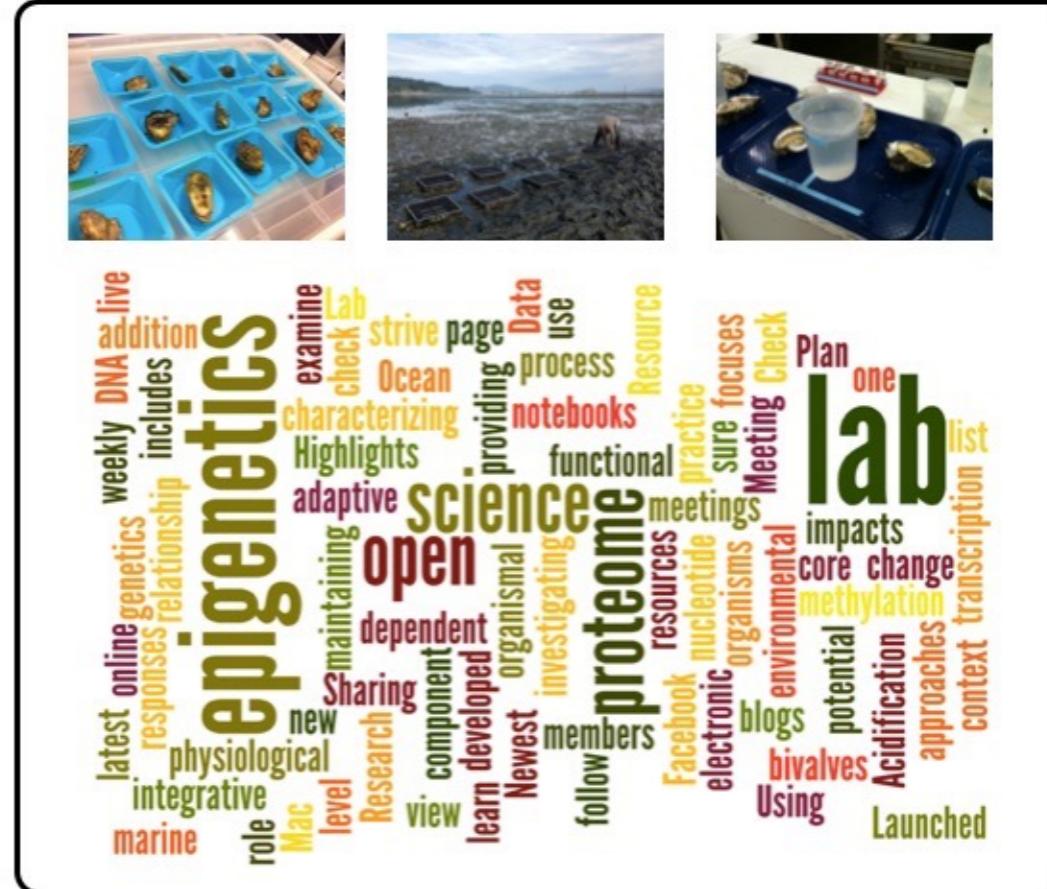


Does DNA Methylation Facilitate Genome Diversity and Phenotypic Plasticity in Marine Invertebrates?

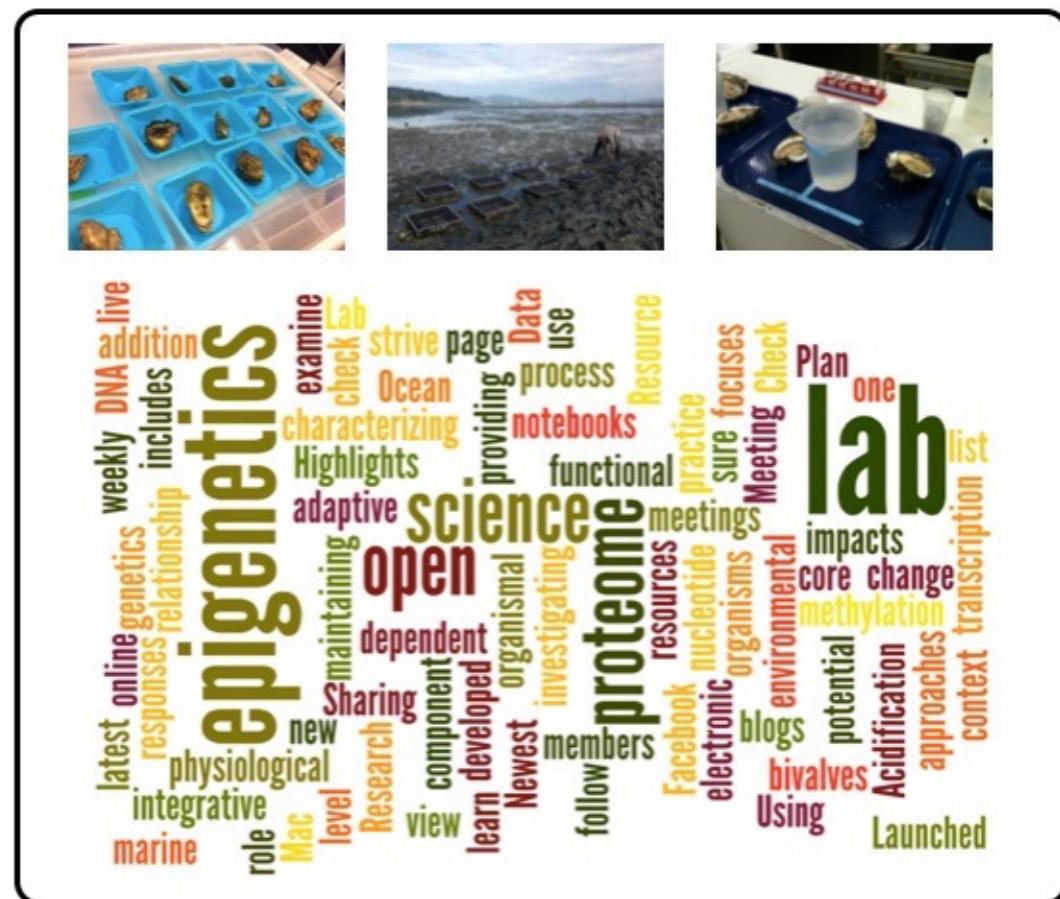
Steven Roberts
Associate Professor
School of Aquatic and Fishery Sciences
robertslab.info
@sr320



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

#tldr ~ probably

Steven Roberts
Associate Professor
School of Aquatic and Fishery Sciences
robertslab.info
[@sr320](https://twitter.com/sr320)

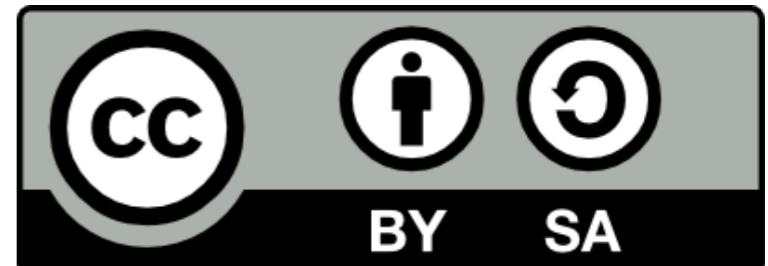


Open Science

- You are free to Share!
- Our lab practices open notebook science



IP[y]: IPython
Interactive Computing



OpenNotebookScience

@ONScience FOLLOWS YOU

Updates from #openscience notebooks,
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yours at onsnetwork.org/joinons/

onsnetwork.org

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

These slides plus links @ robertslab.info

Background

disease resistance

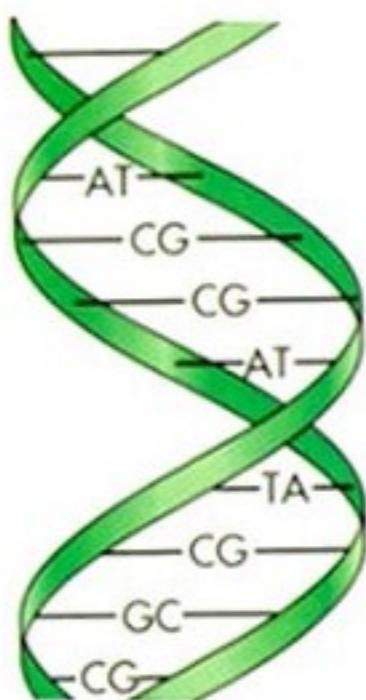


growth

color

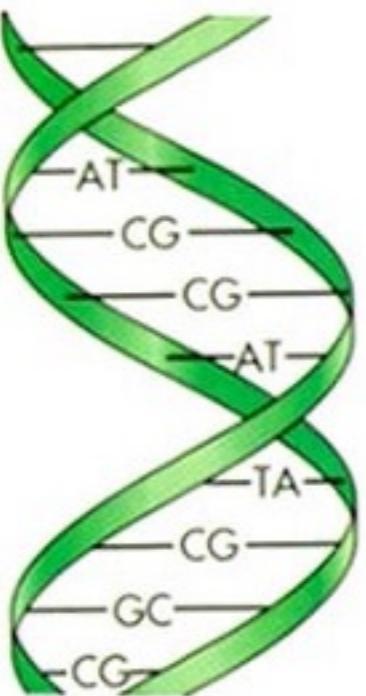
stress
tolerance

Traits



Background

Transcriptome



disease resistance



growth

color

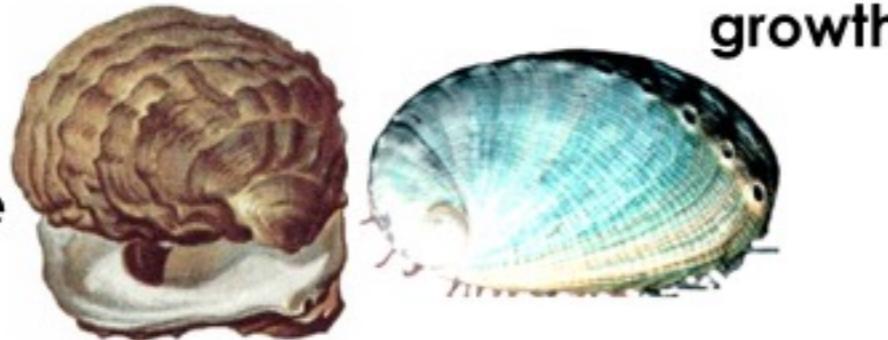
stress
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Traits



