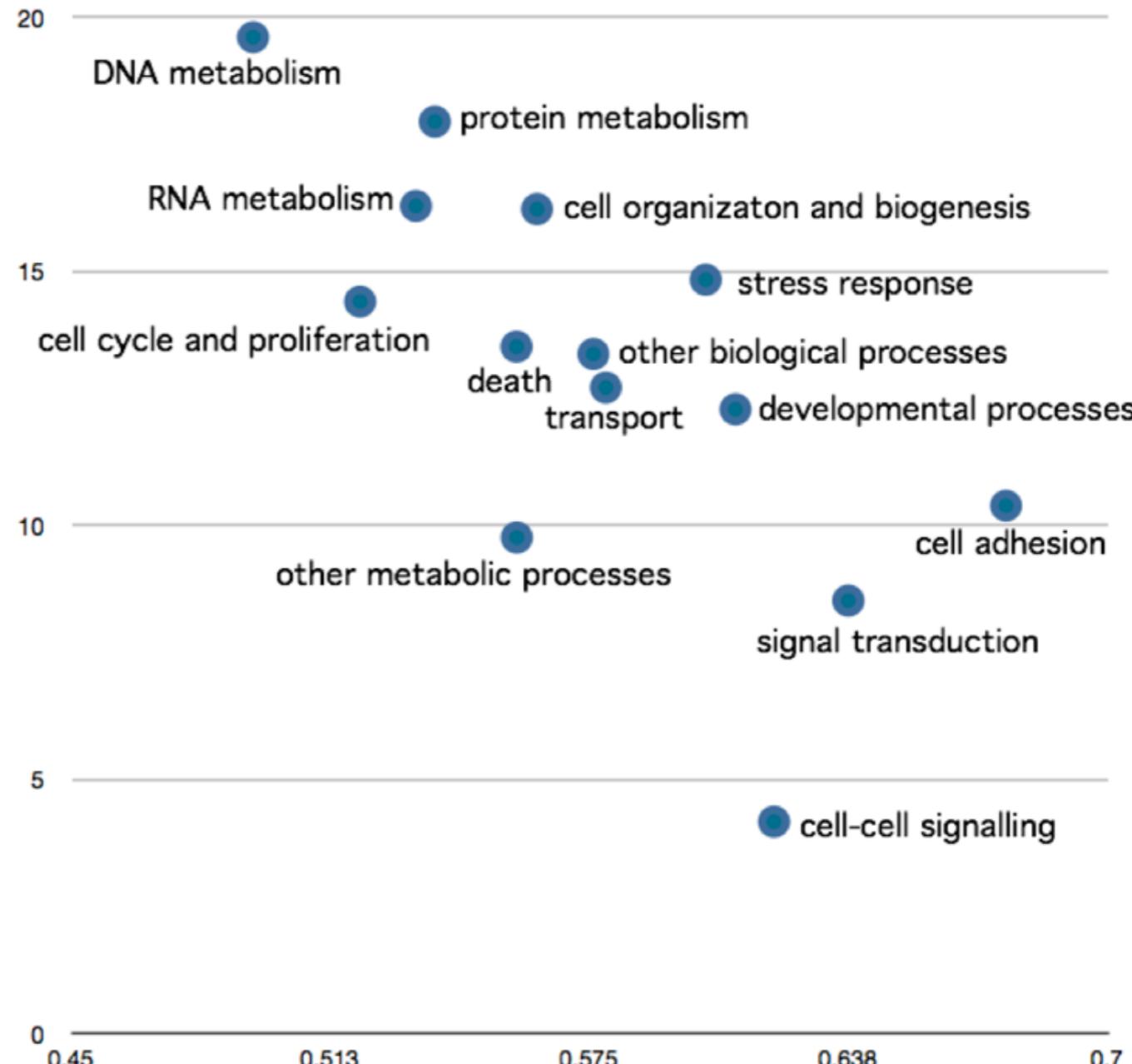


Epigenetic variation 1



Measured degree of DNA methylation

Enrichment level in MBD-Seq library



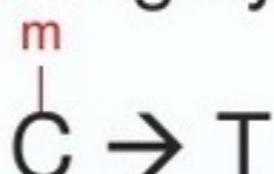
in silico analysis

(modified from Gavery and Roberts 2010)

Predicted degree of DNA methylation

in silico approach

- Principle:
 - Methylated cytosines are highly mutable

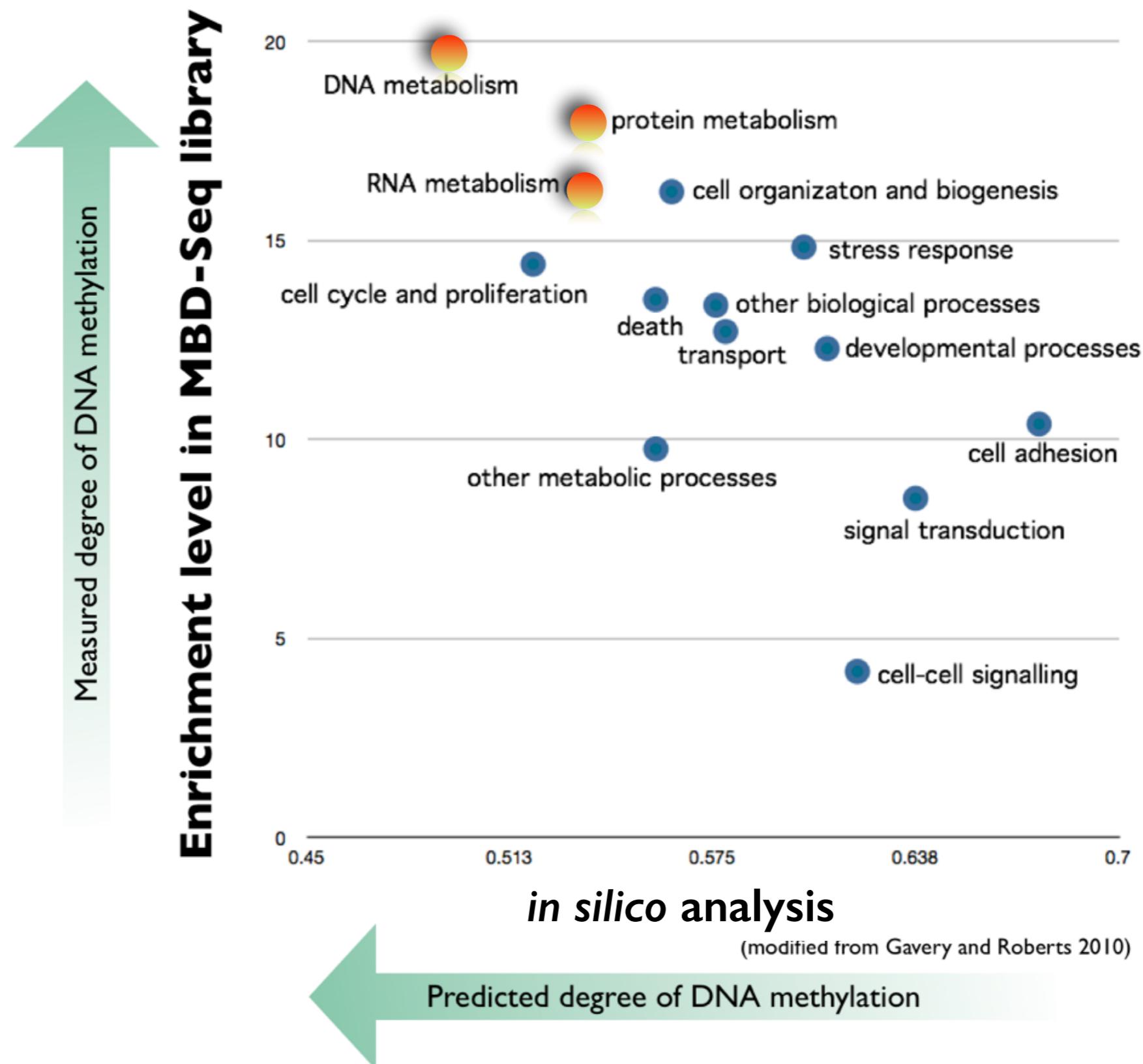


- Methylated regions of DNA are depleted of CpG dinucleotides over evolutionary time (CpG to TpG)

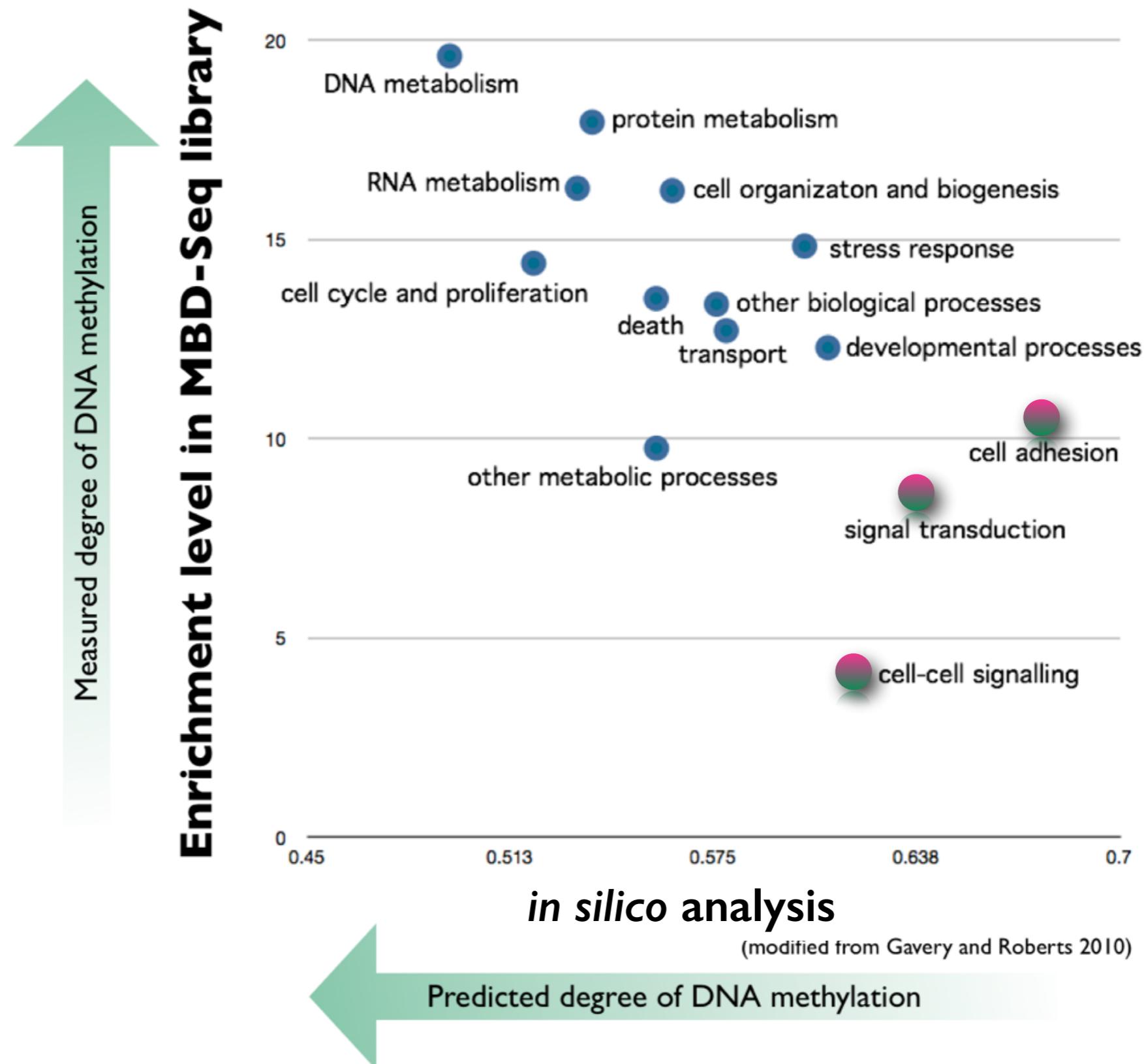
$$\text{CpG O/E} = \frac{\text{CpG observed}}{\text{CpG expected}}$$


high = unmethylated

Epigenetic variation **1**



Epigenetic variation **1**



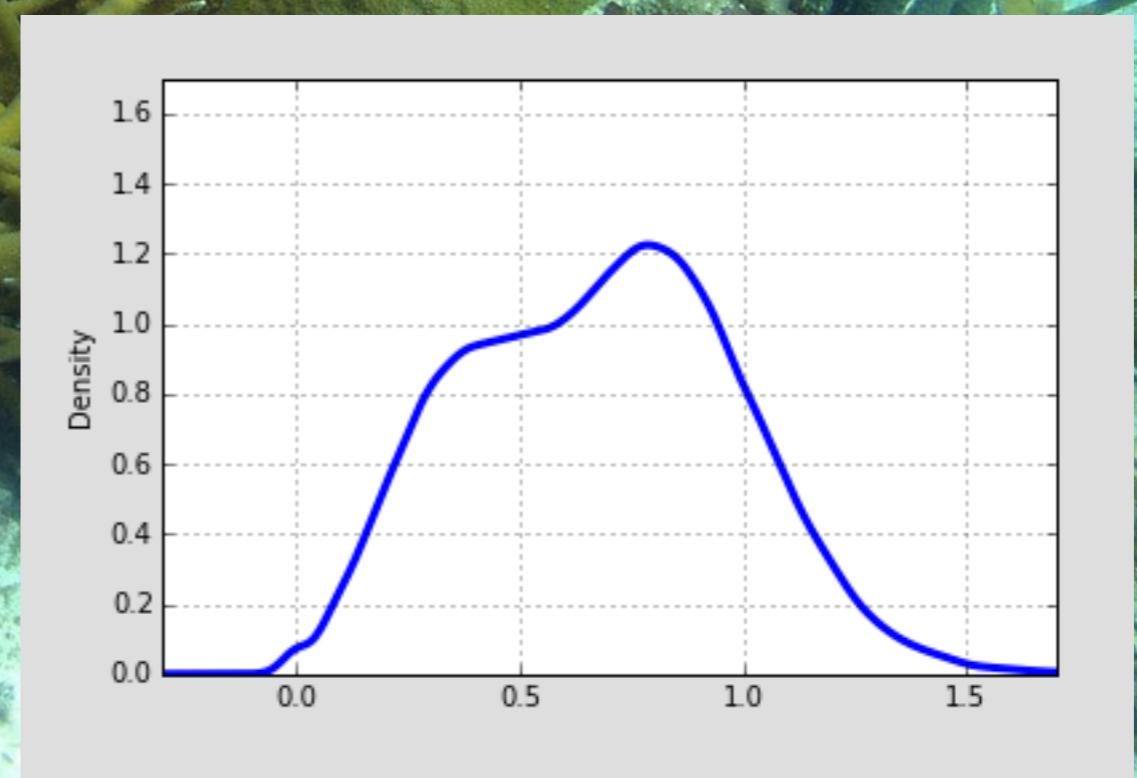
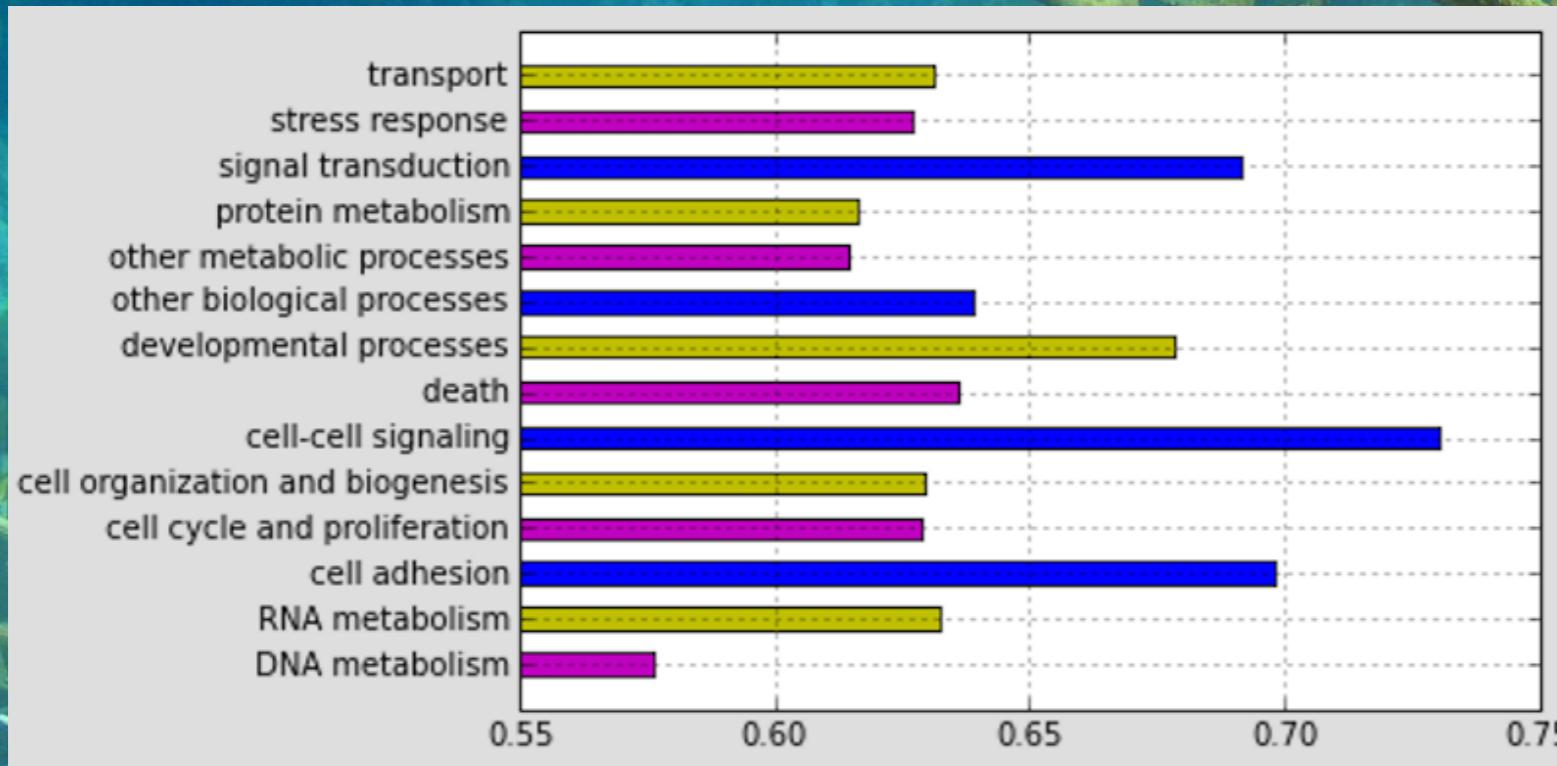
Jay Dimond

Acropora palmata

Acropora cervicornis

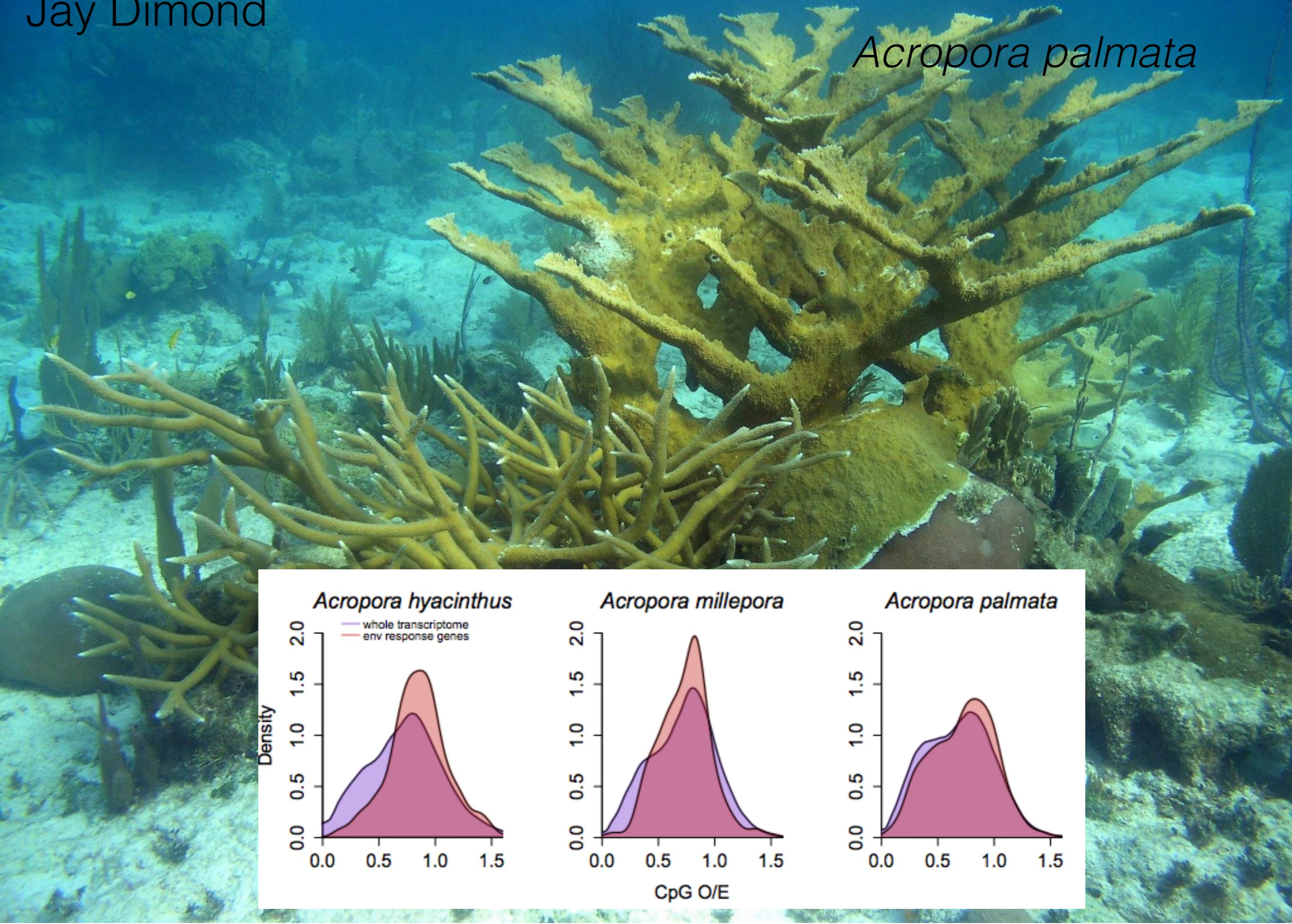
Jay Dimond

Acropora palmata



Jay Dimond

Acropora palmata

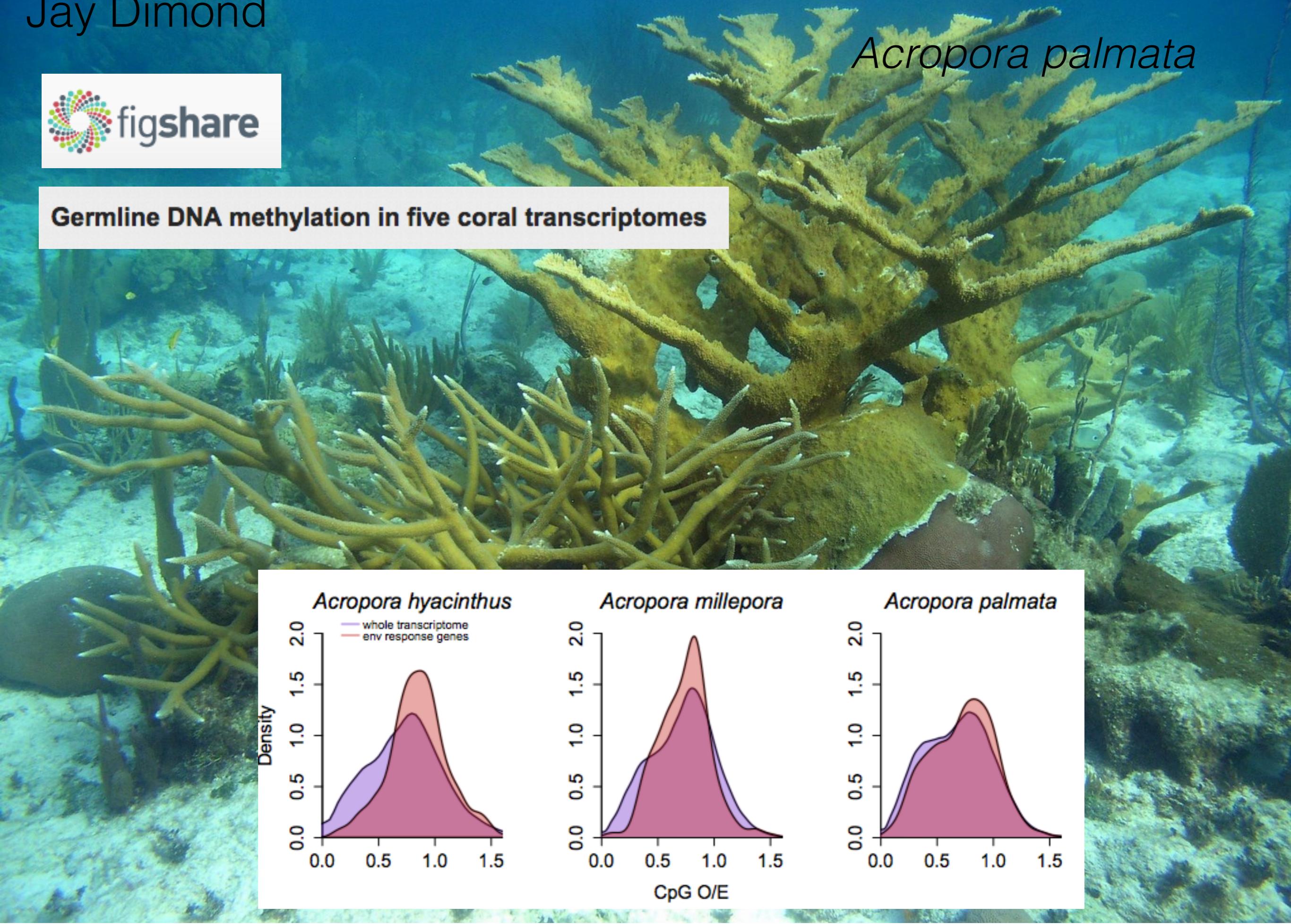


Jay Dimond

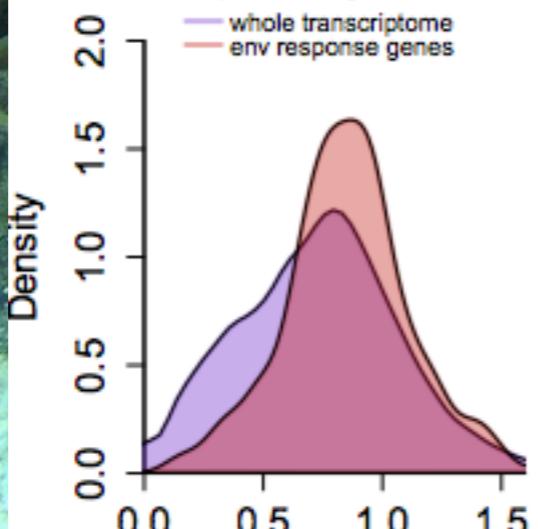
Acropora palmata



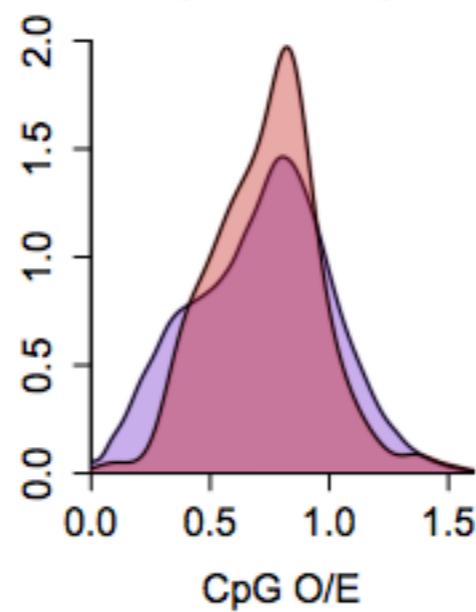
Germline DNA methylation in five coral transcriptomes



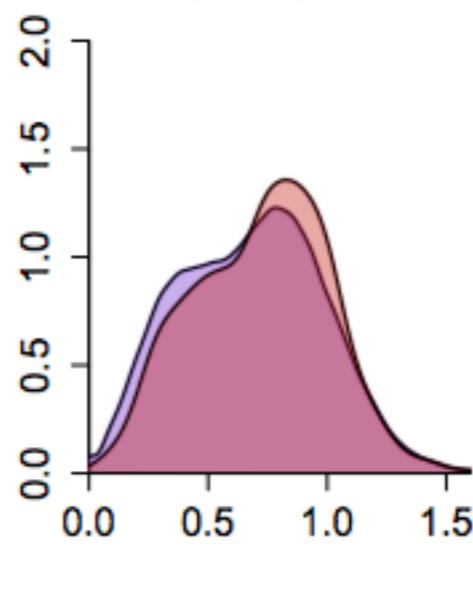
Acropora hyacinthus



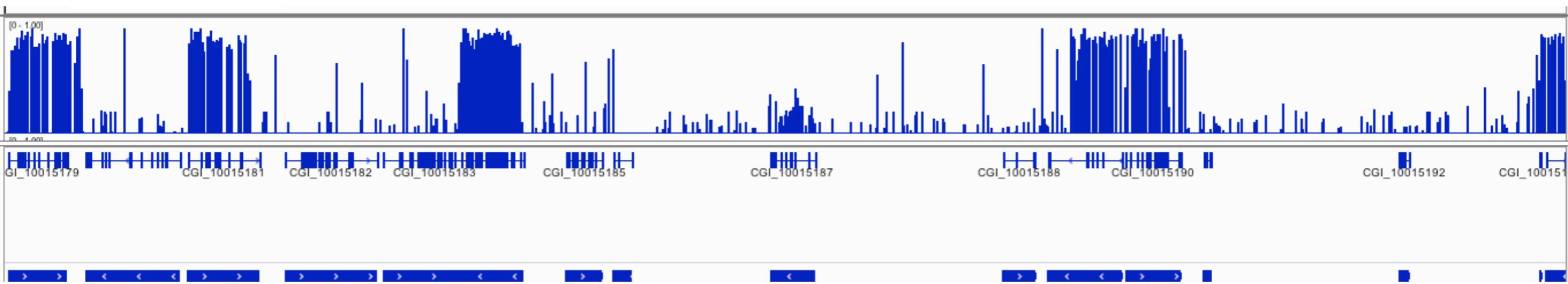
Acropora millepora



Acropora palmata



Epigenetic variation **1**

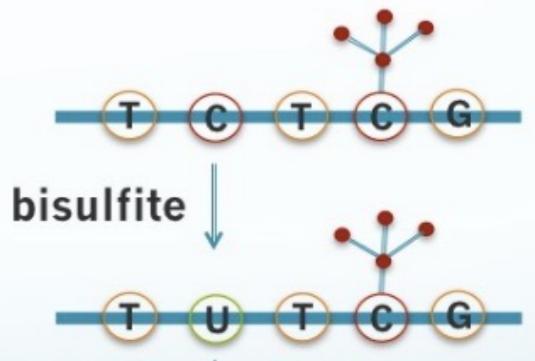


mosaic

associated with gene bodies
based on gene function

Epigenetic variation **1**

Family and Developmental Variation



Sperm &
Larvae
(72h & 120h)



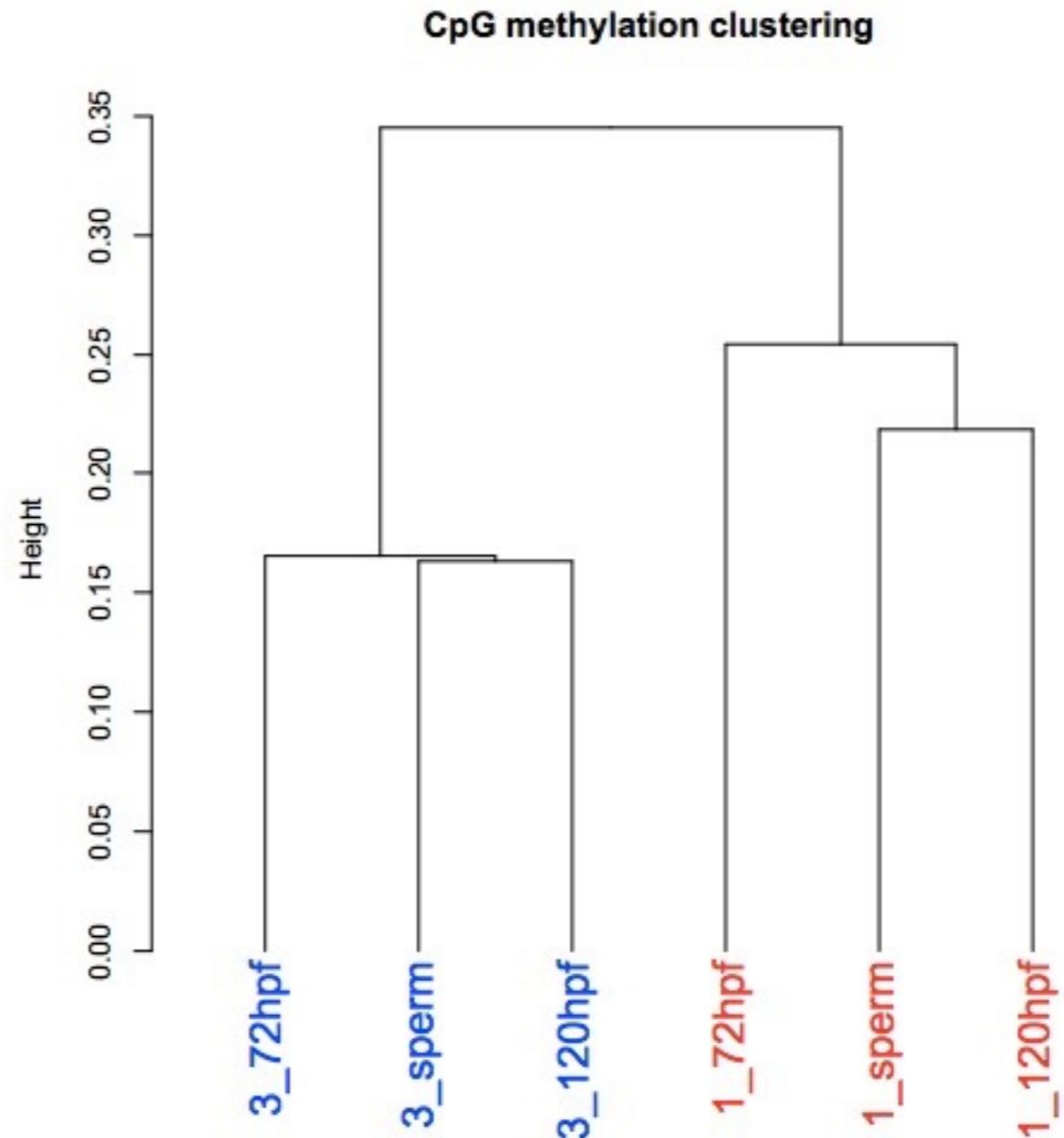
bioRxiv
beta
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New Results

Indication of family-specific DNA methylation patterns in developing oysters

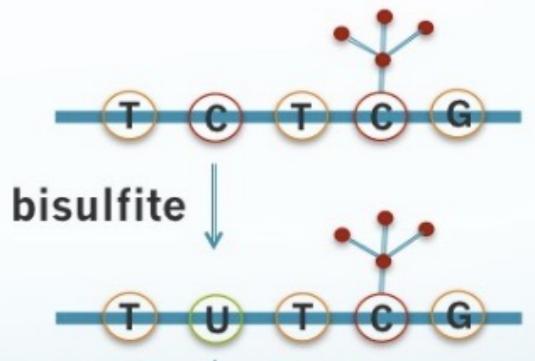
Claire E. Olson , Steven B. Roberts

doi: <http://dx.doi.org/10.1101/012831>



Epigenetic variation **1**

Family and Developmental Variation



Sperm &
Larvae
(72h & 120h)