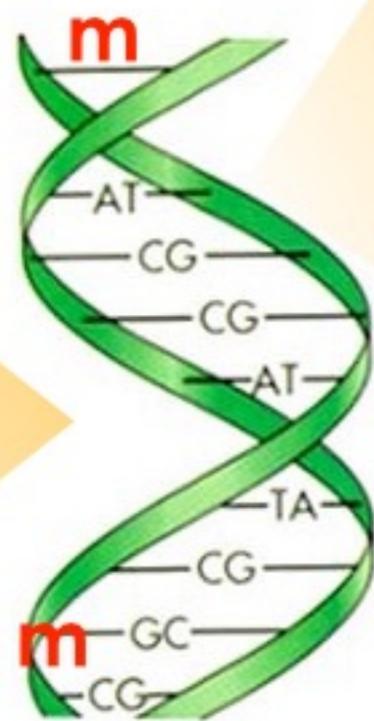
Background

disease resistance



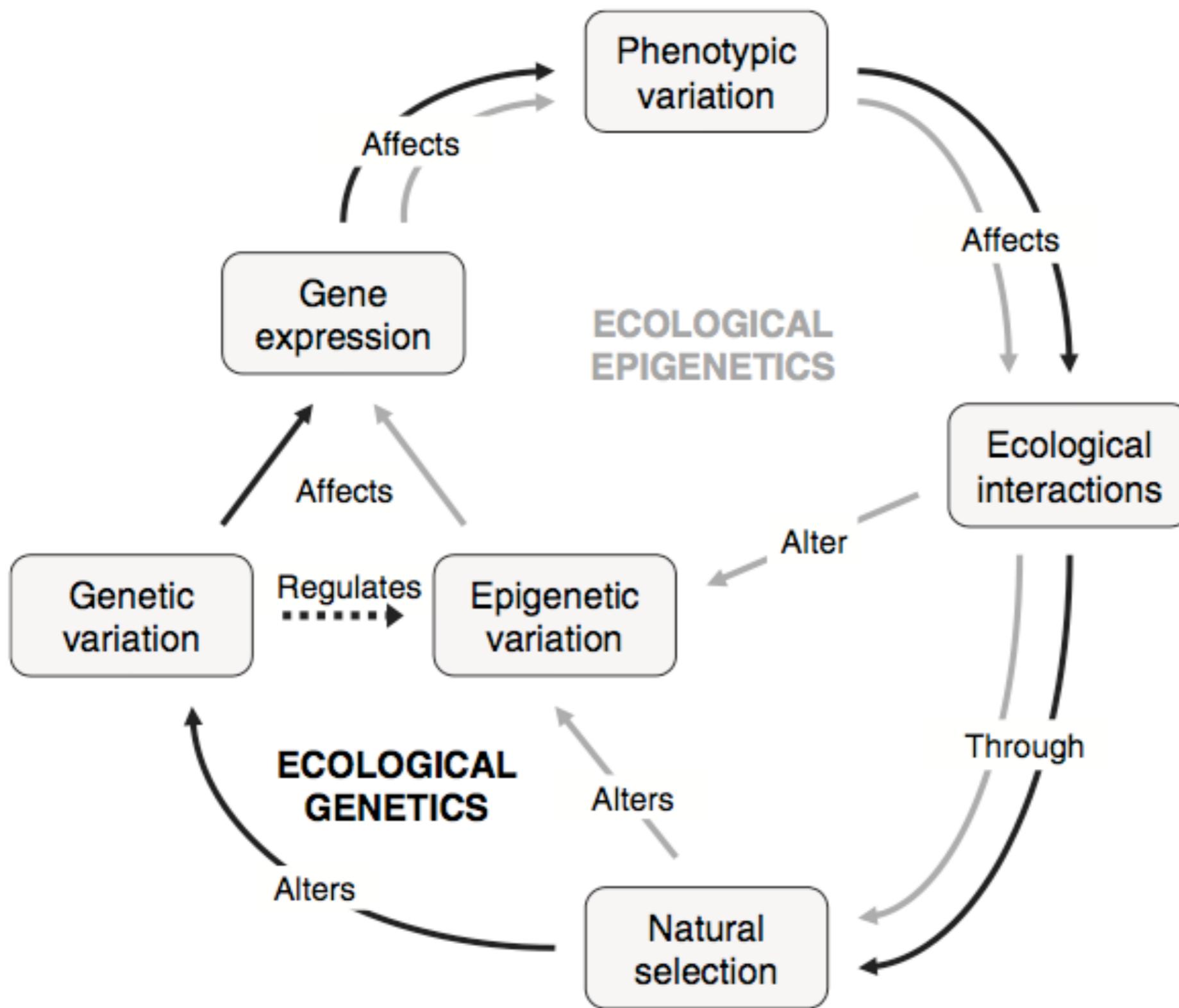
growth

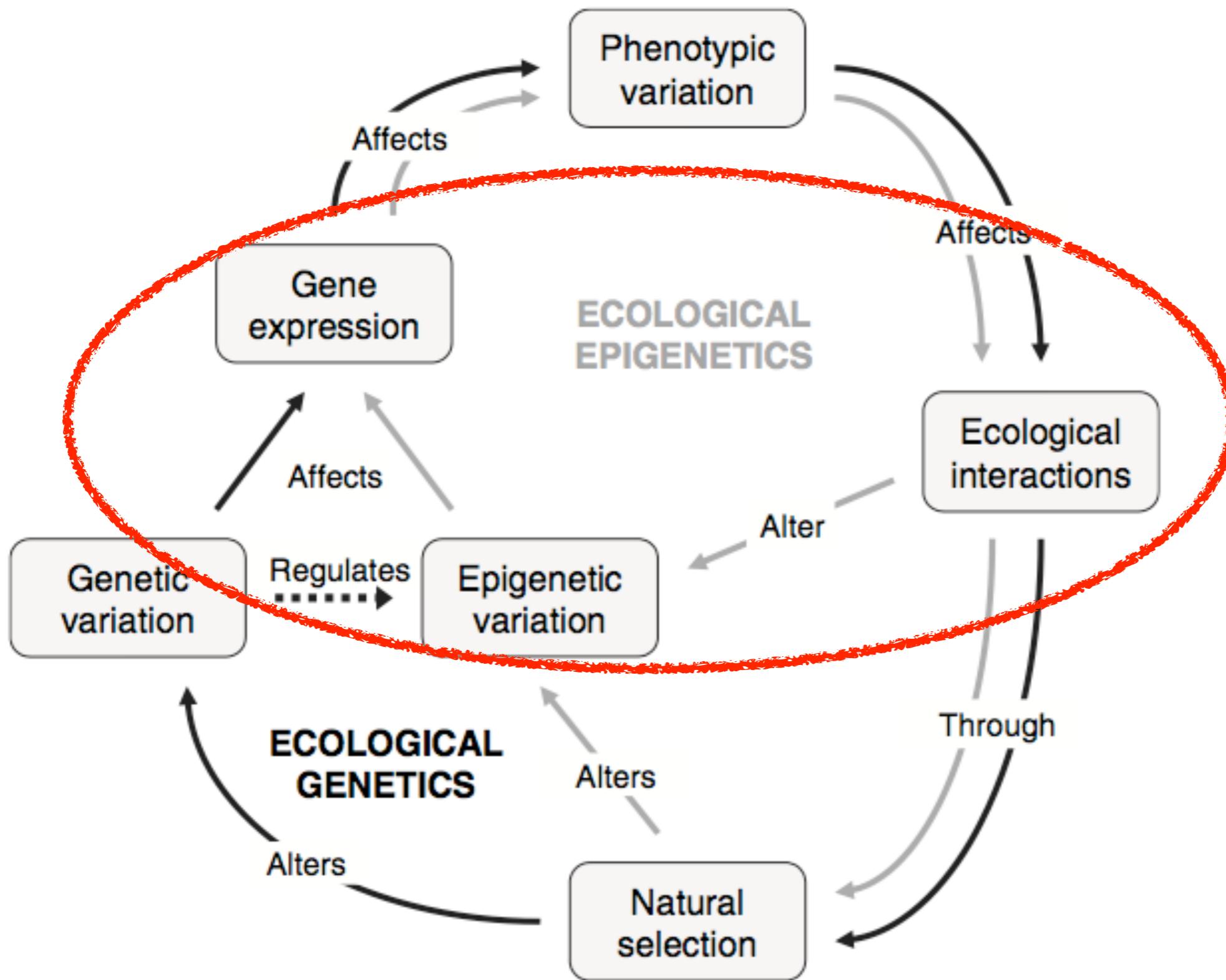
Traits

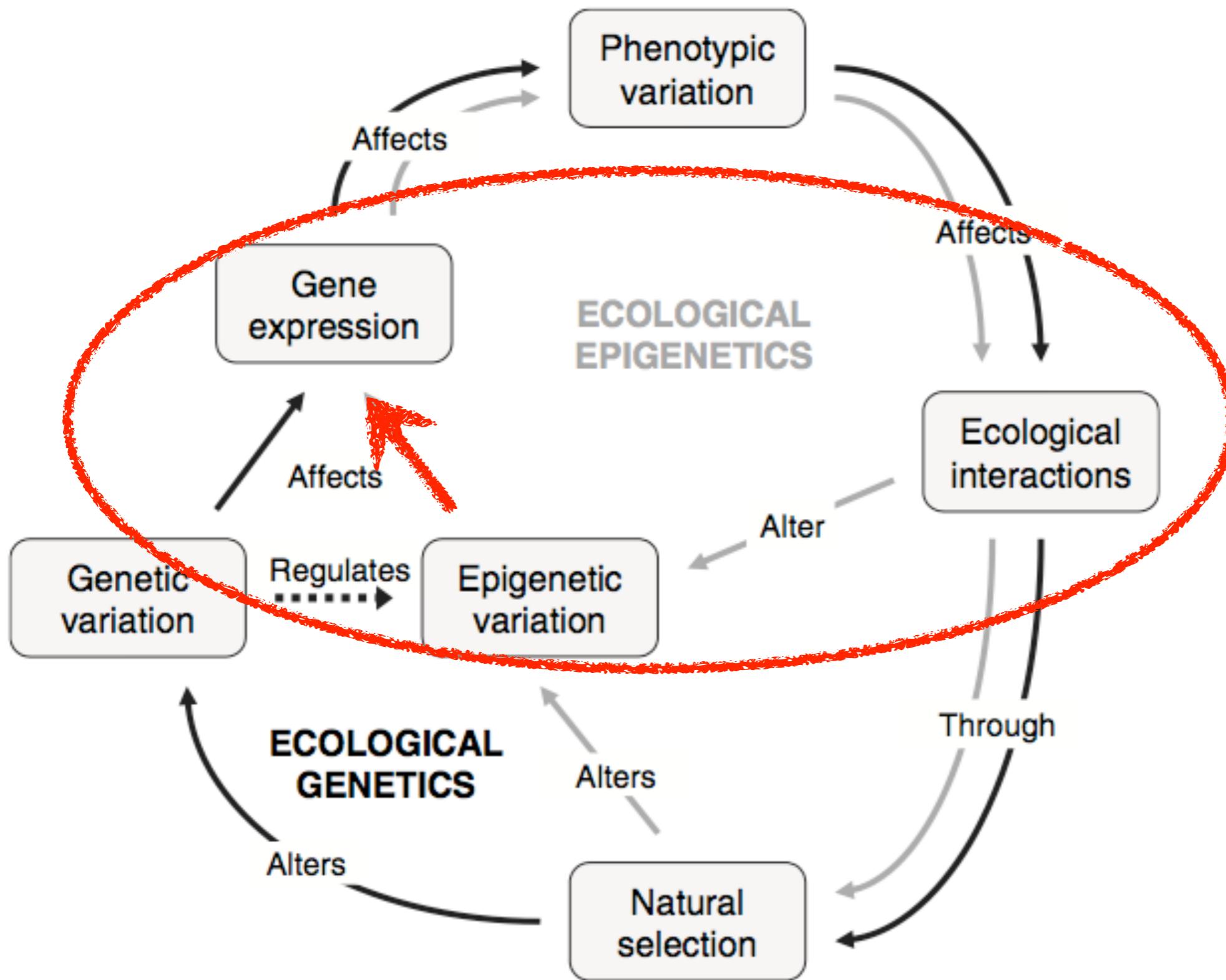


Epigenetics

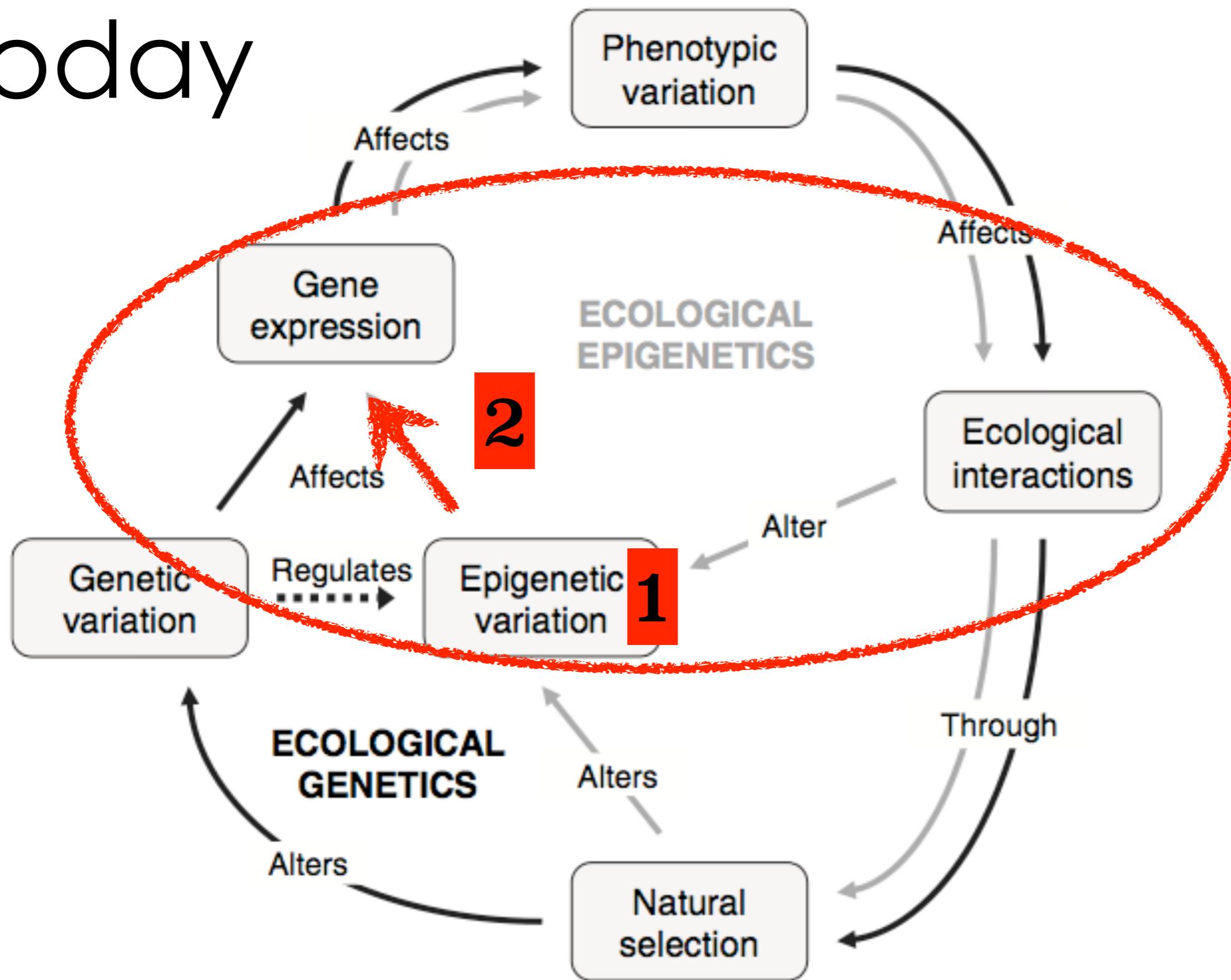








Today



Ecology Letters, (2008) 11: 106–115

doi: 10.1111/j.1461-0248.2007.01130.x

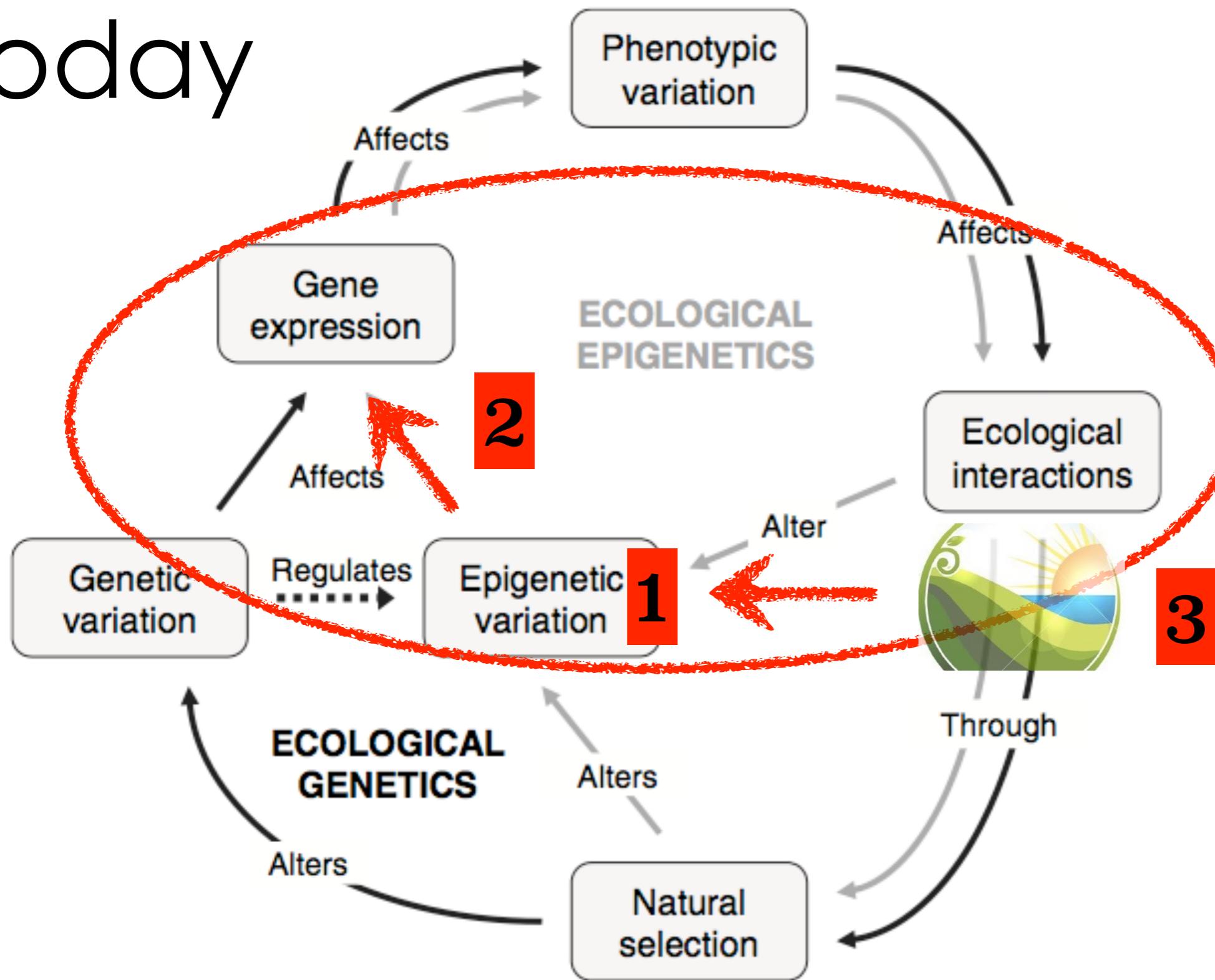
modified from

IDEA AND
PERSPECTIVE

Epigenetics for ecologists

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

Today



Ecology Letters, (2008) 11: 106–115

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IDEA AND
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Epigenetics for ecologists