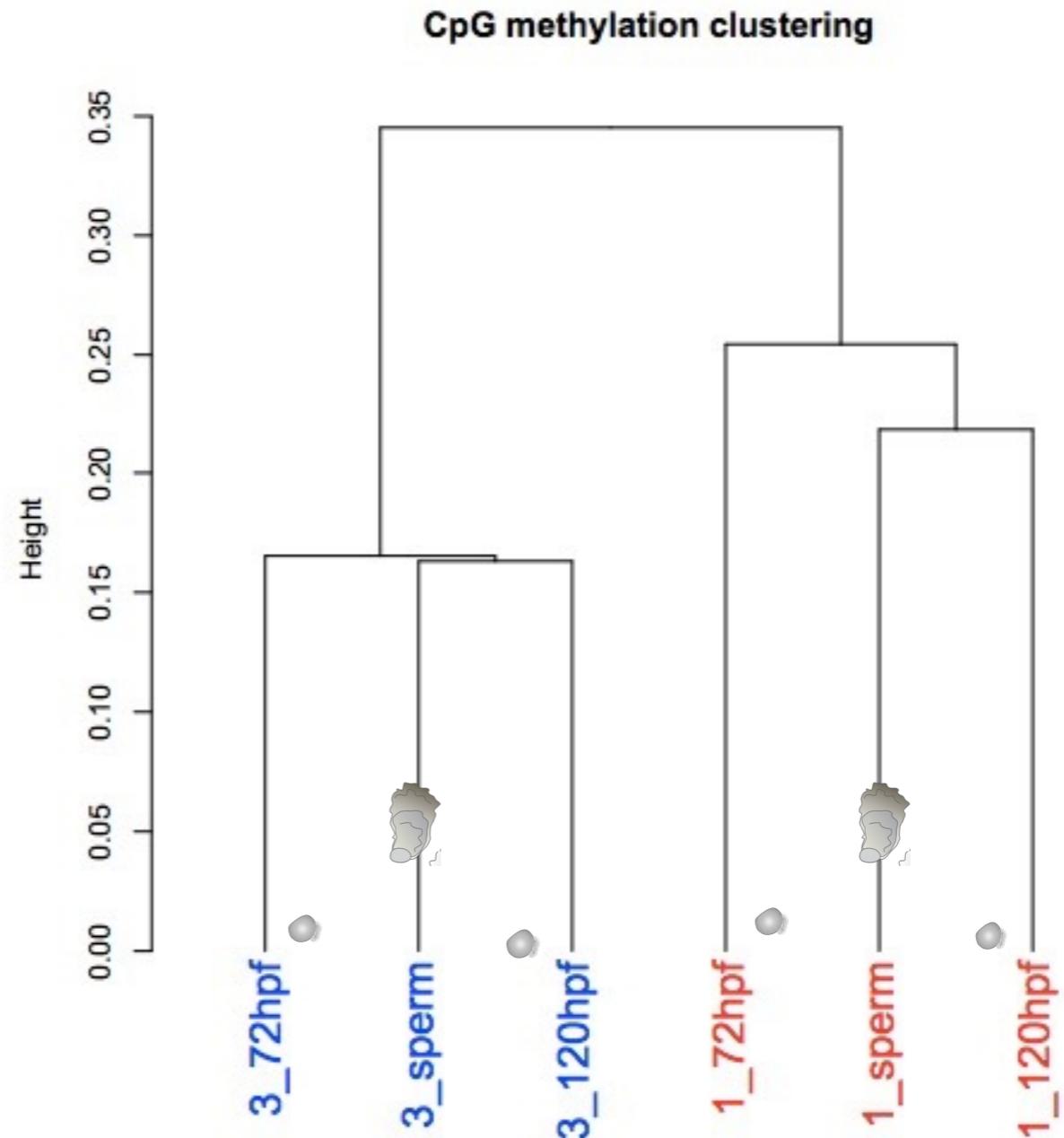
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New Results

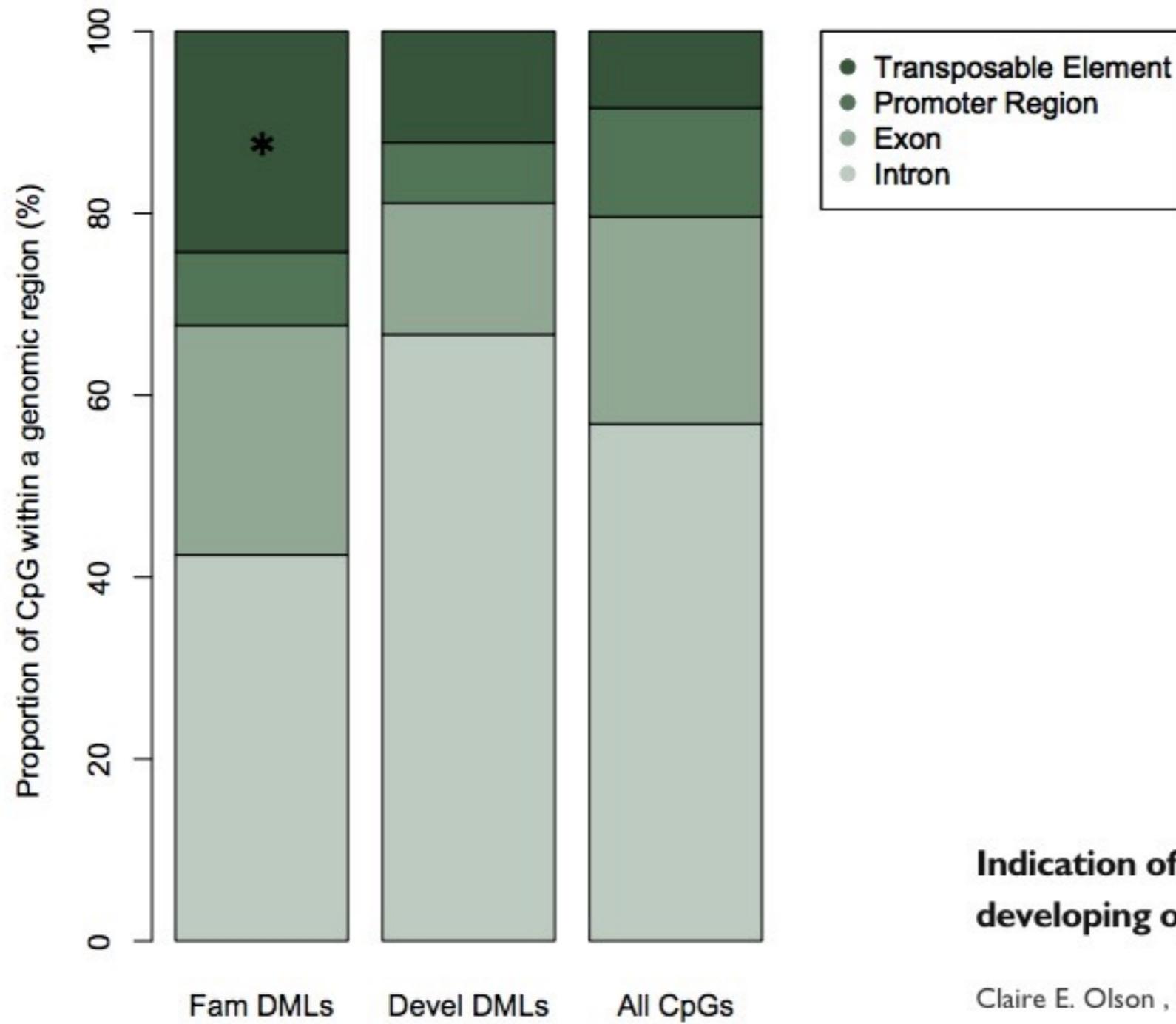
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Epigenetic variation **1**

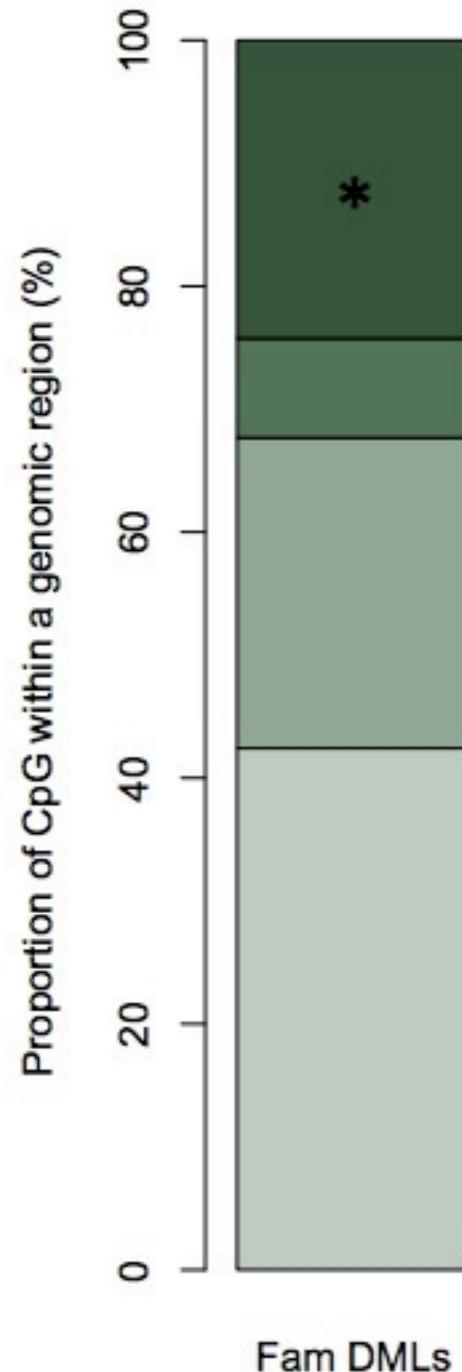


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Epigenetic variation **1**



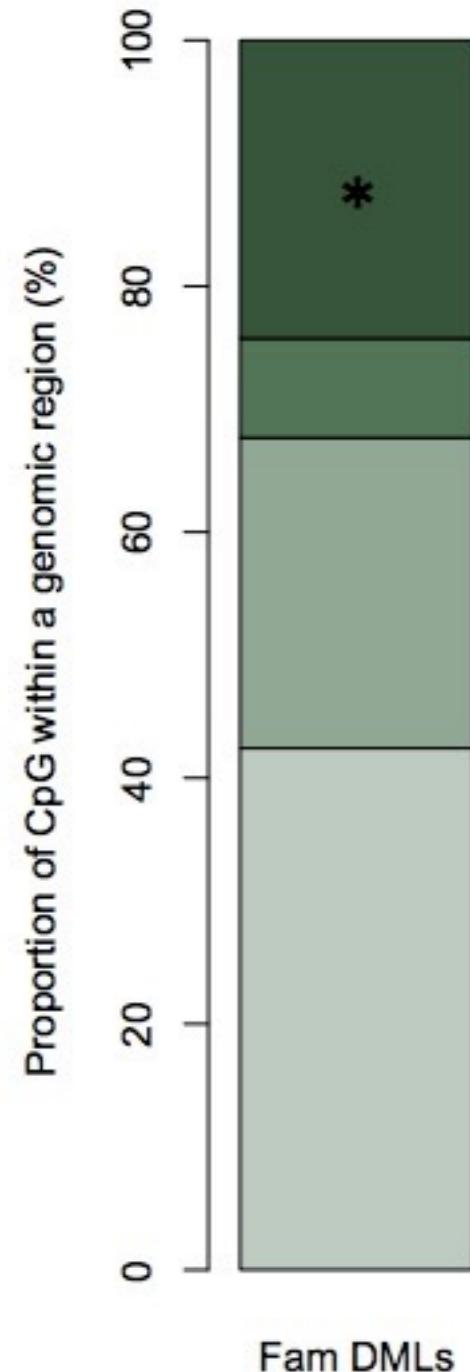
Differentially methylated loci in gene bodies could be lethal or deleterious, as they would alter gene expression.

Another possibility is that differentially methylated loci may provide advantageous phenotypic variation by increasing transposable element mobility.

Indication of family-specific DNA methylation patterns in developing oysters

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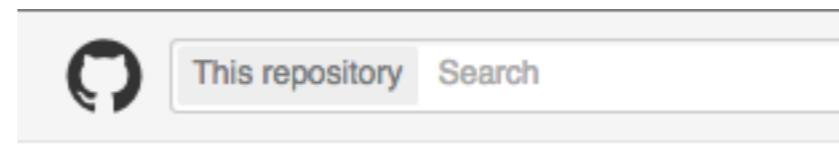
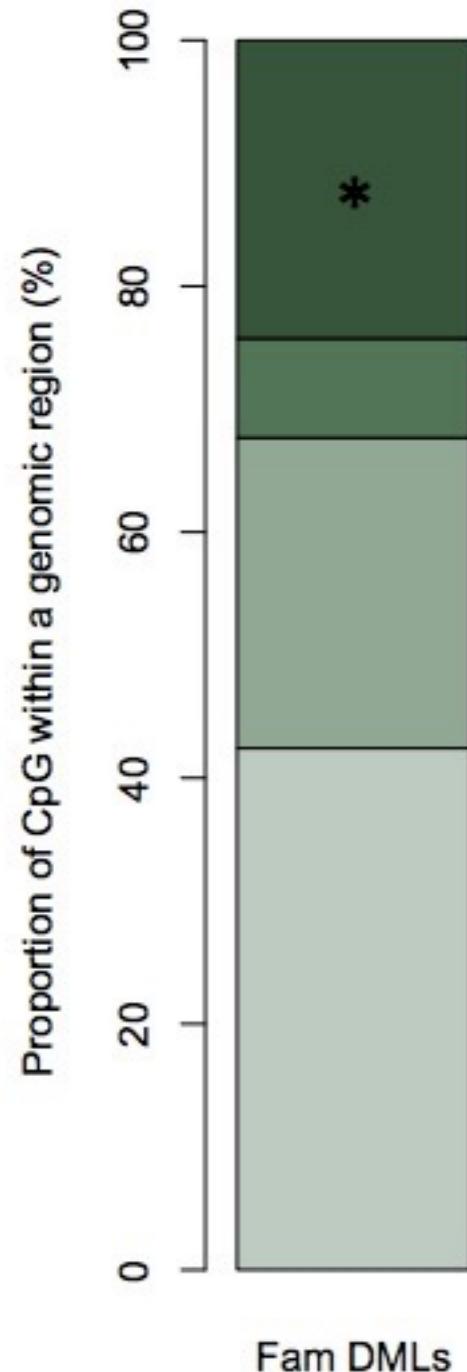


***Assumes some form
of random process***
occurring during
gametogenesis?

Indication of family-specific DNA methylation patterns in developing oysters

Claire E. Olson , Steven B. Roberts
doi: <http://dx.doi.org/10.1101/012831>

Epigenetic variation **1**



 che625 / olson-ms-nb



**IPython Notebook for downloading and analyzing data
the manuscript: "Indication of family-specific DNA
methylation patterns in developing oysters"**

bioRxiv preprint - <http://dx.doi.org/10.1101/012831>

To execute the IPython Notebook in its entirety you will need:

- IPython - [install instructions](#)
- BSMAP - [install instructions](#)
- bedtools - [install instructions](#)
- R - [install instructions](#)
- rpy2 (interface to R from Python) - [install instructions](#)

- Sparsely (~16 %) methylated genome
- Limited variation between cell type
- Gene body methylation correlated with function
- Evidence indicates DMRs are predominant in transposable elements

Gene
expression



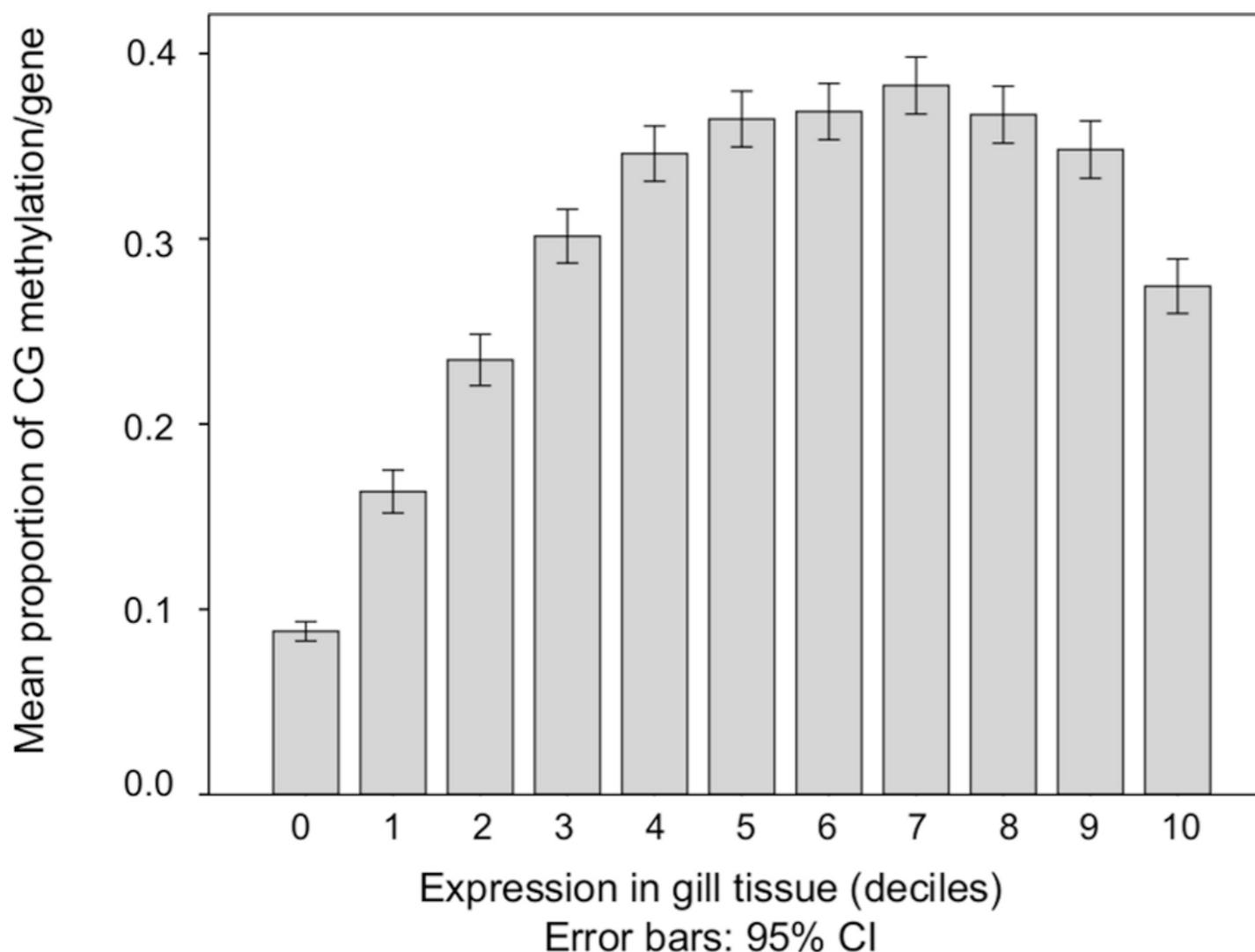
Epigenetic
variation

Function?

Gene expression

2

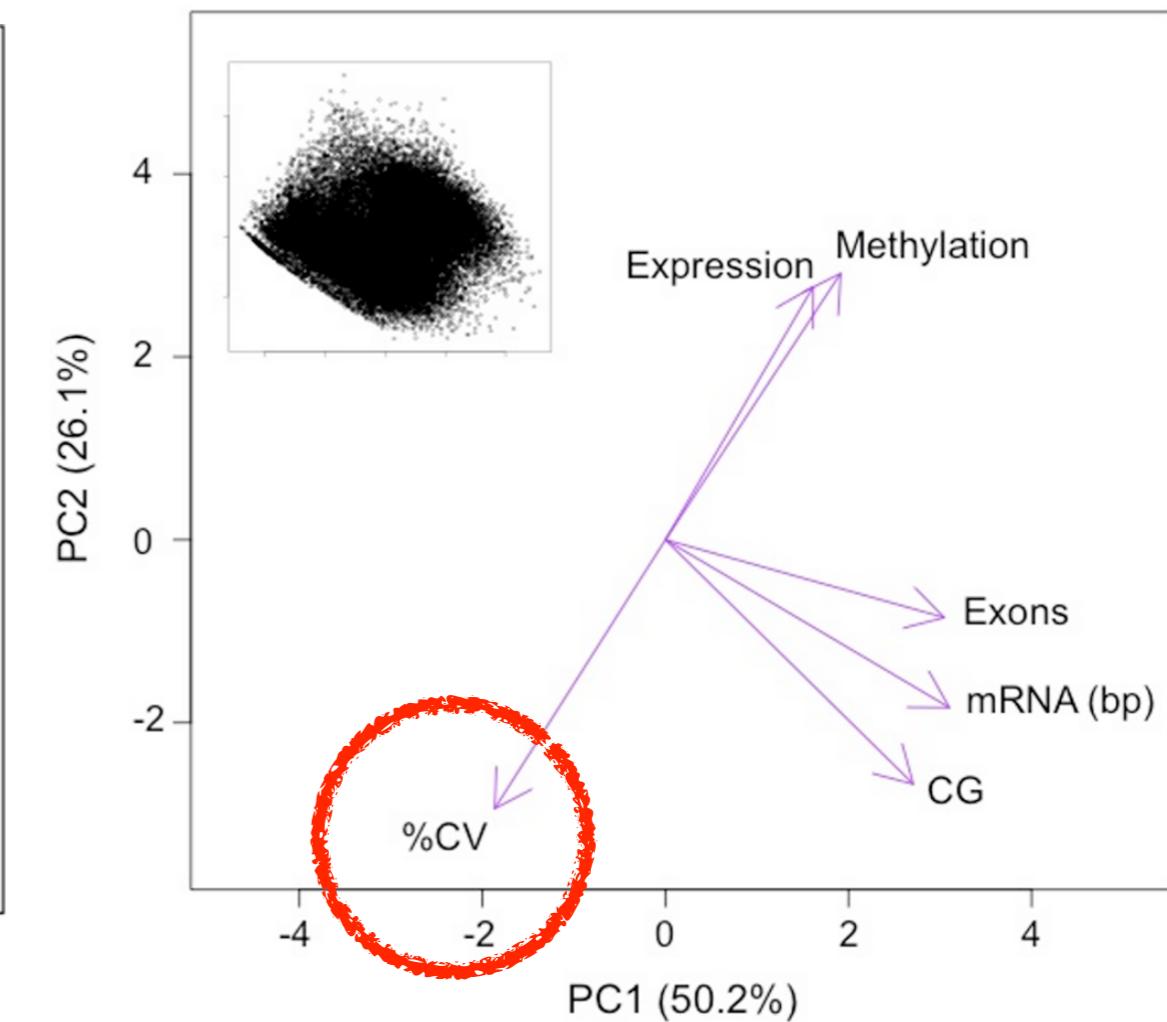
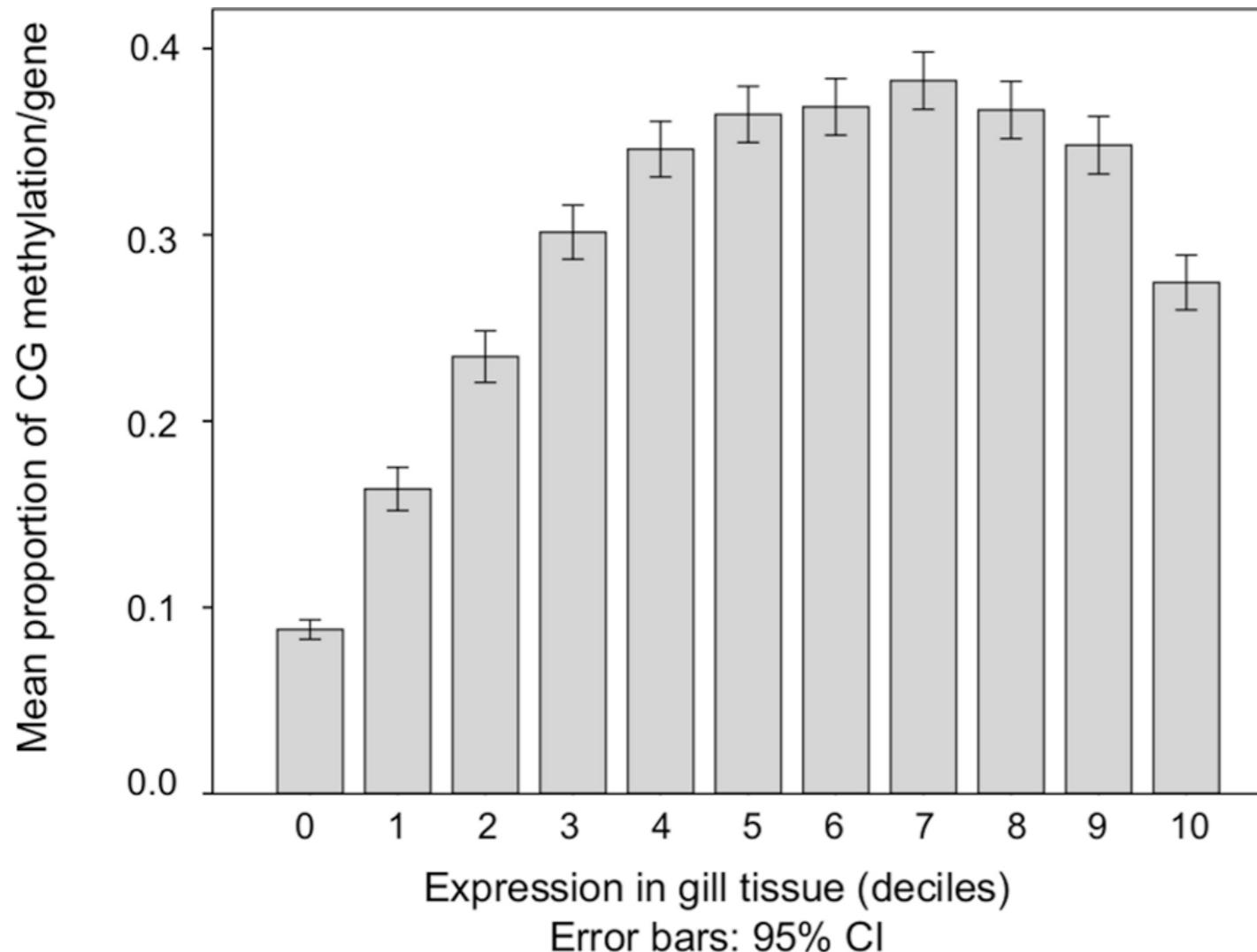
Epigenetic variation



Gene expression

2

Epigenetic variation



Predominant intragenic methylation is associated with gene expression characteristics in a bivalve mollusc

Mackenzie R. Gavery and Steven B. Roberts

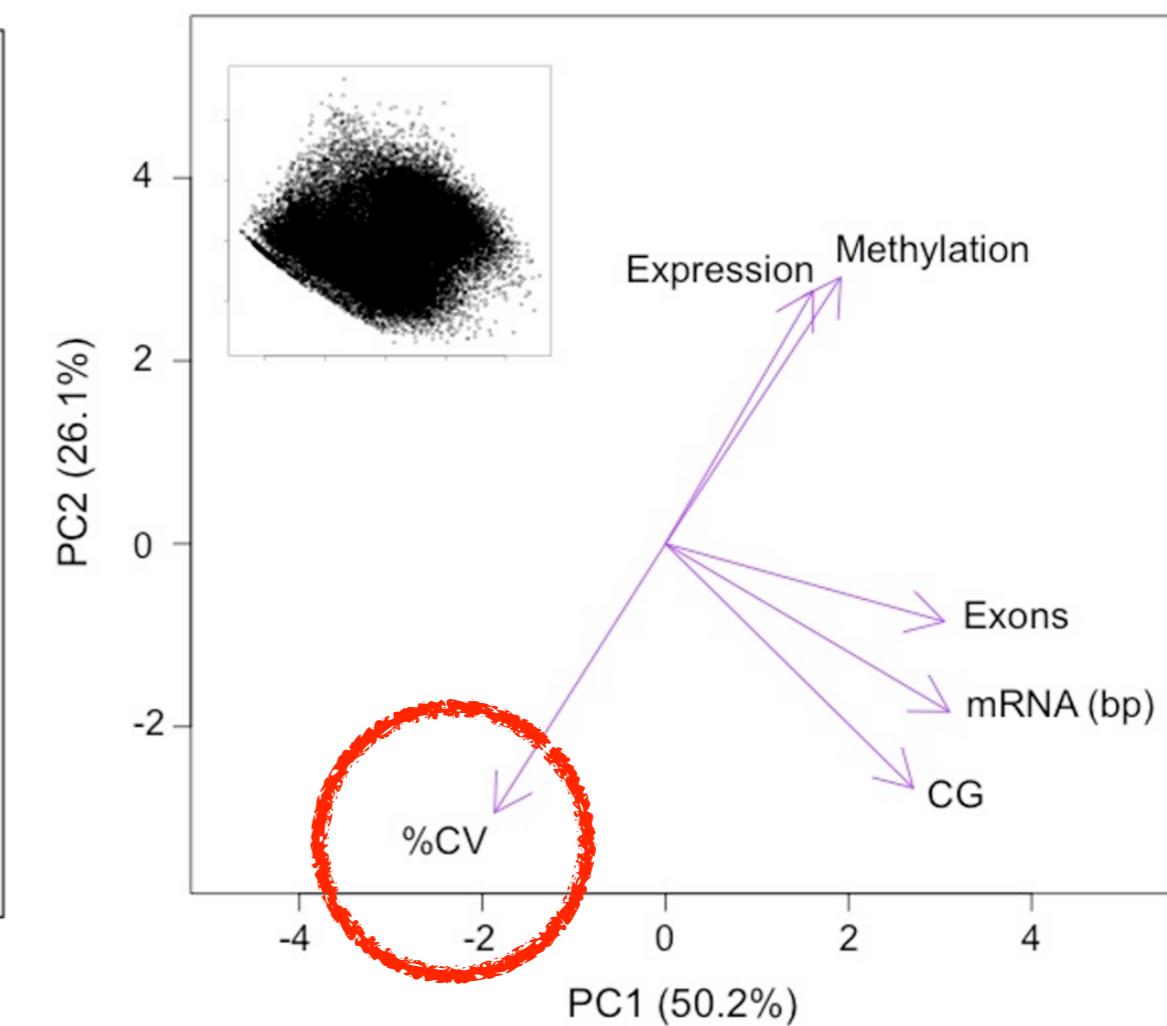
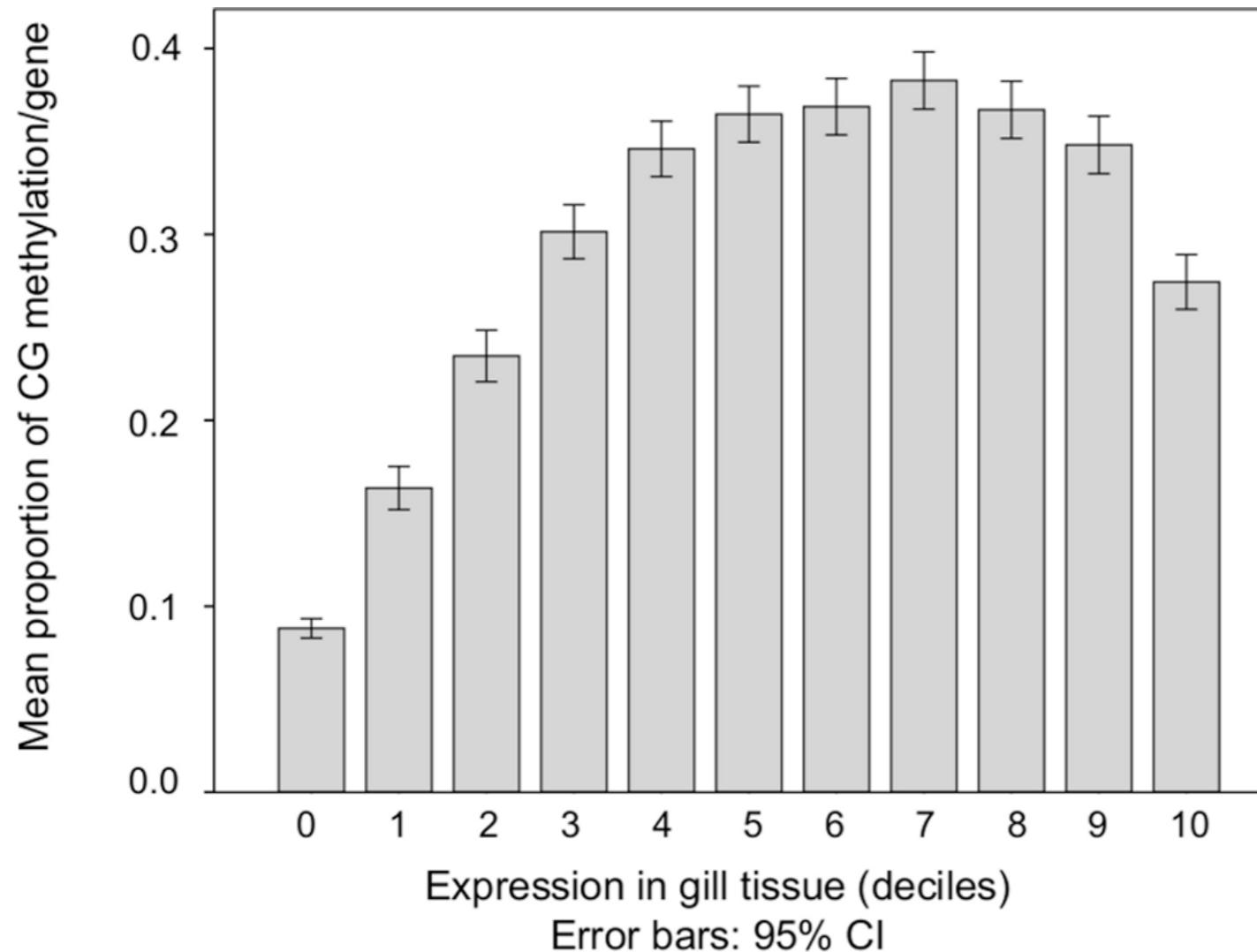
School of Aquatic and Fishery Sciences, University of Washington, Seattle, WA, USA

Gene expression

2

Epigenetic variation

Theory: **Does not** influence expression level
but rather alternative splicing.



PeerJ

Predominant intragenic methylation is
associated with gene expression
characteristics in a bivalve mollusc

Mackenzie R. Gavery and Steven B. Roberts

School of Aquatic and Fishery Sciences, University of Washington, Seattle, WA, USA

What?