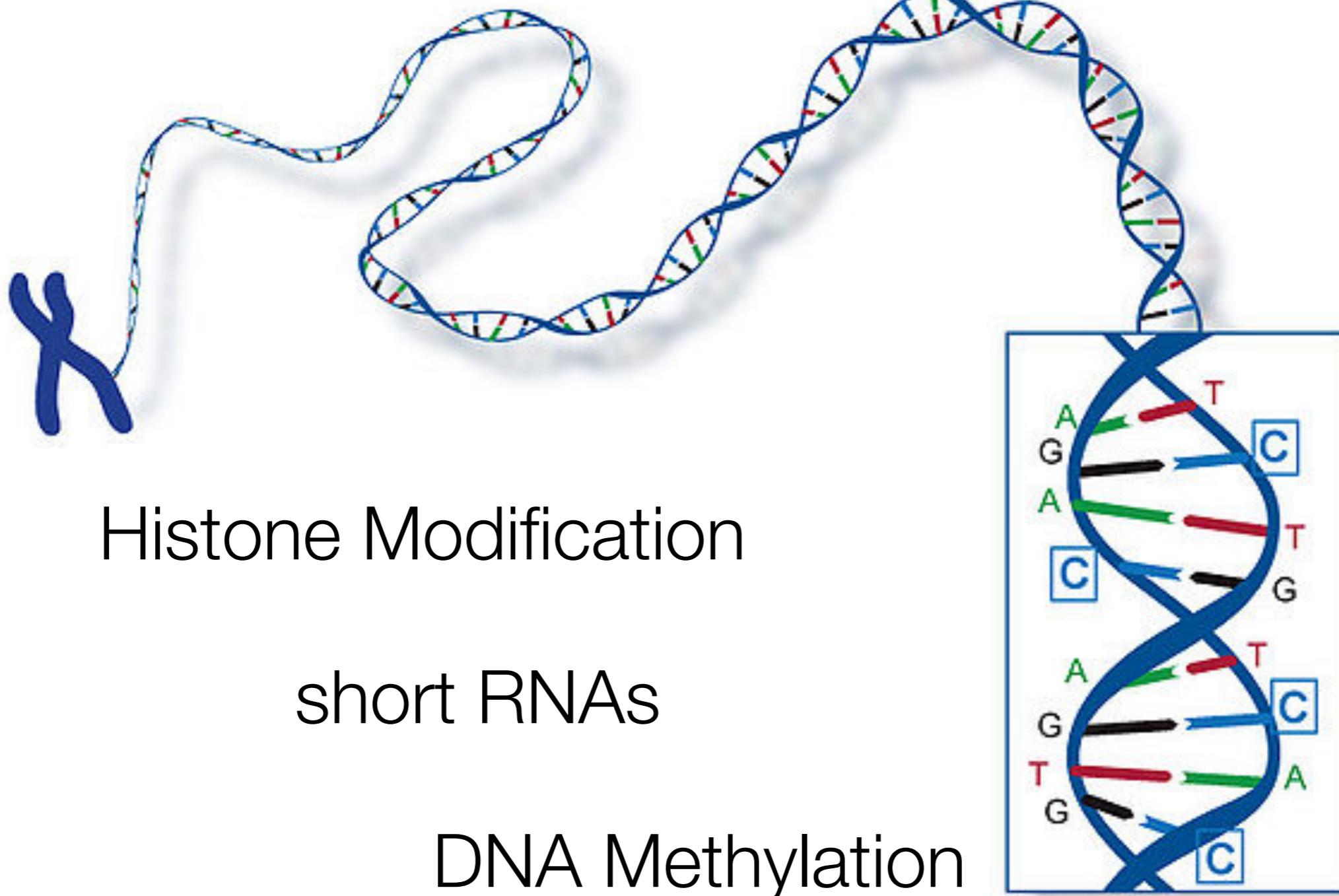
Oliver Bossdorf,^{1,*} Christina L.
Richards² and Massimo Pigliucci³



Genome Resources



Epigenetics



Epigenetics



Photo credit: Flickr, Creative Commons, he-boden



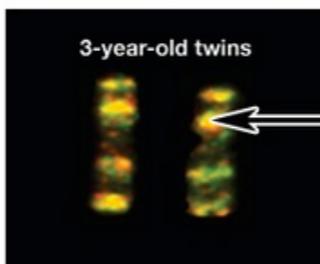
Epigenetics



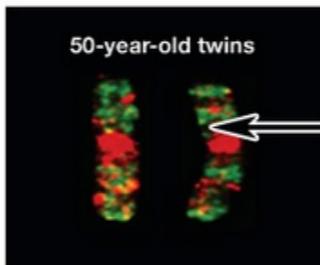
Nature AND Nurture

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.

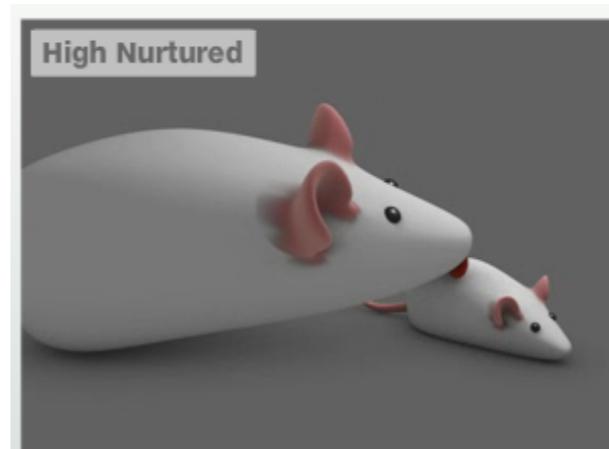
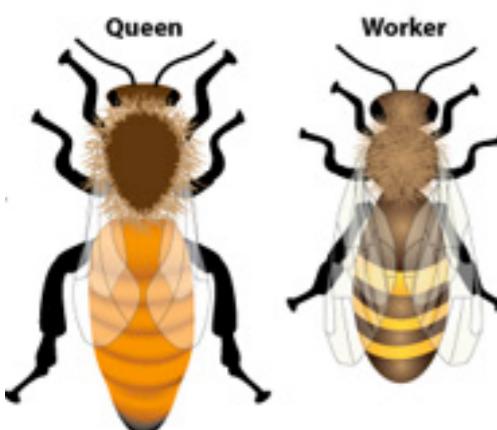
While pregnant, both of their mothers were fed Bisphenol A (BPA) but DIFFERENT DIETS:

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

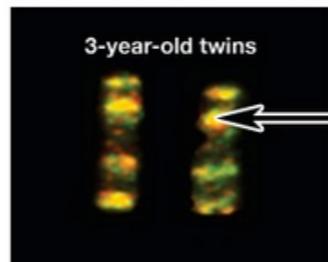
These Two Mice are Genetically Identical and the Same Age