A context dependent role for DNA methylation in bivalves

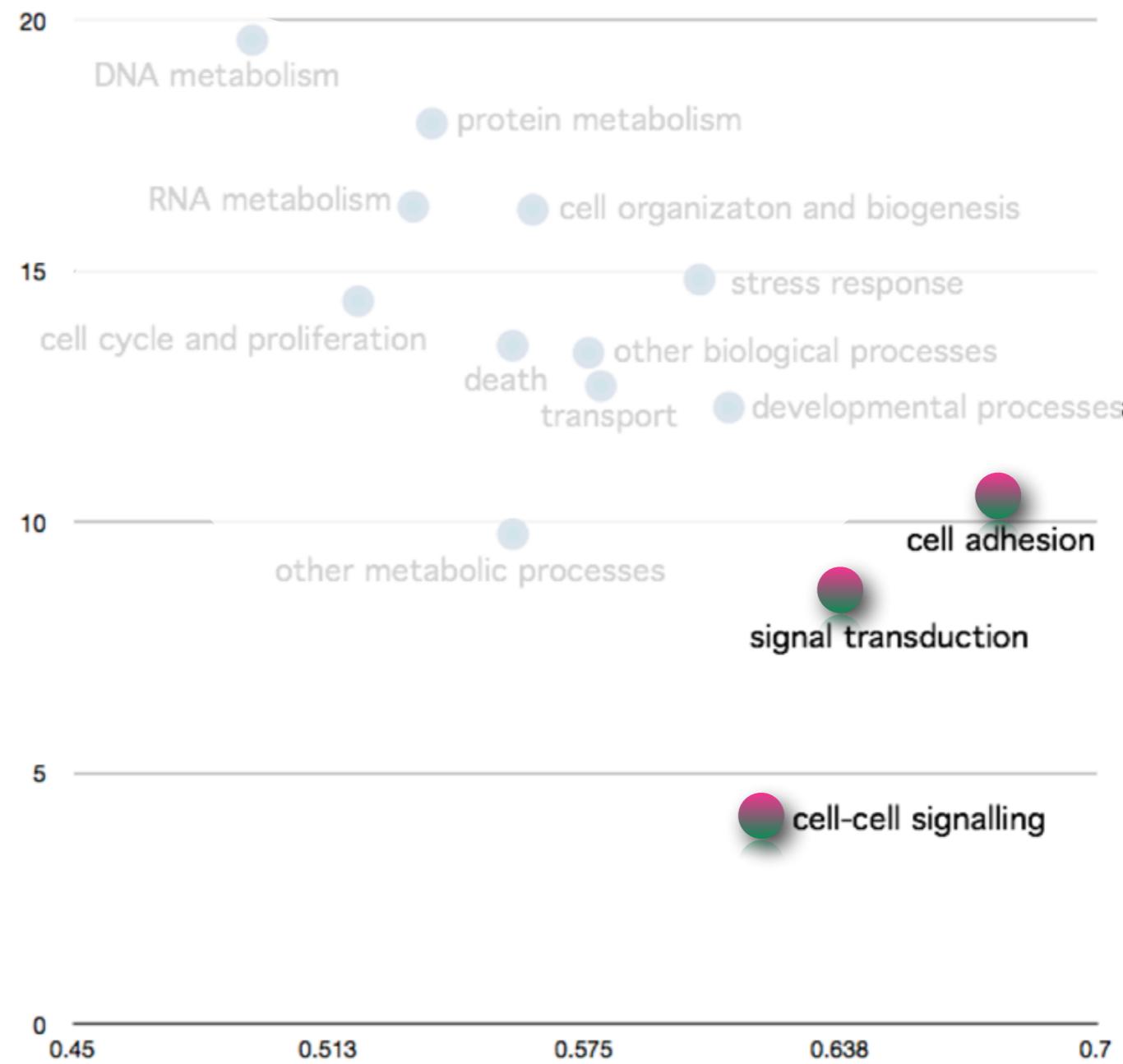
Mackenzie R. Gavery and Steven B. Roberts

Advance Access publication date 7 January 2014

In species that experience a diverse range of environmental conditions, processes have evolved to increase the number of potential phenotypes in a population in order to improve the chances for an individual's survival.

Gene expression

Epigenetic variation
2



Roberts and Gavery 2012

Gene expression

2

Epigenetic variation

cell adhesion

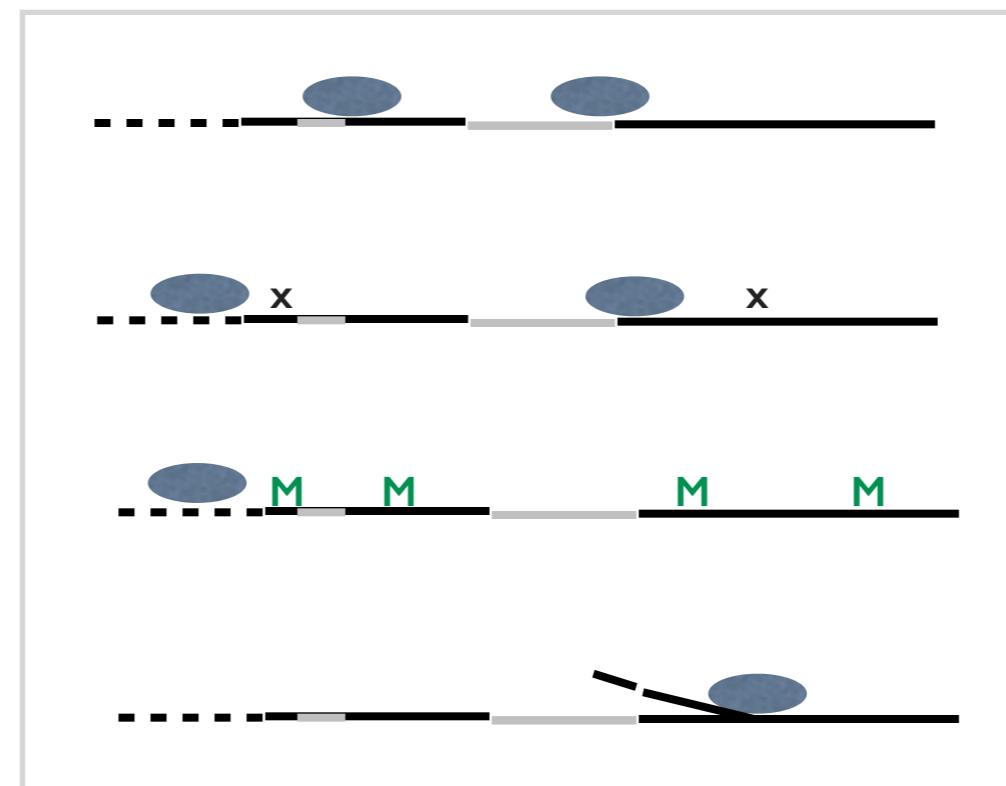
signal transduction

cell-cell signalling

sparse methylation

tissue / temporal specific and inducible genes

Transcriptional opportunities



alternative start sites

sequence mutation
change AA, premature stop codon

conventional transcription
transient methylation

alternate transcript
exon skipping

Gene expression



Epigenetic variation

DNA metabolism

protein metabolism

RNA metabolism



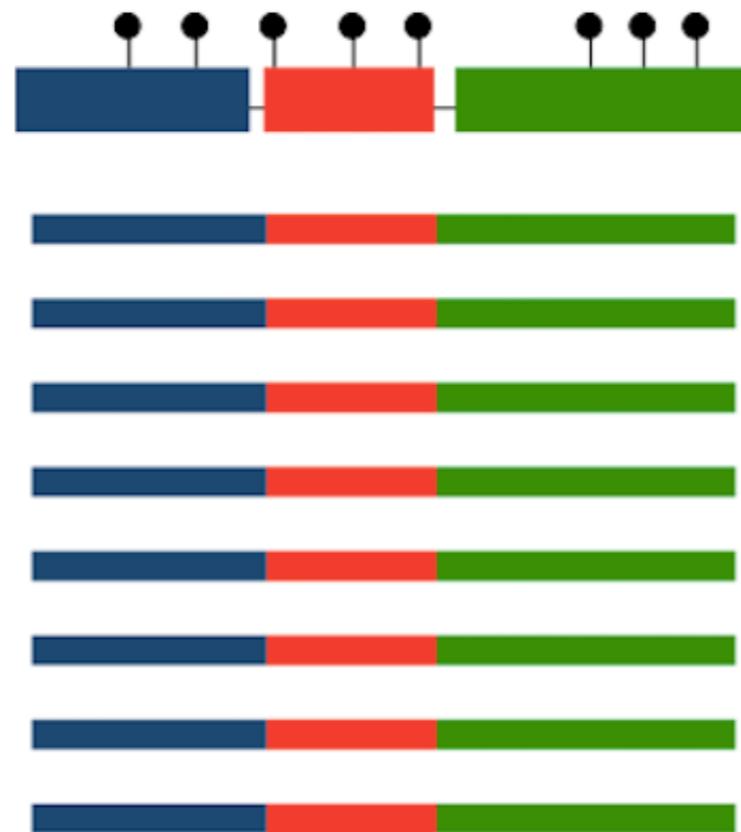
germline methylation

*ubiquitously expressed,
critical genes*

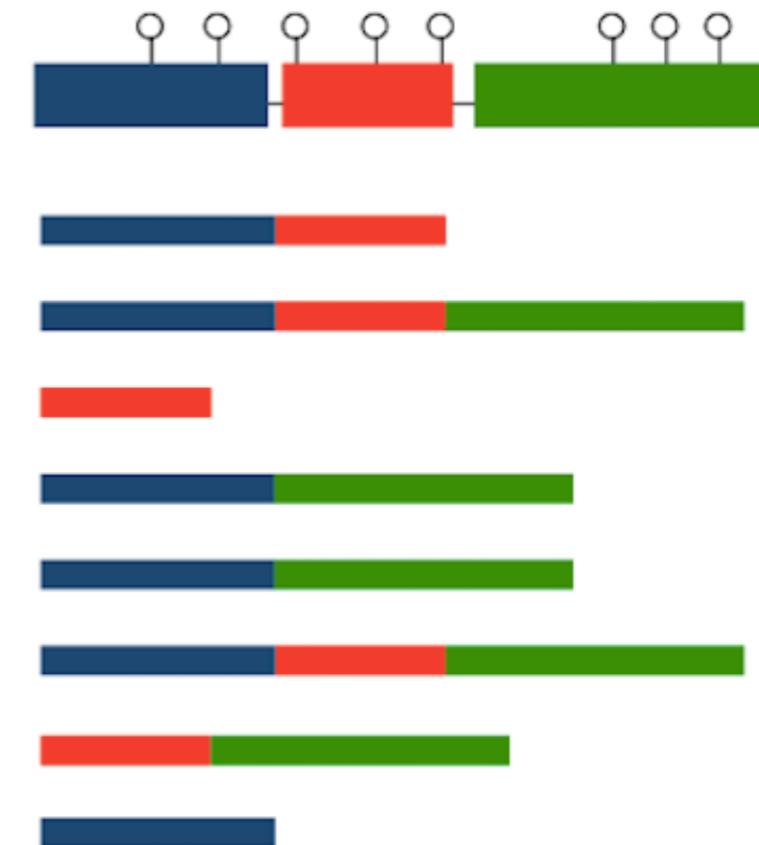
Transcriptional opportunities



conventional transcription
5' UTR promotor



housekeeping



response to
change

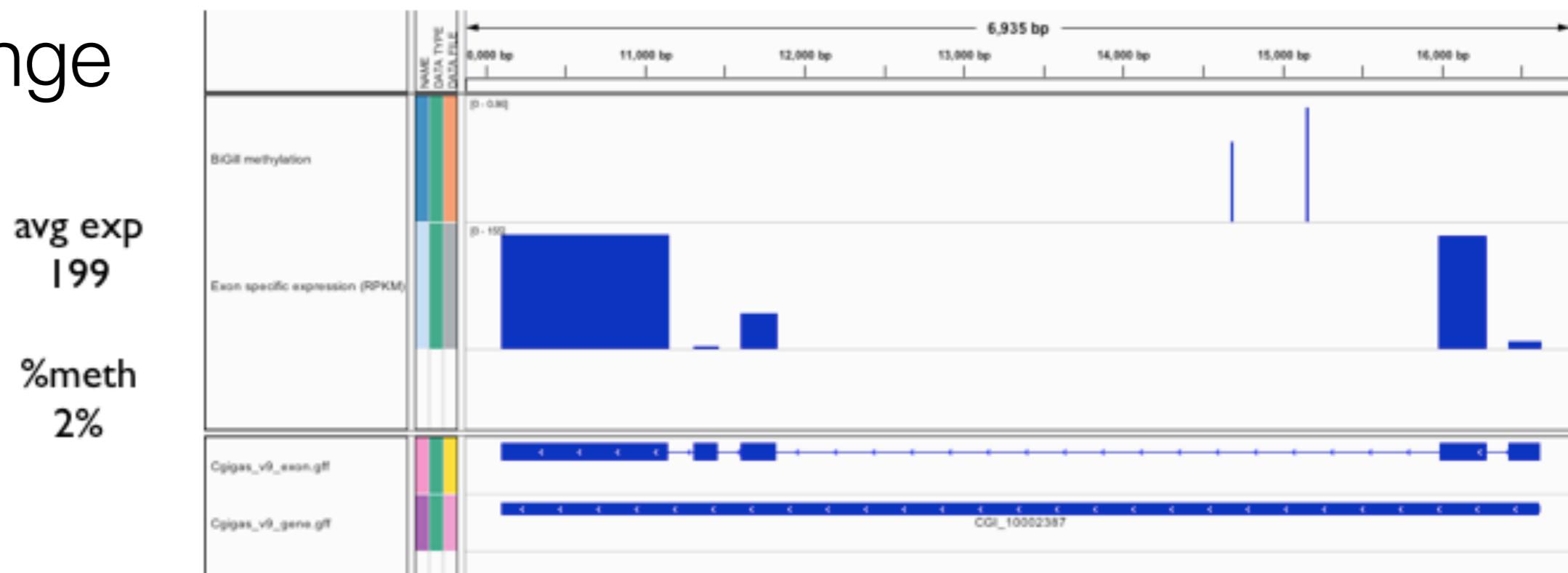
A context dependent role for DNA methylation in bivalves

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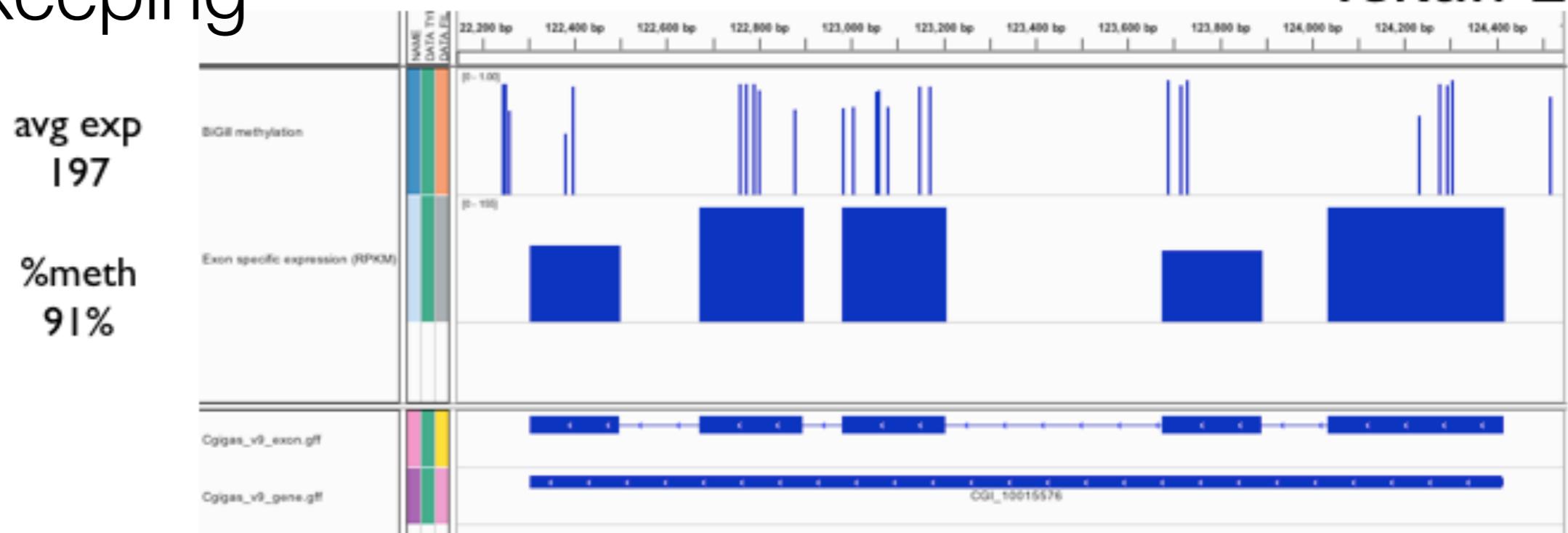
response to
change

Heat shock 70 kDa protein 12A



housekeeping

Tektin-2



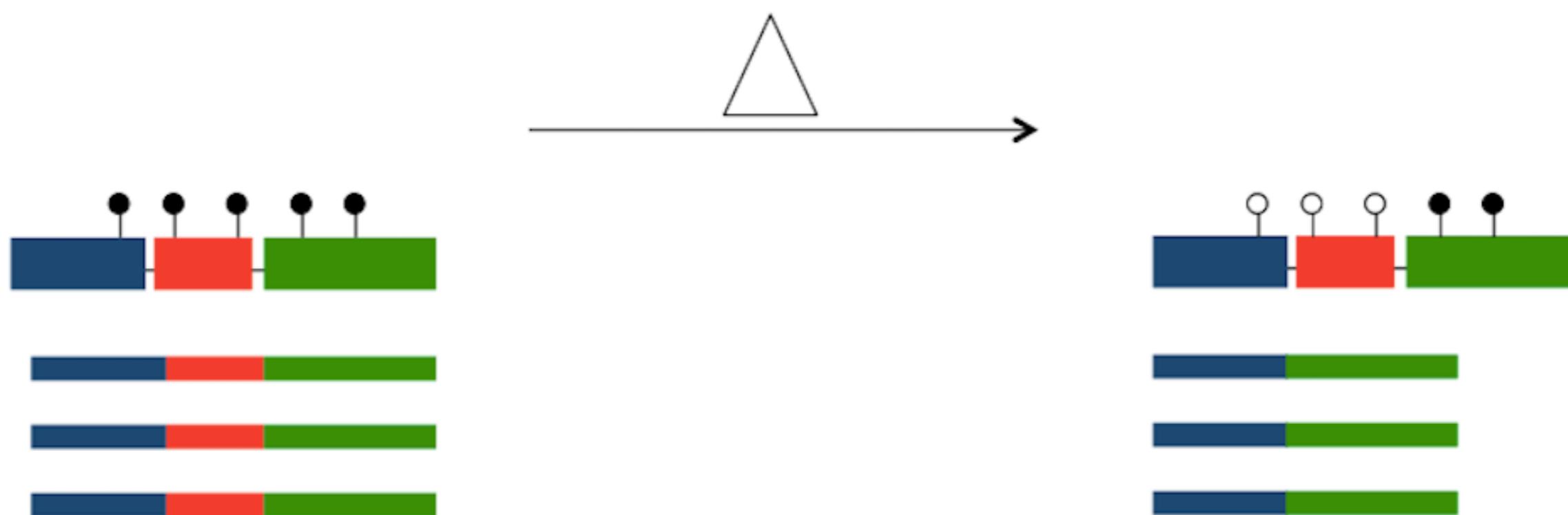


Targeted Regulation

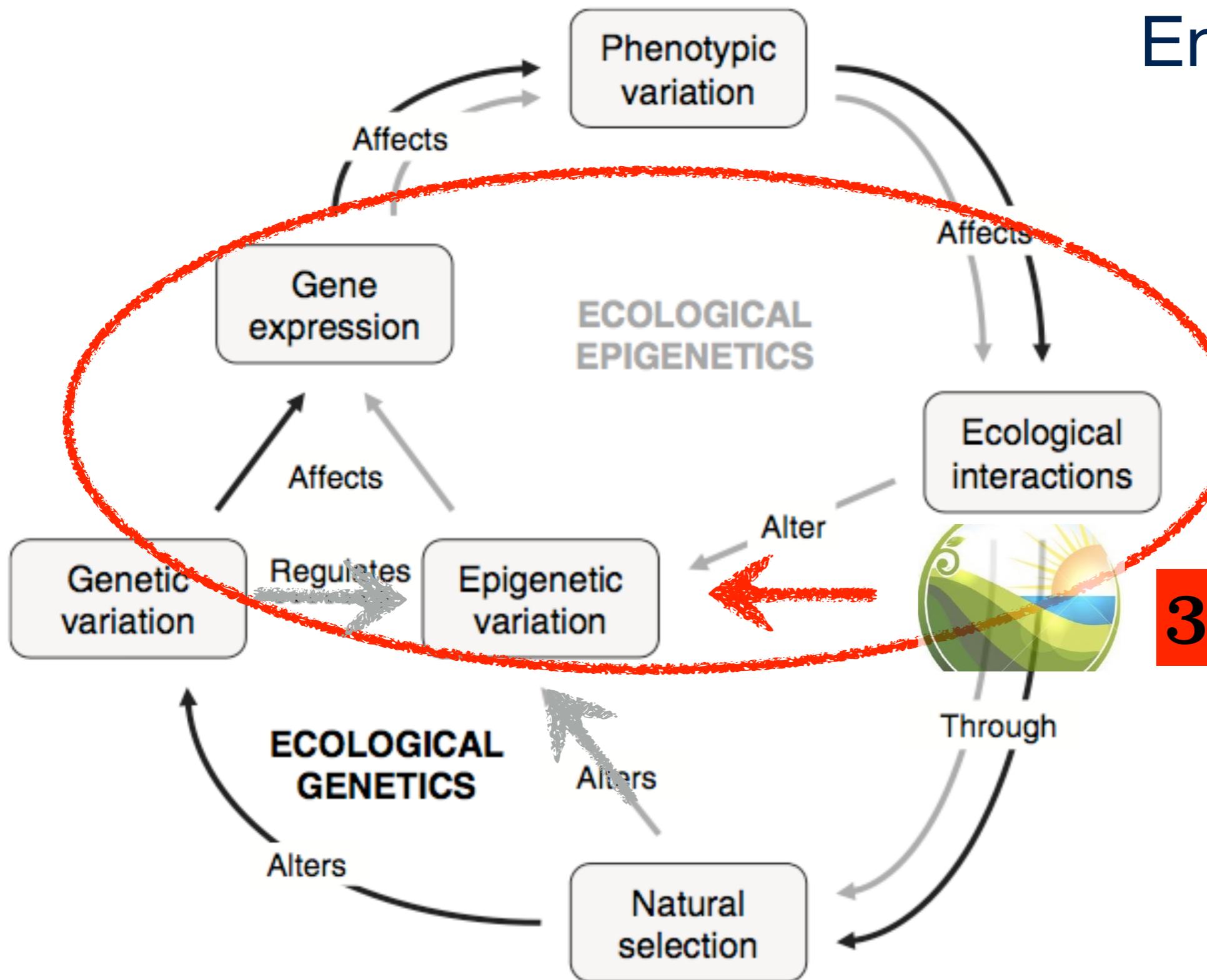
A context dependent role for DNA methylation in bivalves

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Environmental Influence



Ecology Letters, (2008) 11: 106–115

doi: 10.1111/j.1461-0248.2007.01130.x

modified from

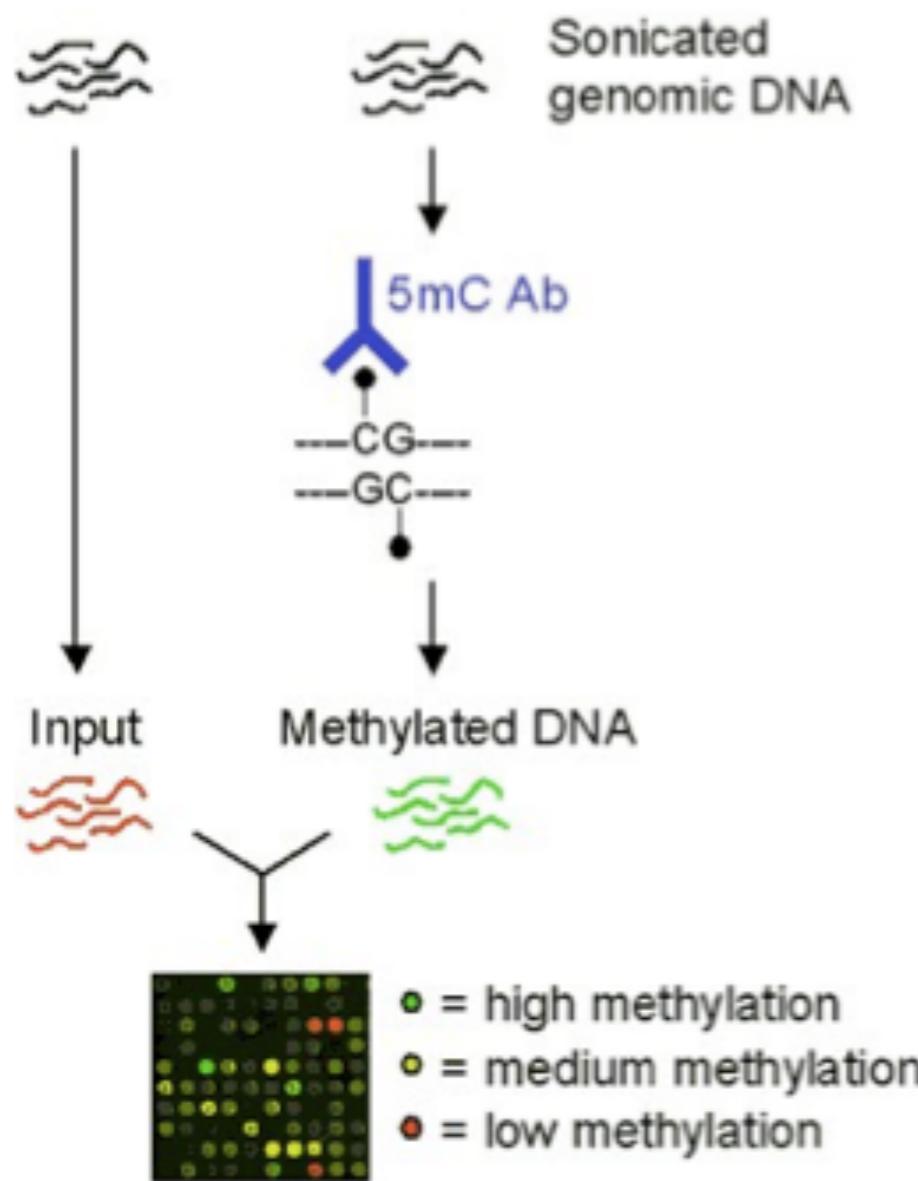
IDEA AND
PERSPECTIVE

Epigenetics for ecologists

Oliver Bossdorf,^{1,*} Christina L.
Richards² and Massimo Pigliucci³

Very new data

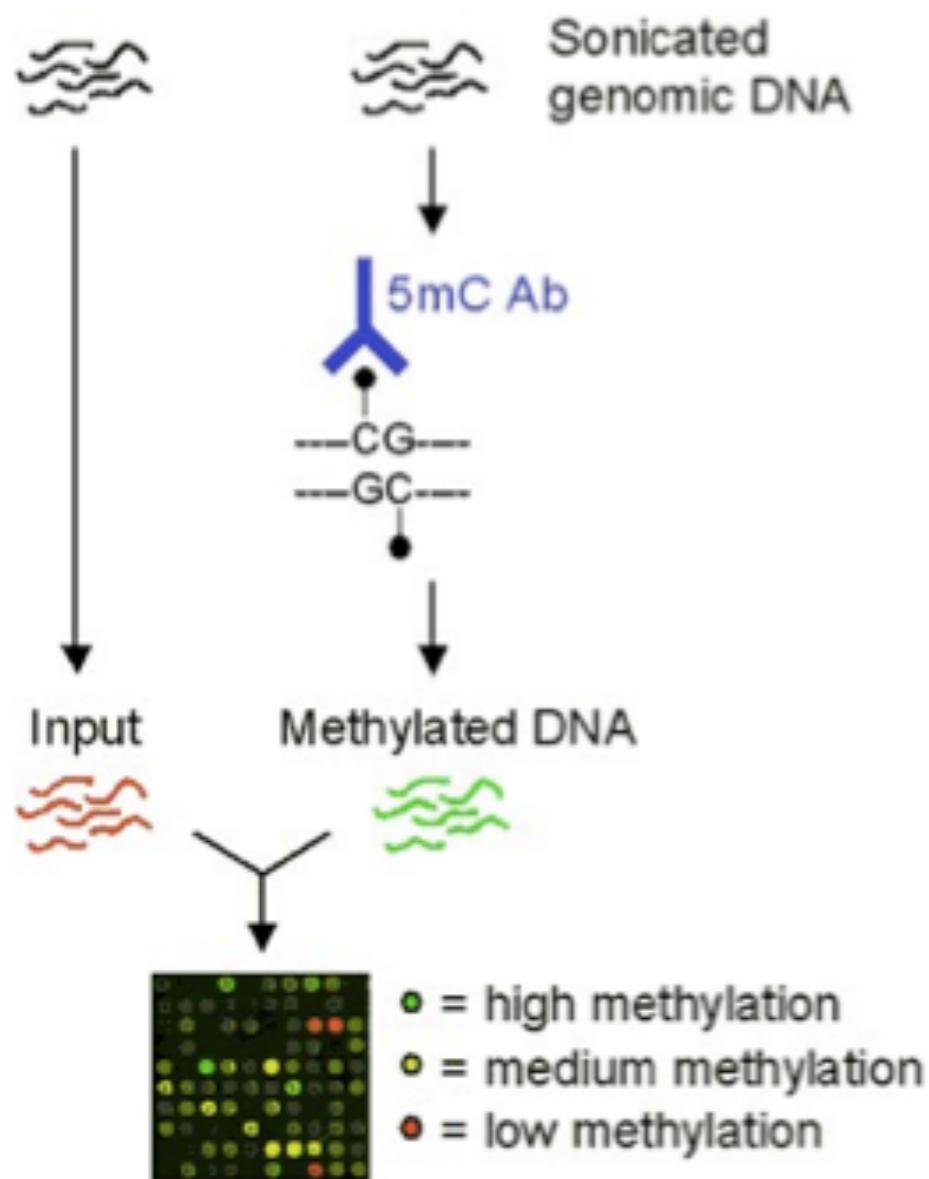
Environmental impact (Estrogens)



- 96 regions that were hypermethylated in EE2
 - 90 are in genes
 - 52 of these cross exon/intron boundary another
 - 32 are in introns
 - 6 are just in exons
- 287 regions that were hypomethylated in EE2
 - 256 are in genes
 - 138 cross exon/intron boundary
 - 114 are in introns only and
 - 4 are just in exons

Very new data

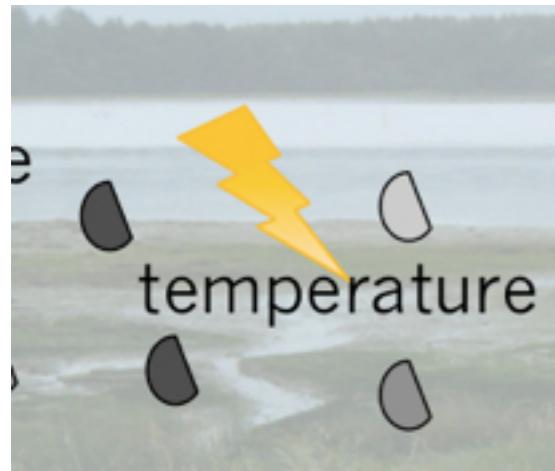
Environmental impact (Estrogens)



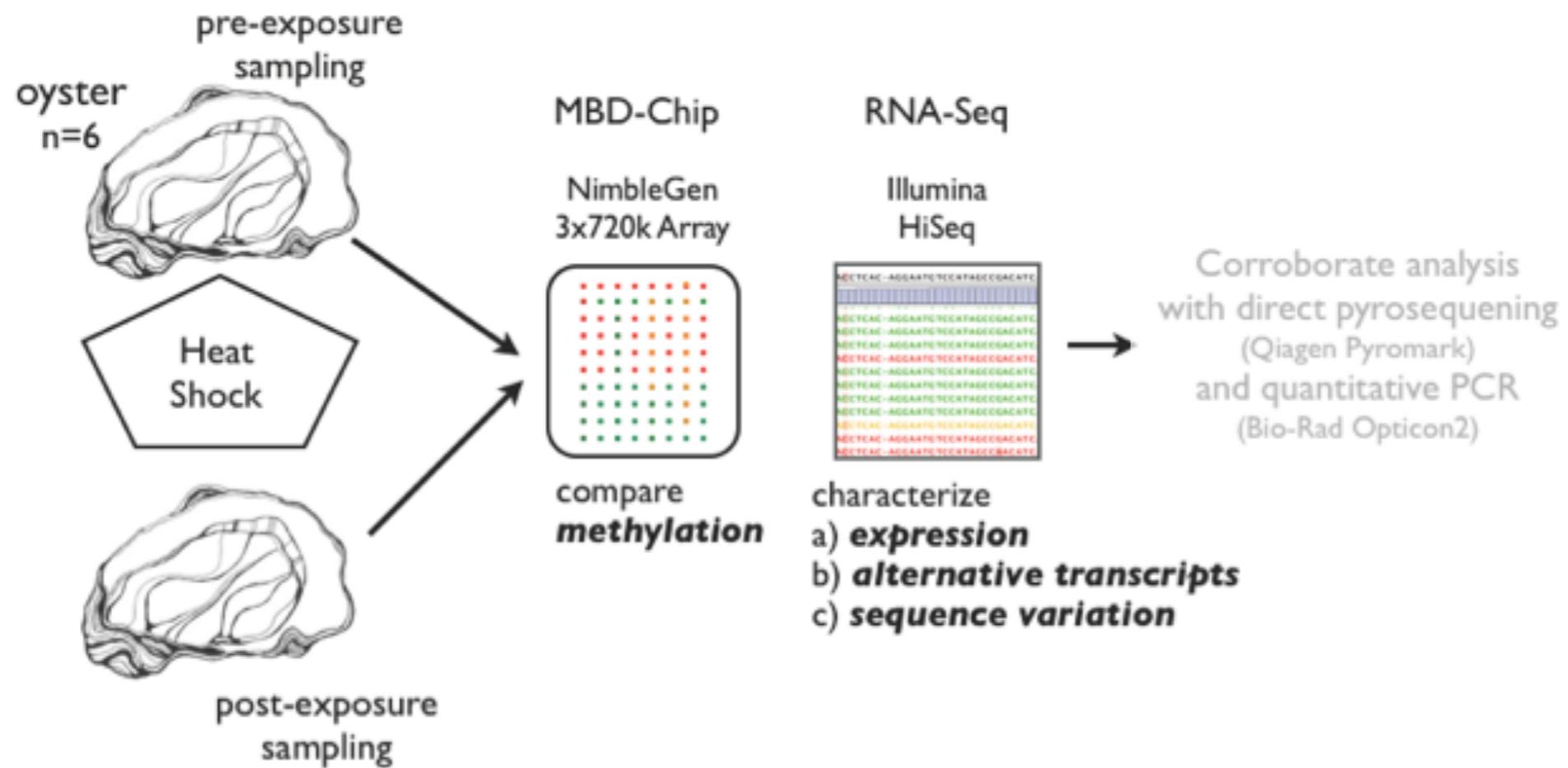
Exposure results in significant hypomethylation

Very new data

Environment and gene expression

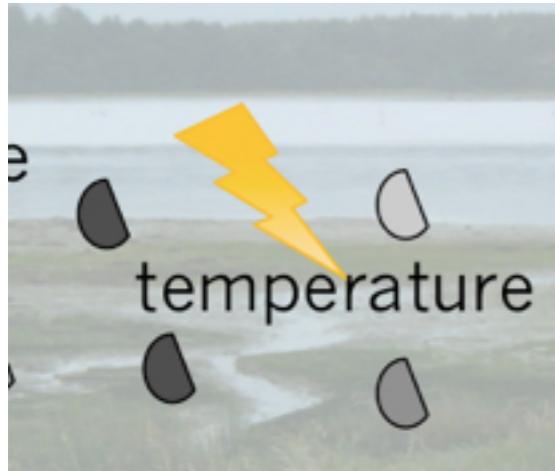


stochastic or targeted?