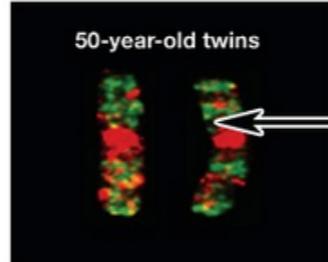
Nature AND Nurture

Chromosome 3 Pairs

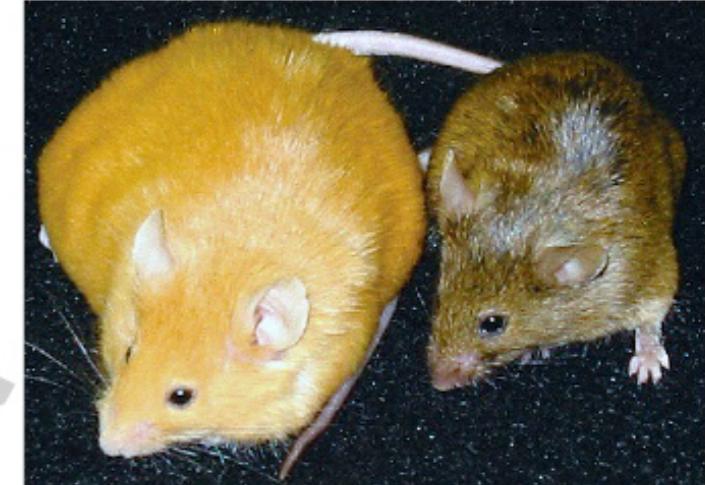
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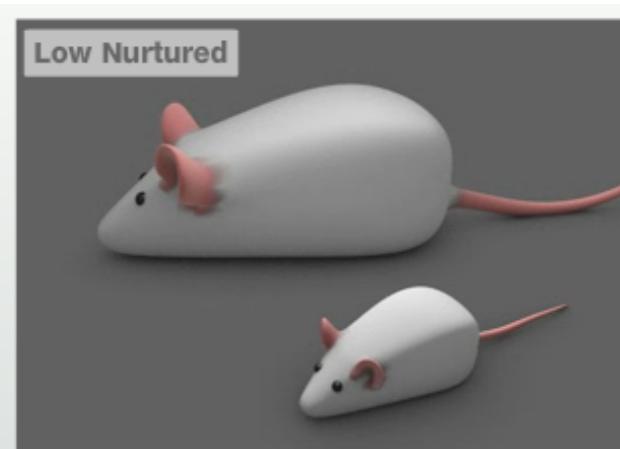
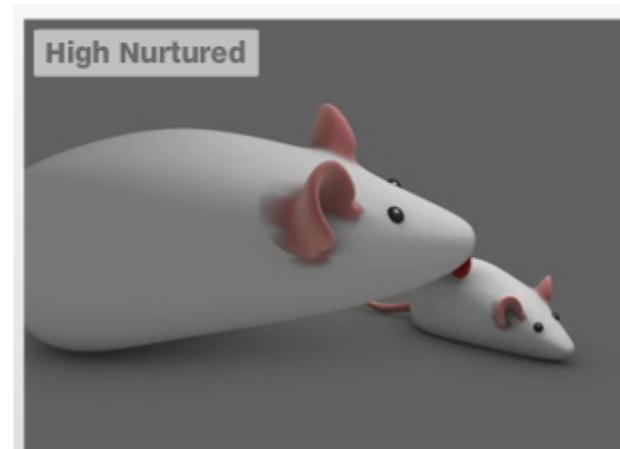
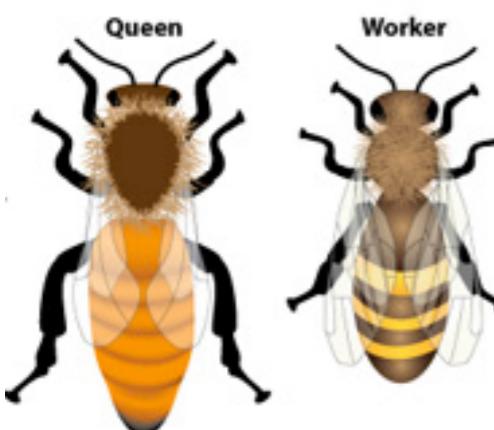
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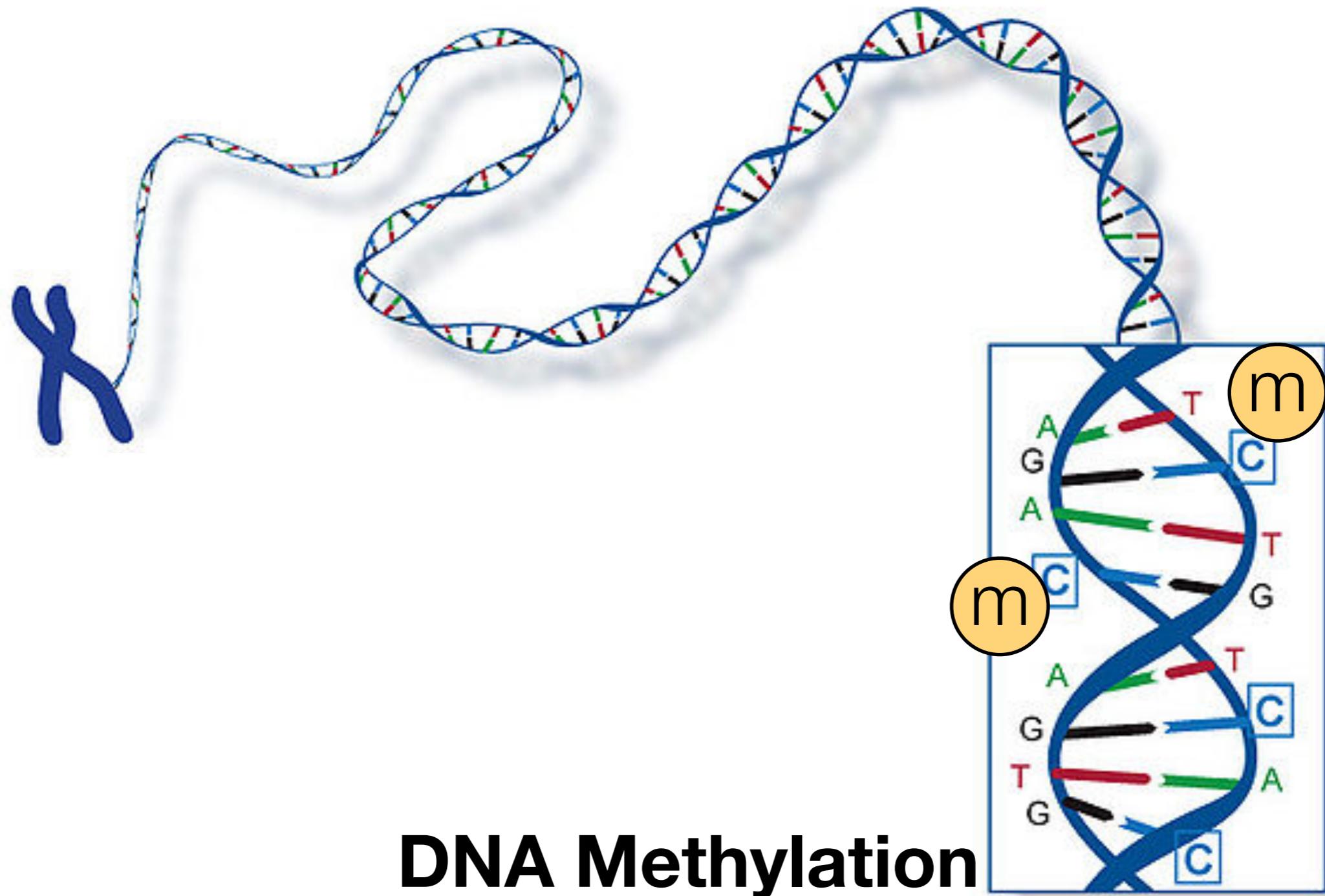