Very new data

Environment and gene expression

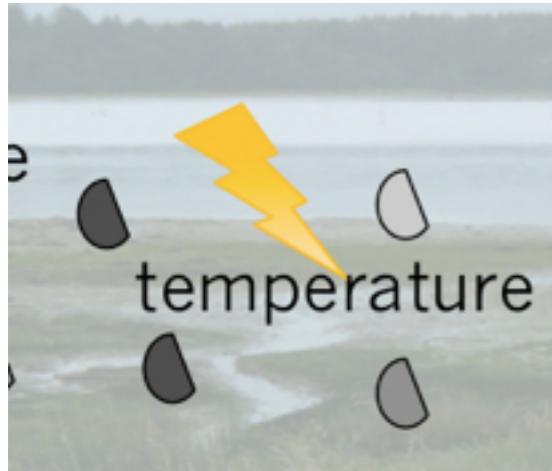


stochastic or targeted?

Oyster	Hypo-methylated	Hyper-methylated
2	7224	2803
4	6560	3587
6	7645	4044

Very new data

Environment and gene expression



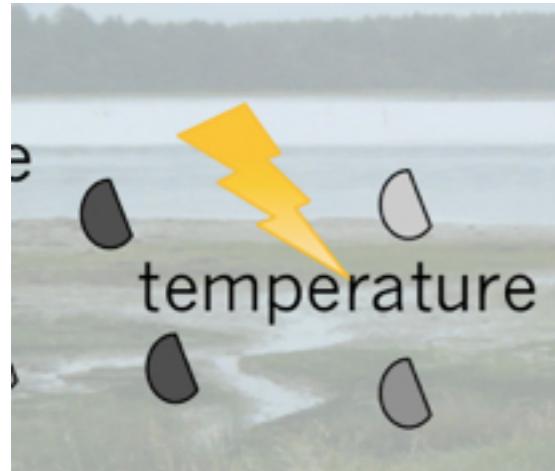
stochastic or targeted?

Oyster	Hypo-methylated	Hyper-methylated
2	7224	2803
4	6560	3587
6	7645	4044

No obvious association
with genome feature
including *differentially*
expressed
genes

Very new data

Environment and gene expression

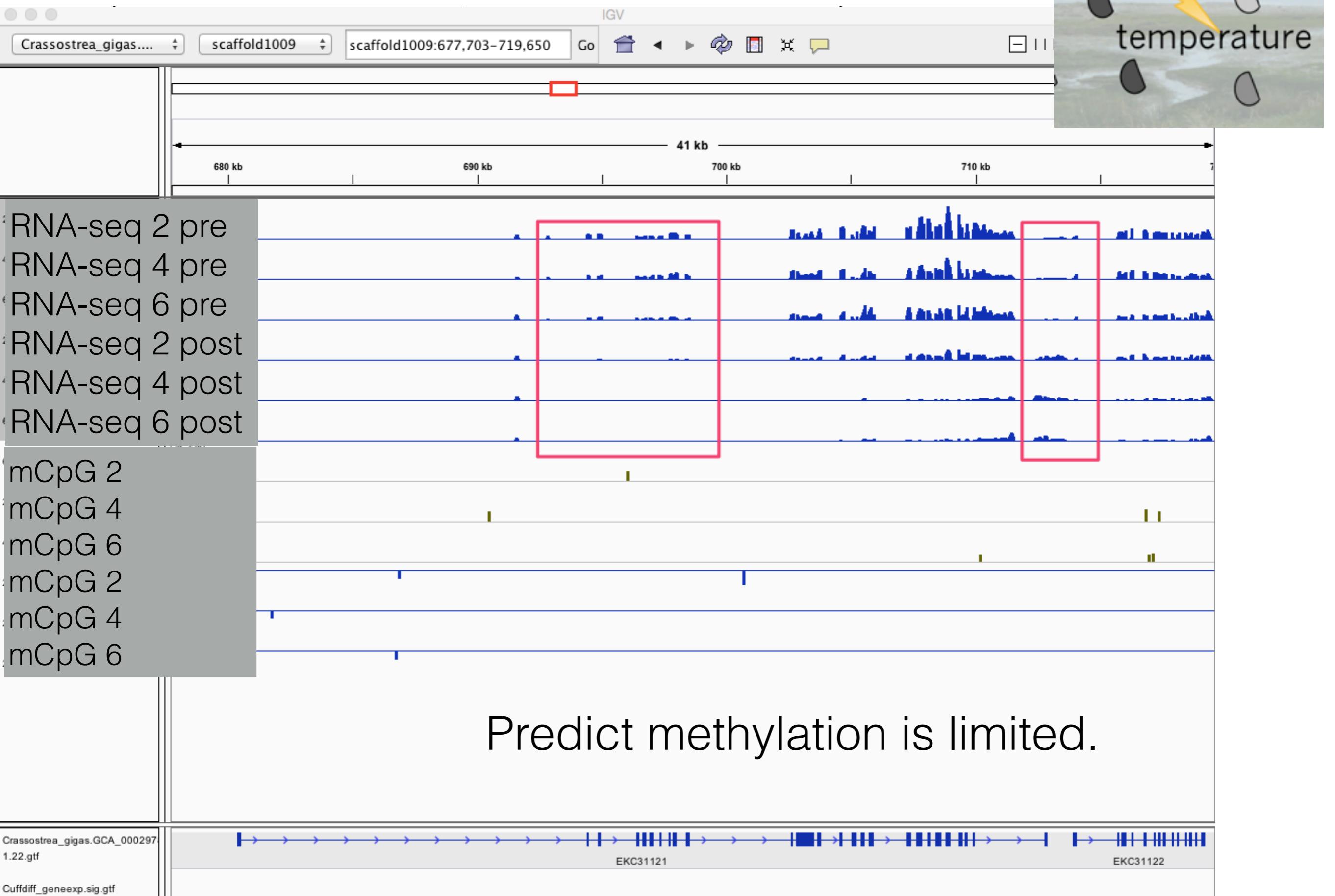


*stochastic or targeted
or ..?*

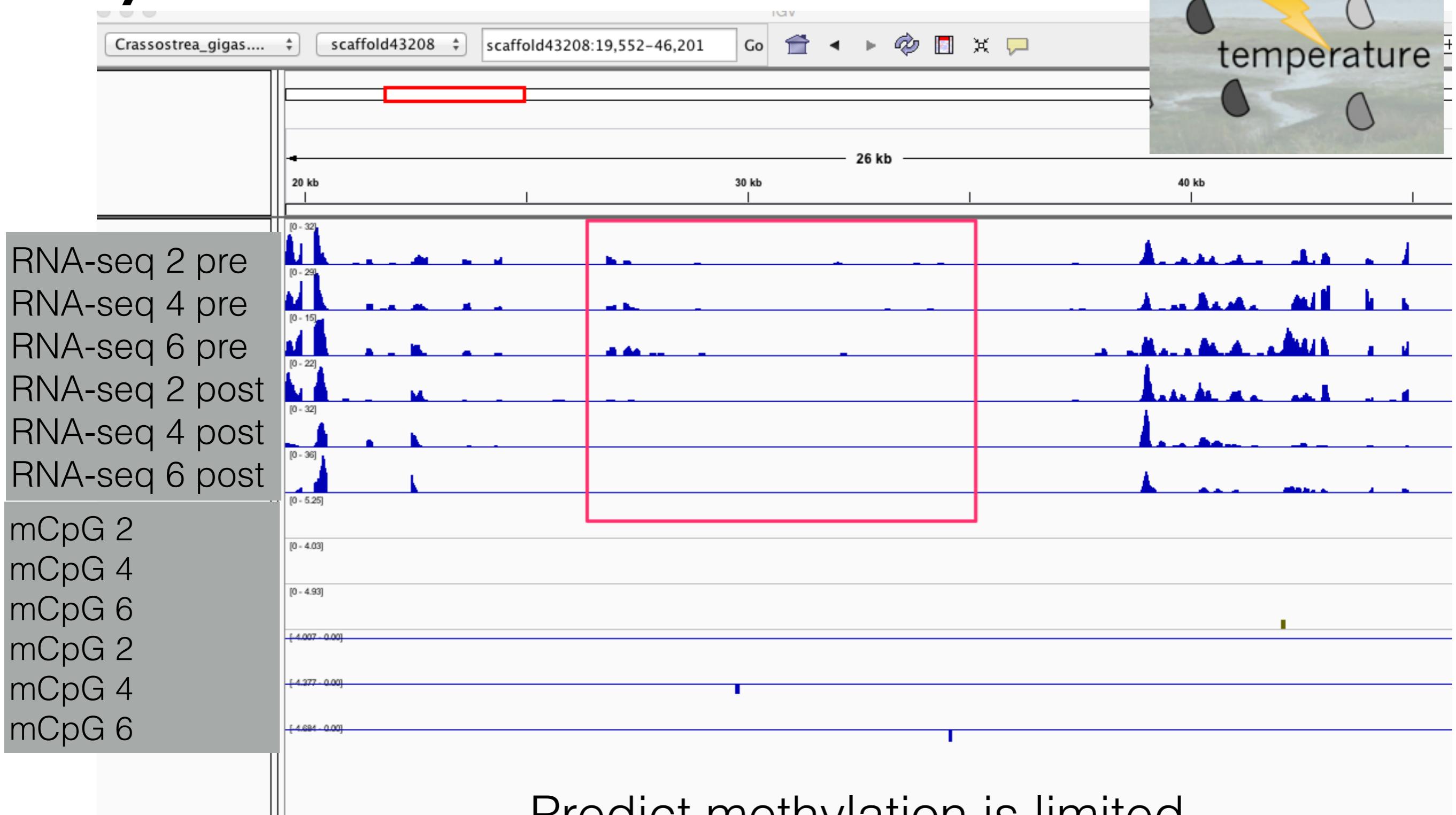
Oyster	Hypo-methylated	Hyper-methylated
2	7224	2803
4	6560	3587
6	7645	4044

Changes in methylation (either direction) are more prevalent in introns, repeats, and transposable elements.

Very new data



Very new data

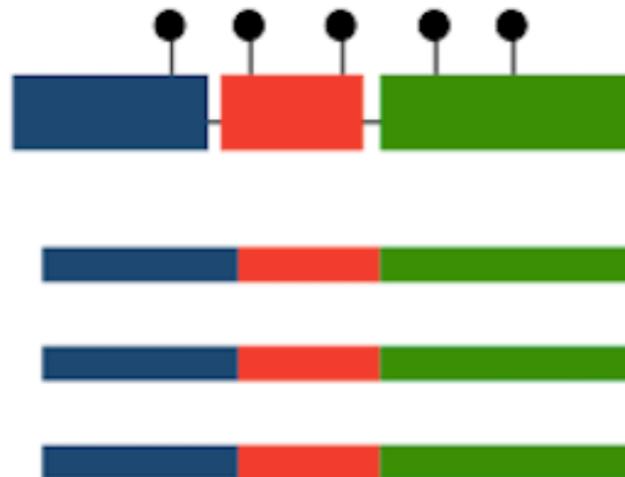


Predict methylation is limited.

Gene
expression

2

Epigenetic
variation



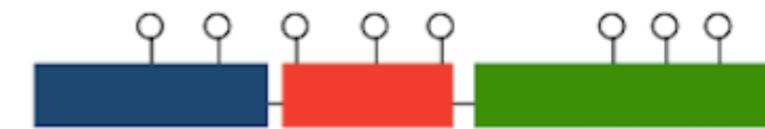
not in this experiment

not even consistent methylation changes at loci level

Gene
expression

2

Epigenetic
variation

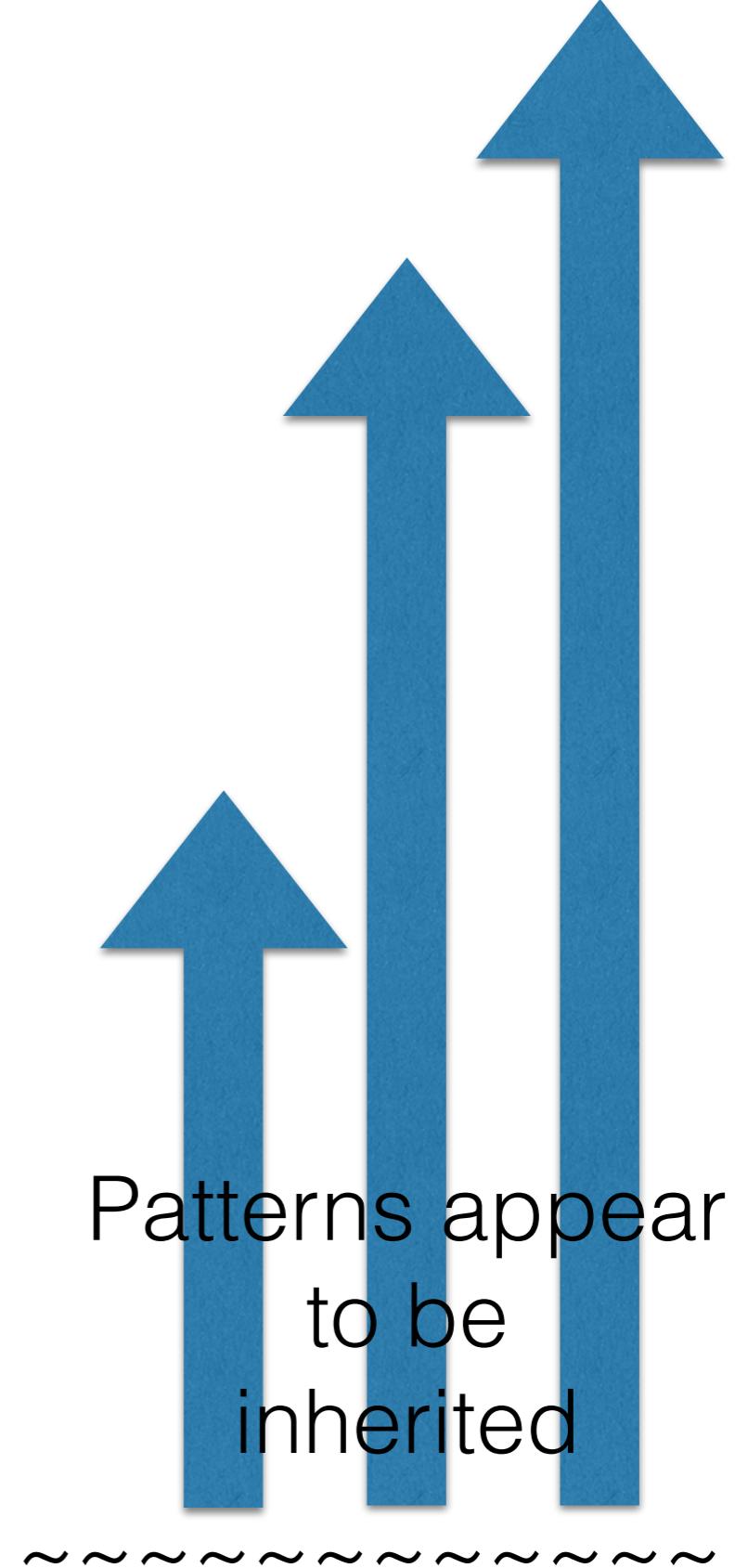


more questions....
interesting but what is controlling?

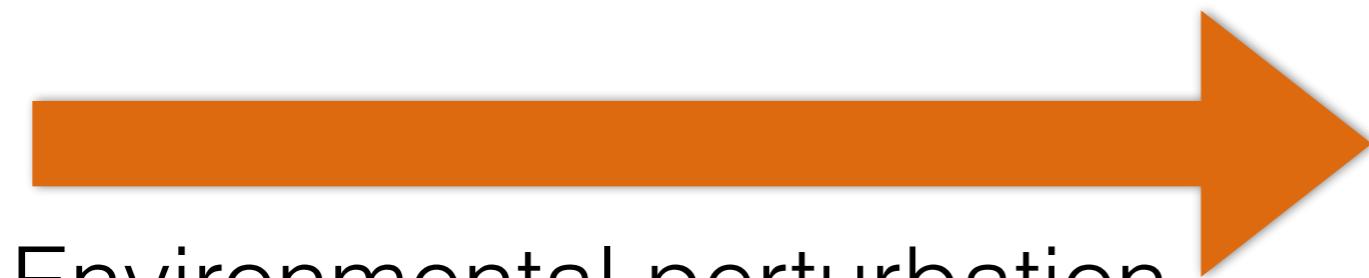
Considerations



Germline methylation encoded with a pattern
product of evolutionary forces



Considerations



Environmental perturbation
impacts DNA methylation
(predominantly demethylation)