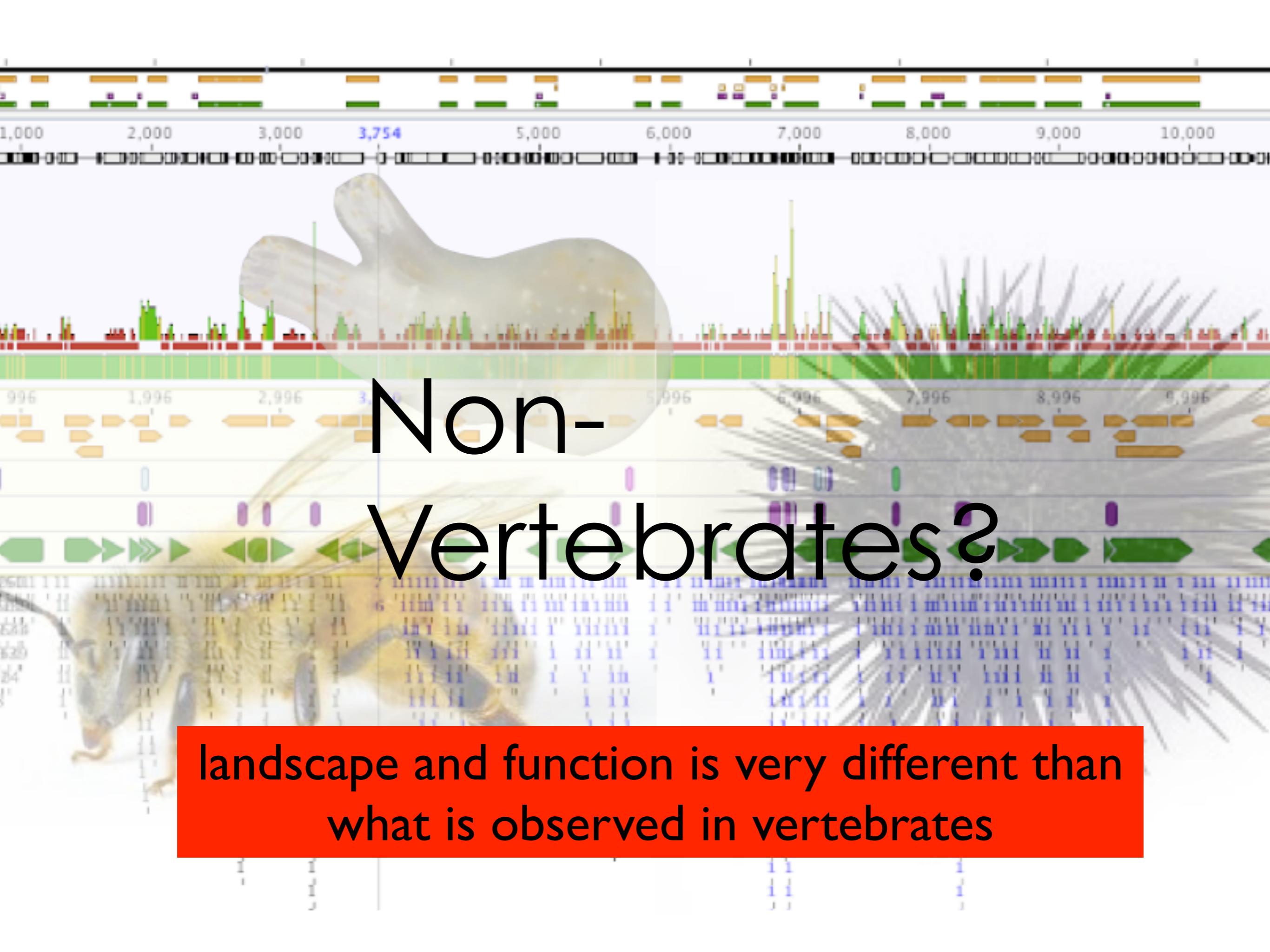
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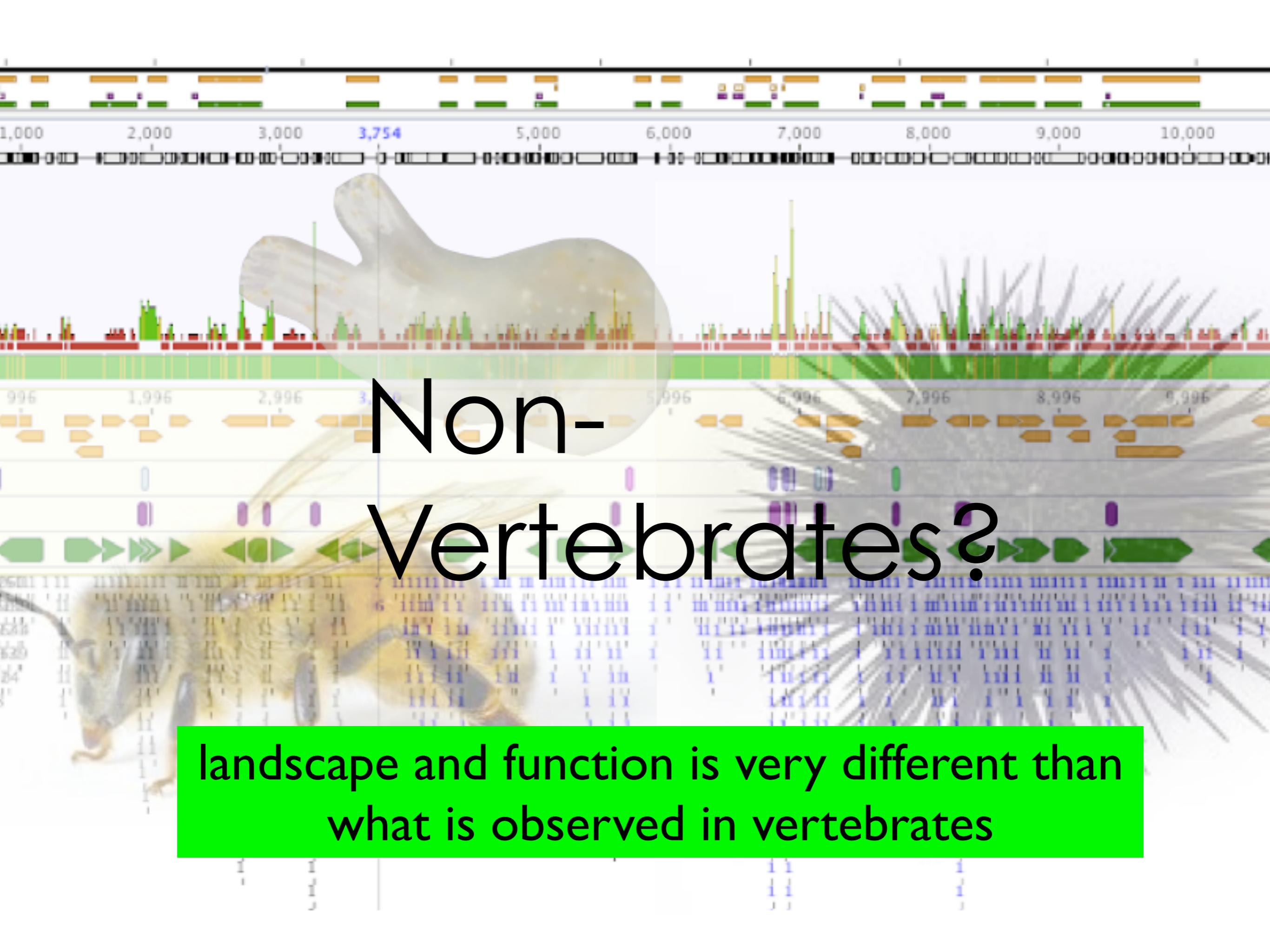
AUDIO





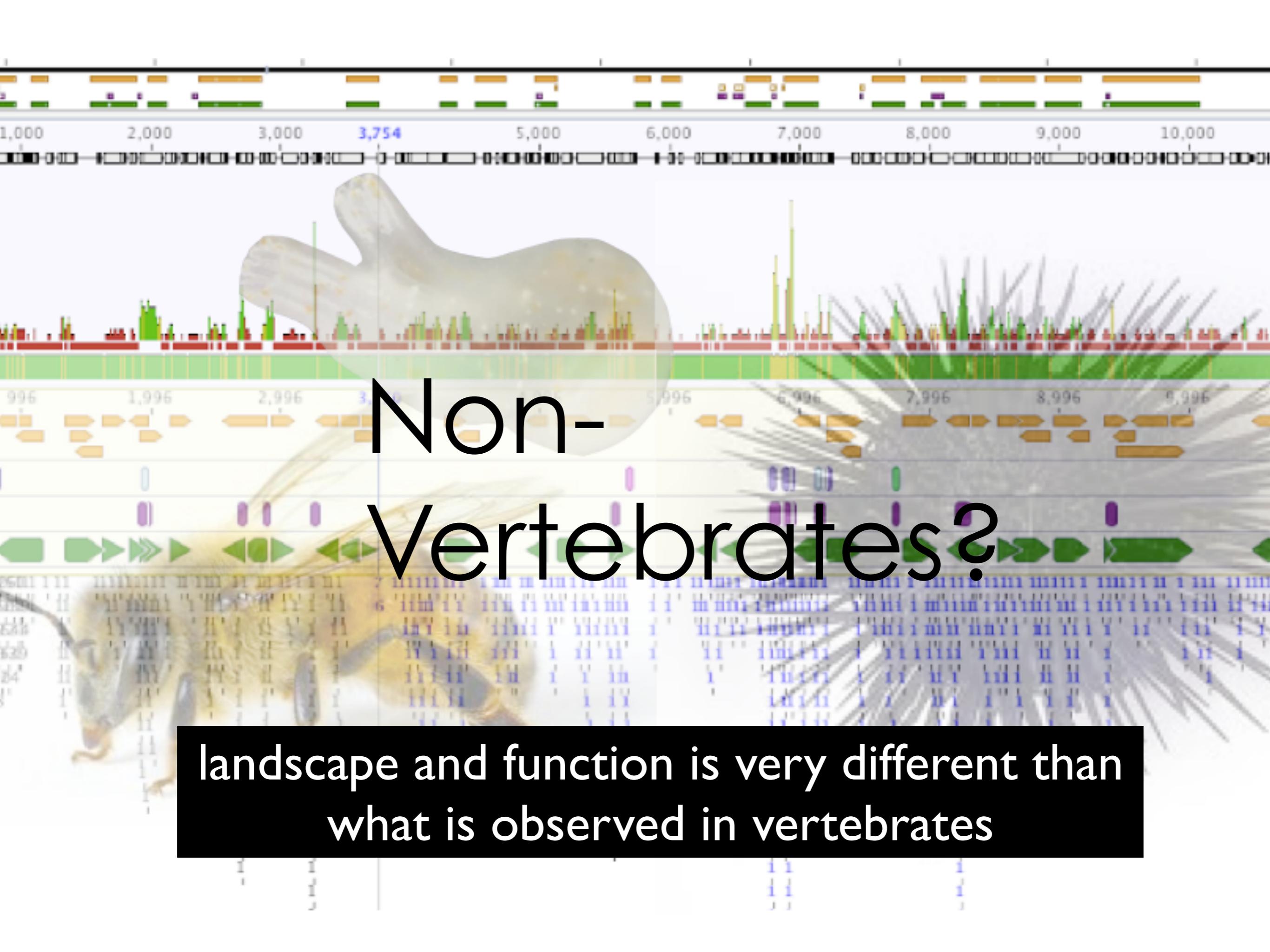
Non- Vertebrates?

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?

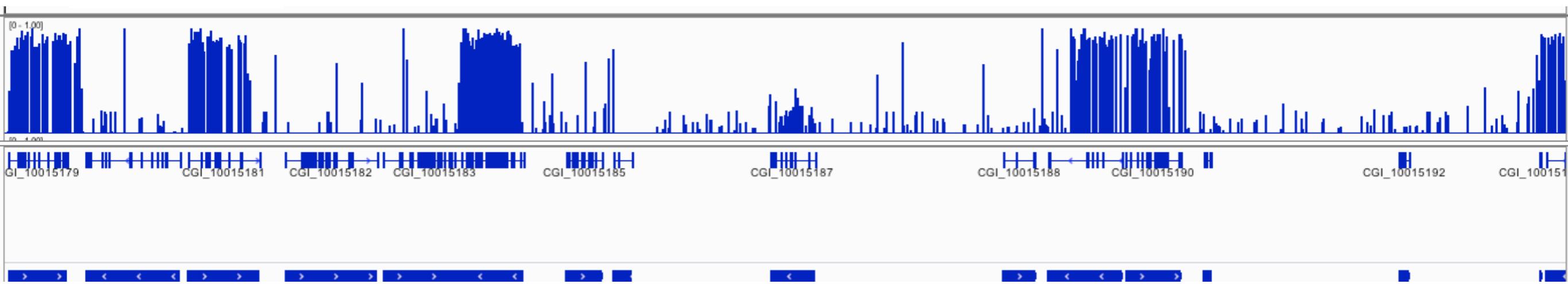
landscape and function is very different than
what is observed in vertebrates

*Absent in
several
model
organisms*



Oysters?