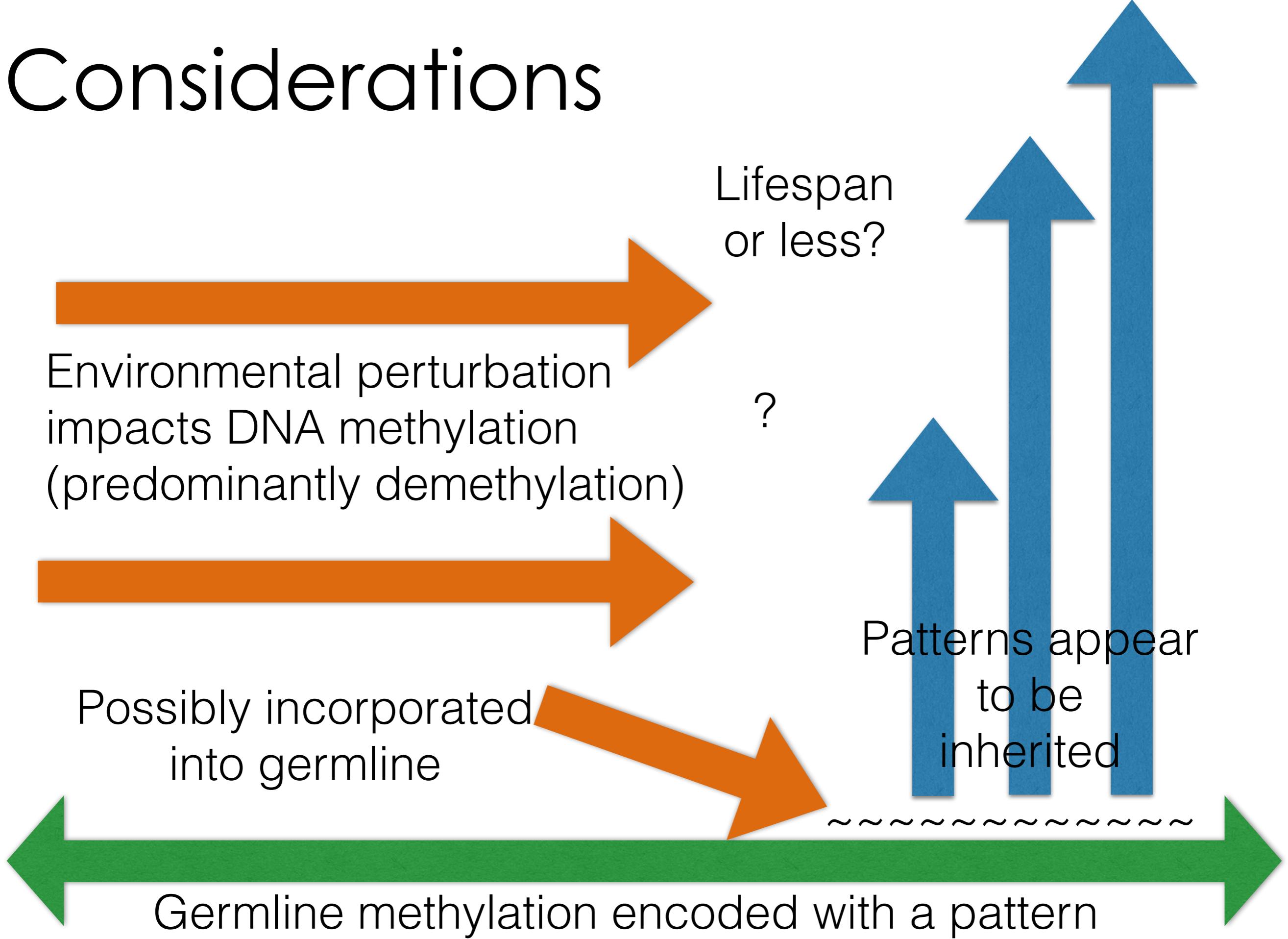


Patterns appear
to be
inherited



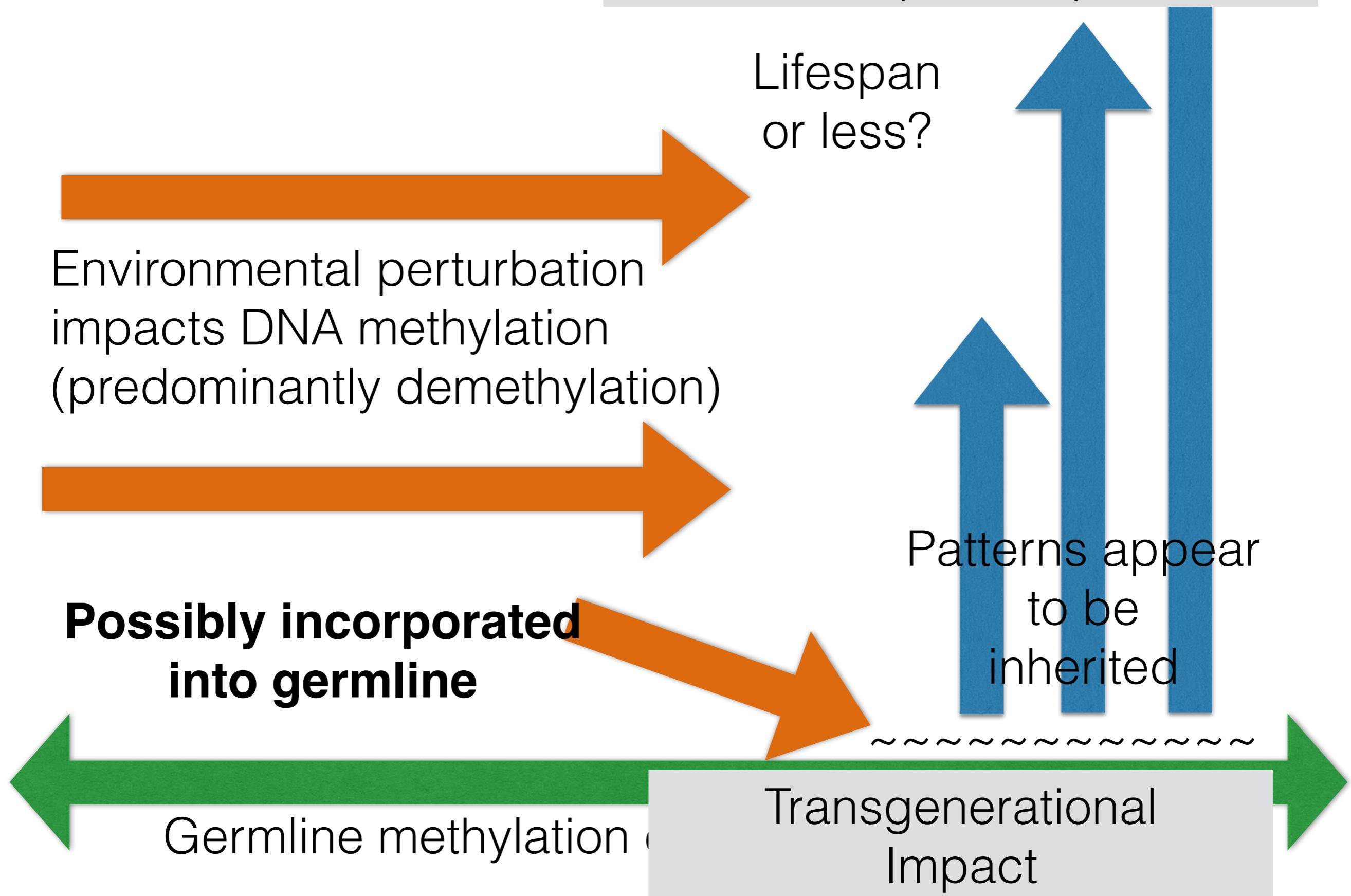
Germline methylation encoded with a pattern
product of evolutionary forces

Considerations



Consideration

Could this provide a “memory”
for subsequent exposure?



Next Steps

Dig into the
heat-shock data

Transposable
Elements

Consider other
epigenetic process

Next Steps

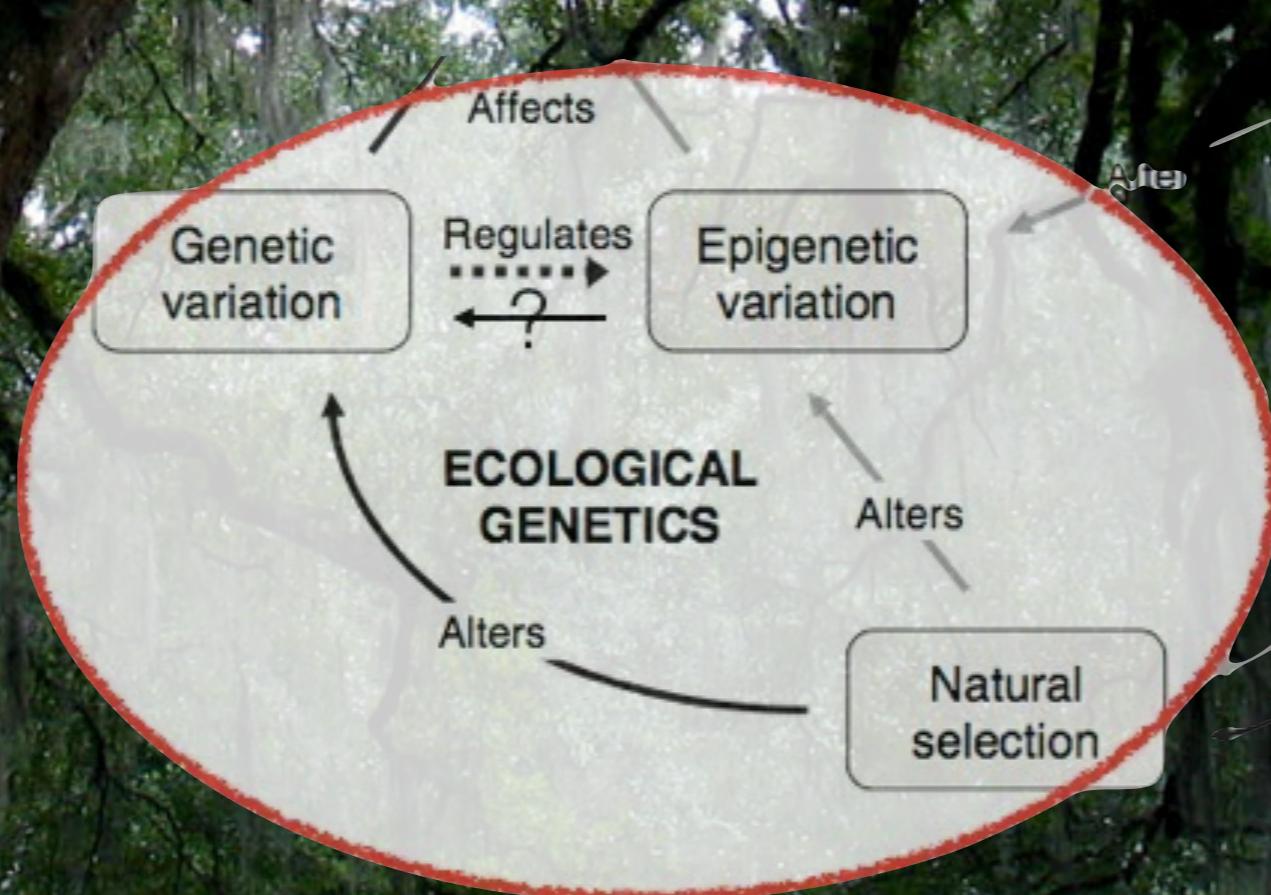


Photo credit: Flickr, Creative Commons, csessums

~~Very new data~~
Heritability
Plasticity
Local Adaptation

*Genetics
versus
Epigenetics*

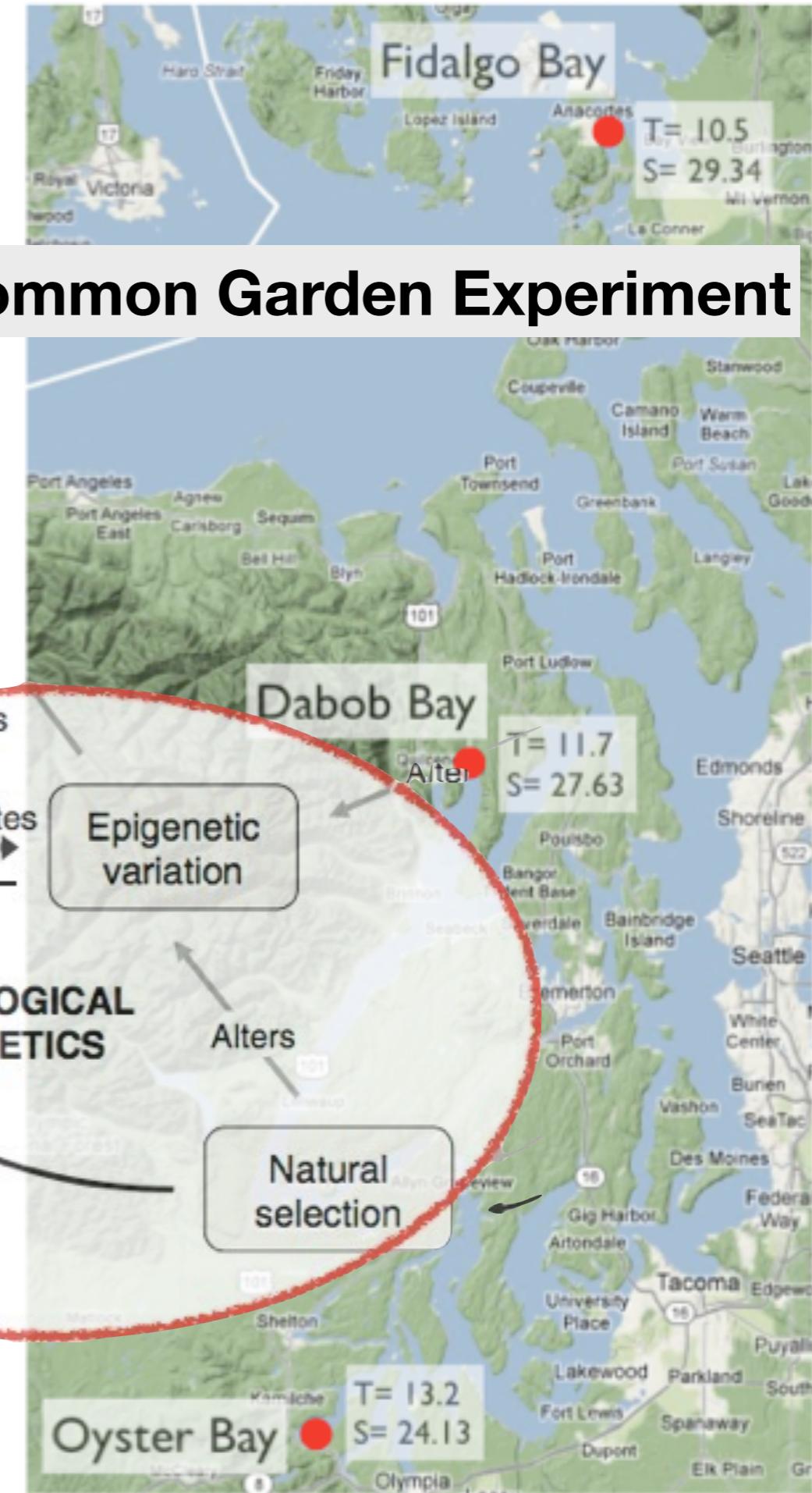
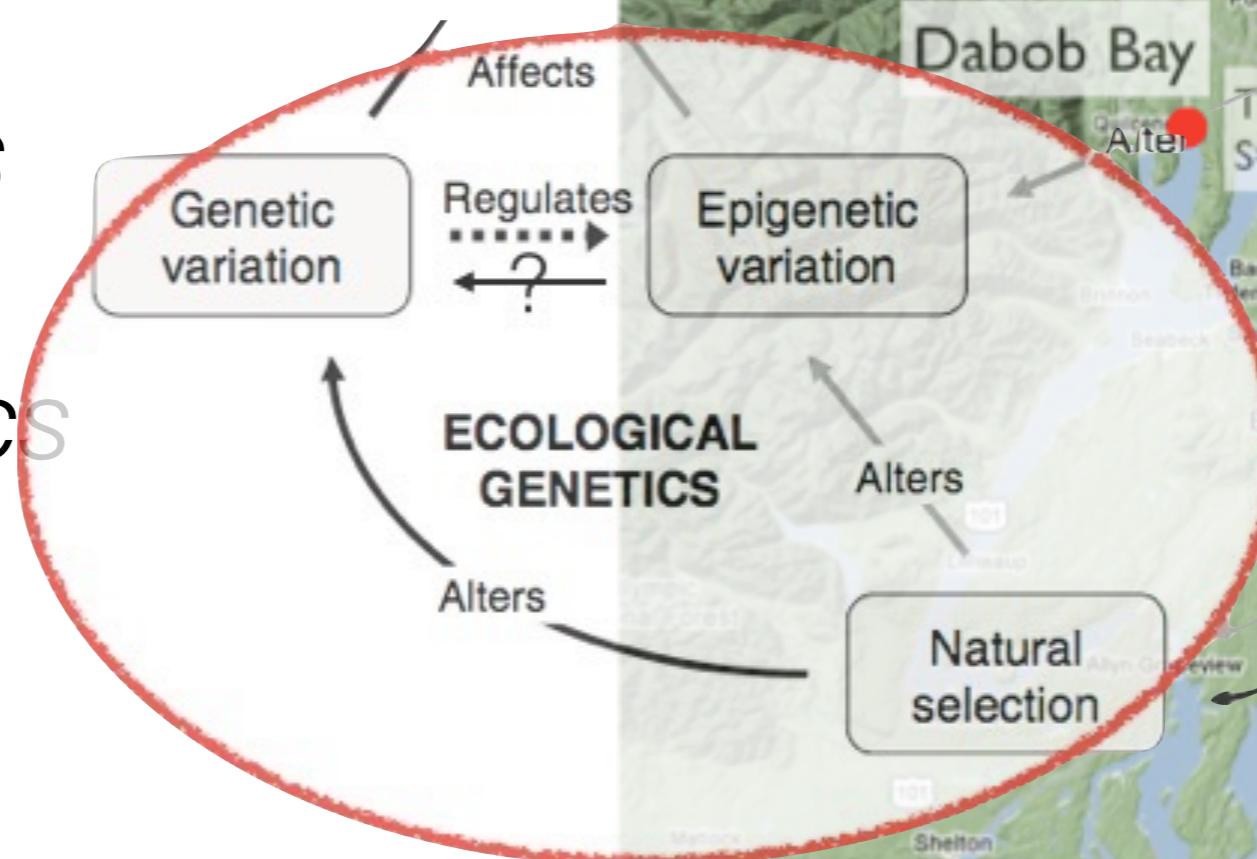


Common Garden Experiment



~~Very new data~~
Heritability
Plasticity
Local Adaptation

Genetics
versus
Epigenetics



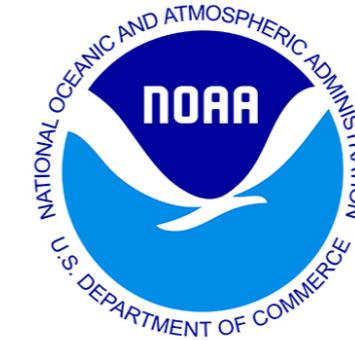
Common Garden Experiment

Acknowledgements

Mackenzie Gavery
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slides, data & more @ robertslab.info