Epigenetic variation **1**



mosaic

associated with gene bodies

Epigenetic variation **1**

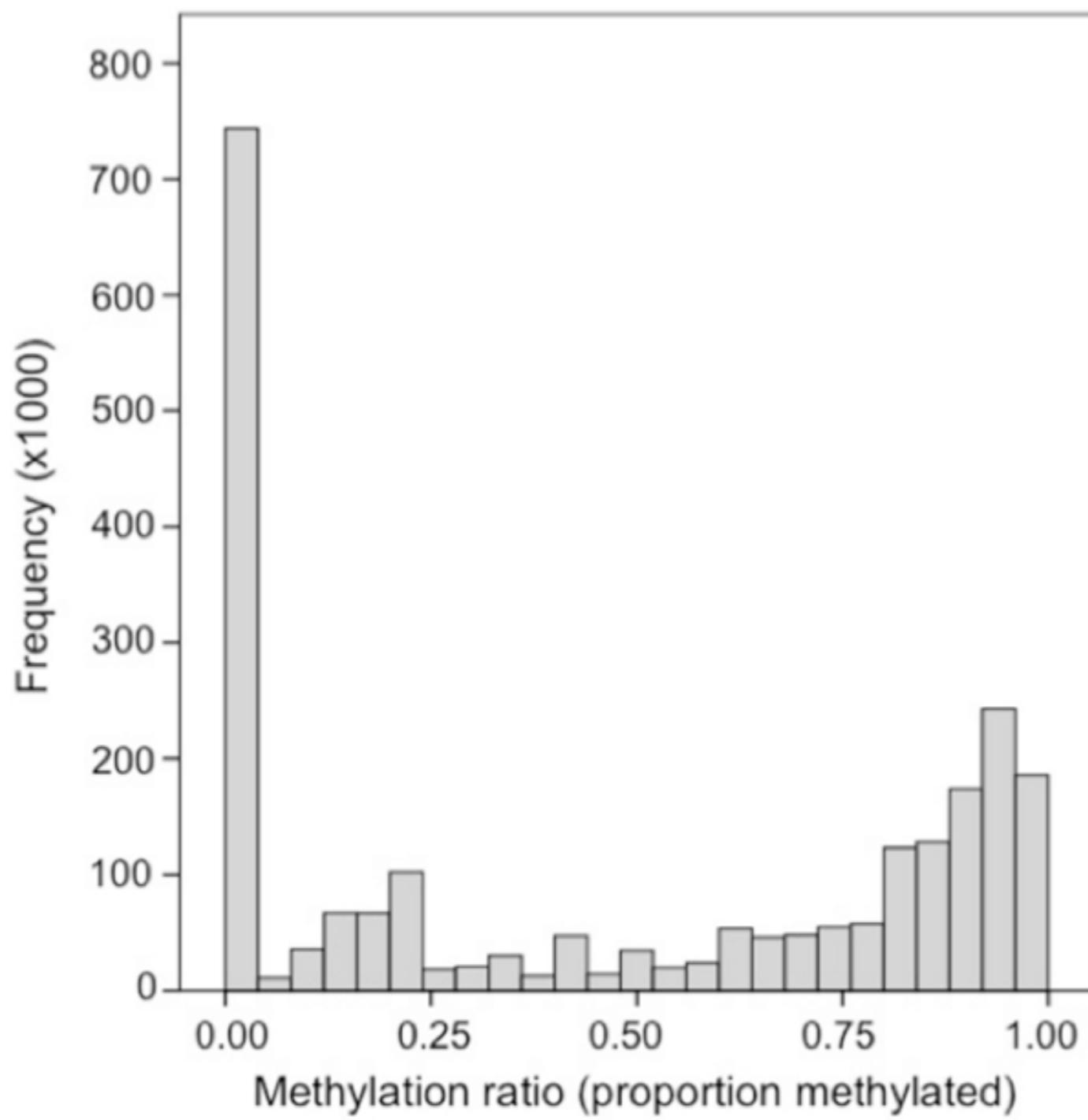
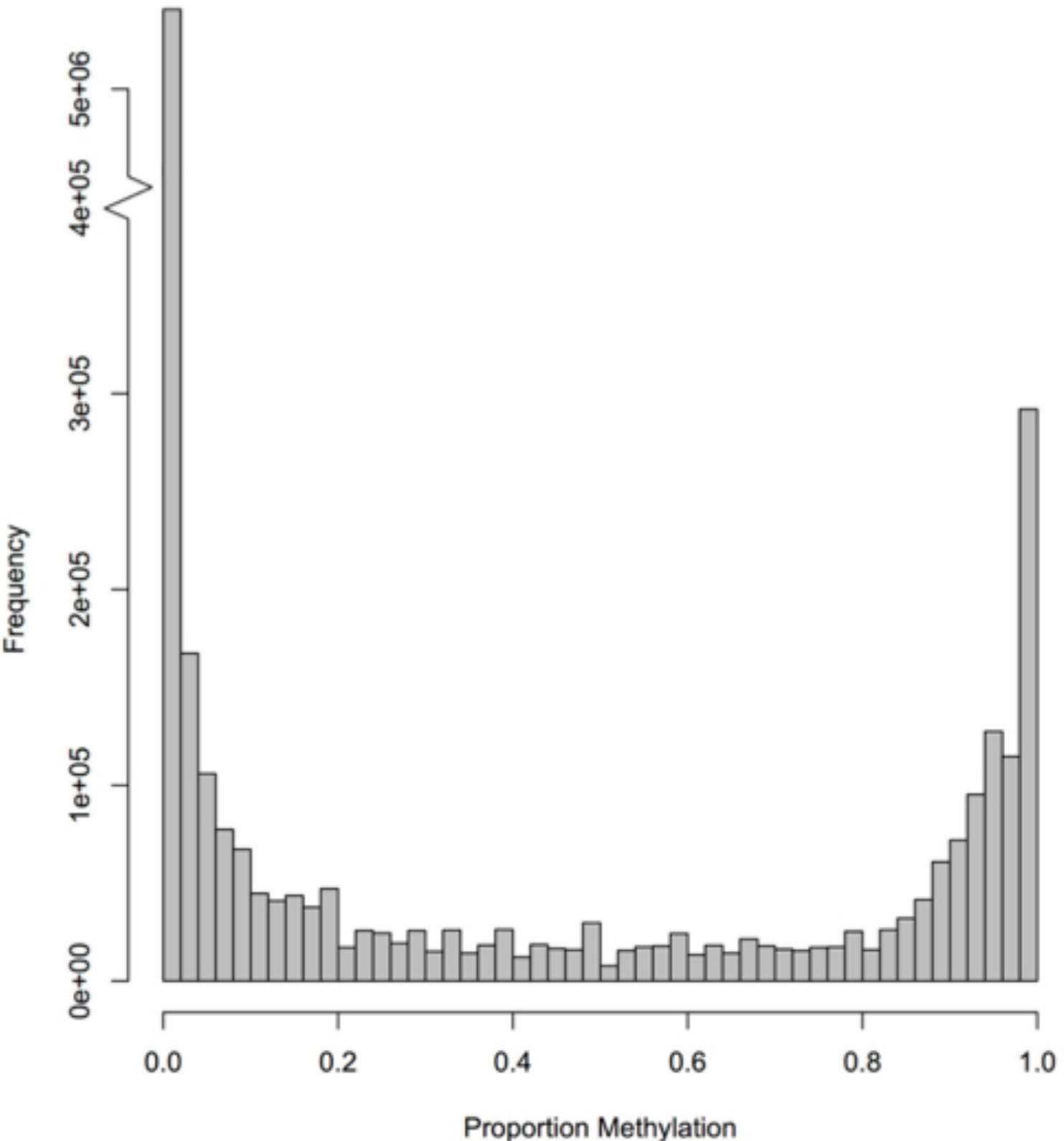
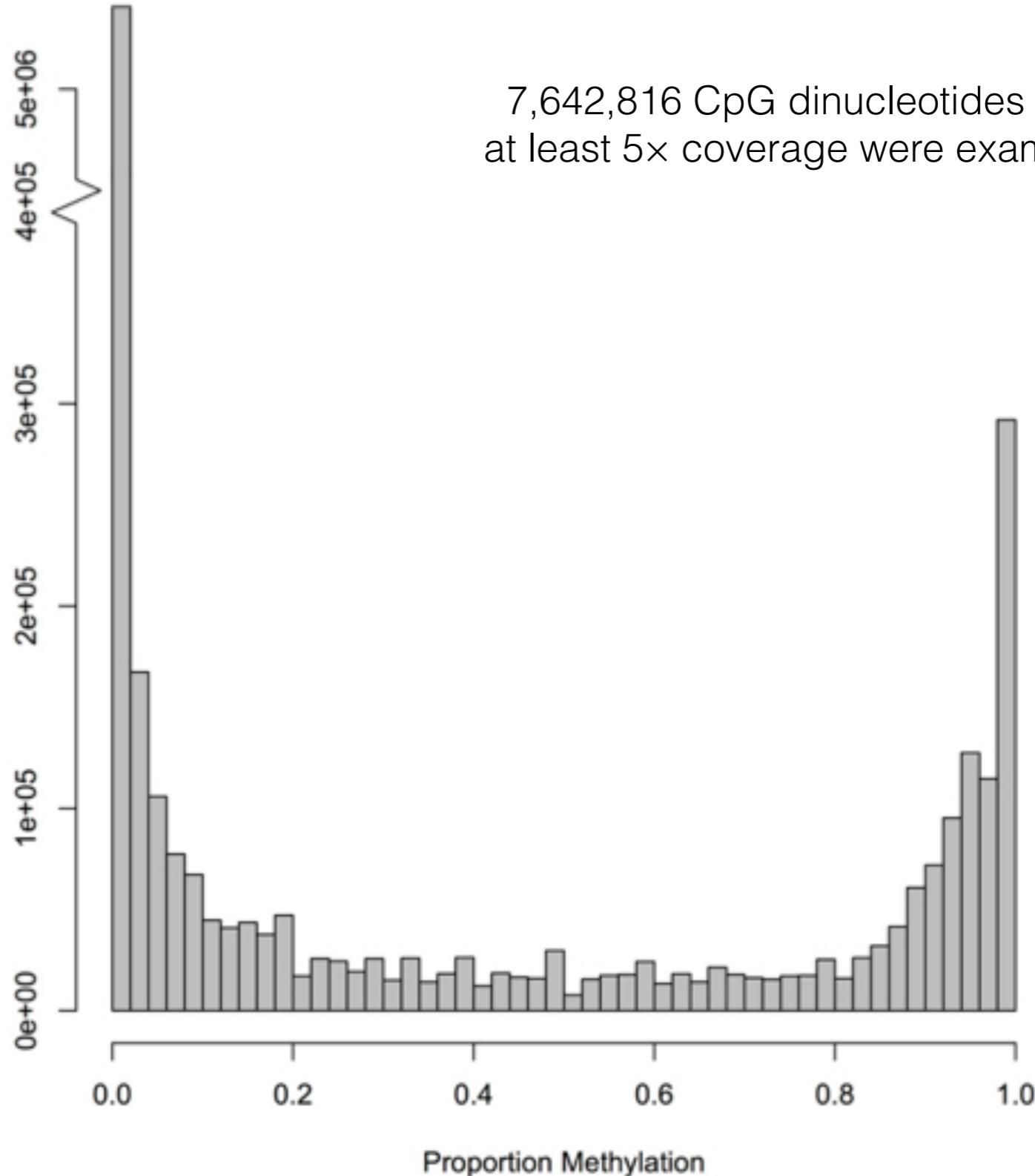
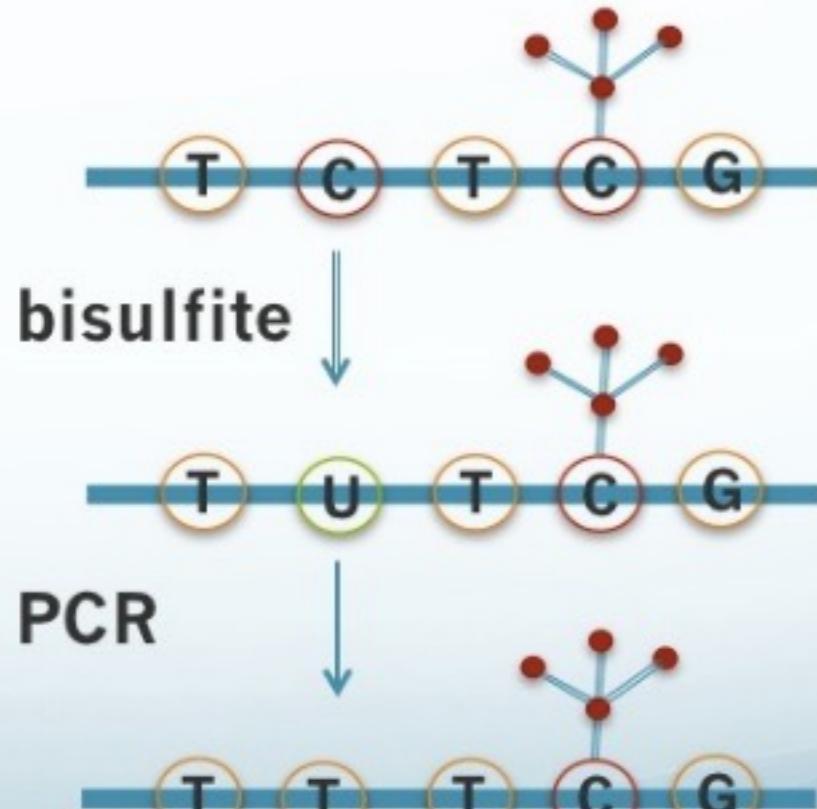


Figure 1 Frequency distribution of methylation ratios for CpG dinucleotides in oyster gill tissue. A total of 2,625,745 CpG dinucleotides with $\geq 5 \times$ coverage are represented.



Epigenetic variation **1**

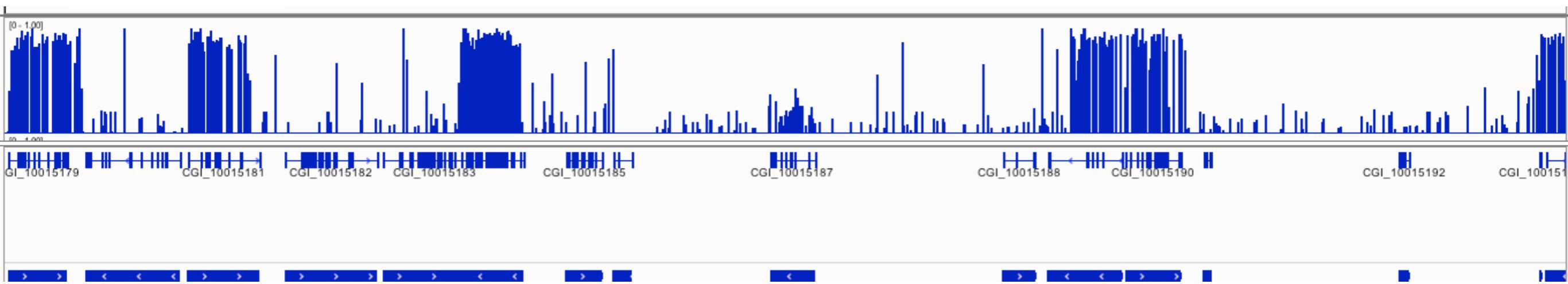
– Bisulfite conversion



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



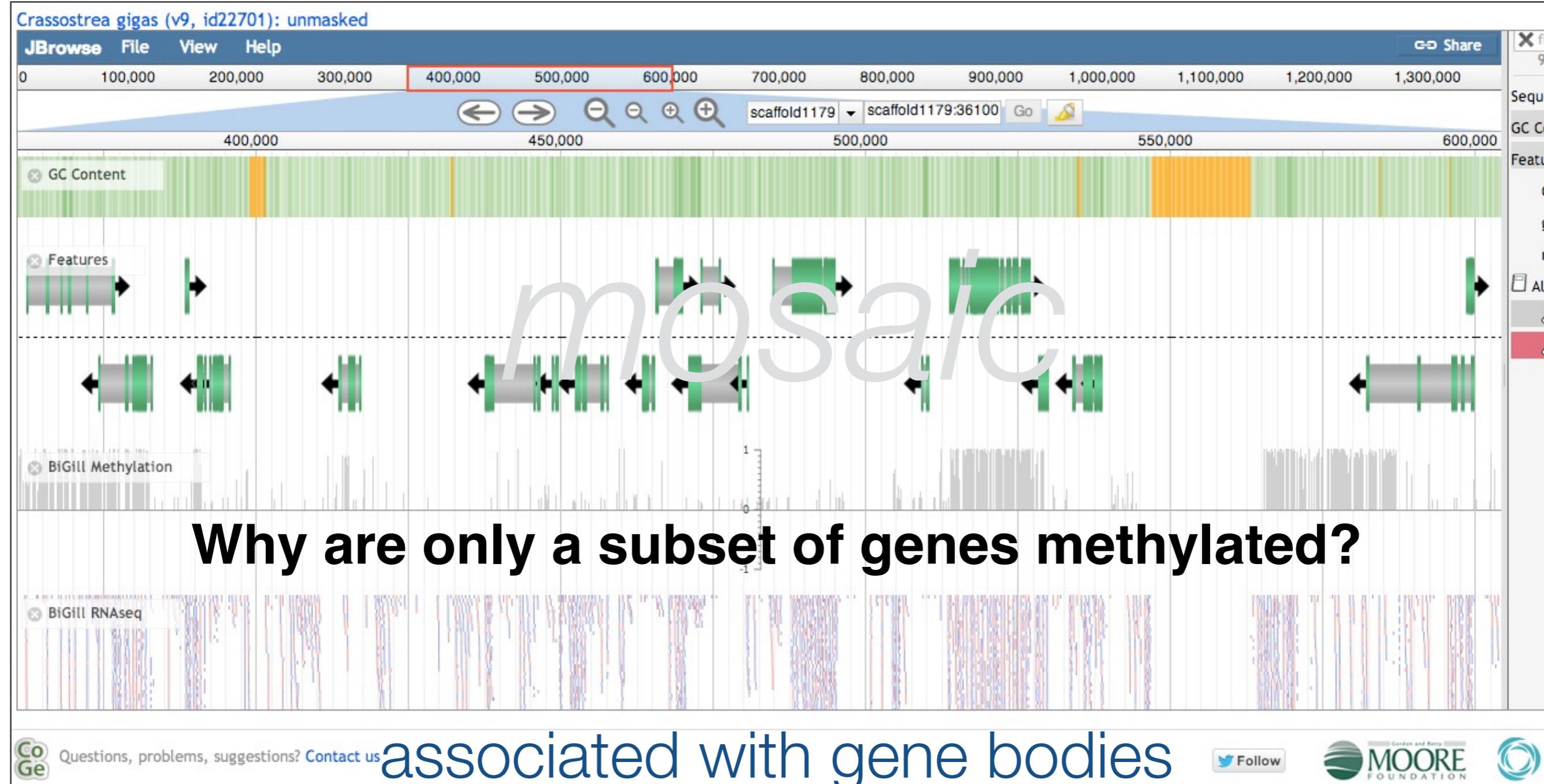
Epigenetic variation **1**



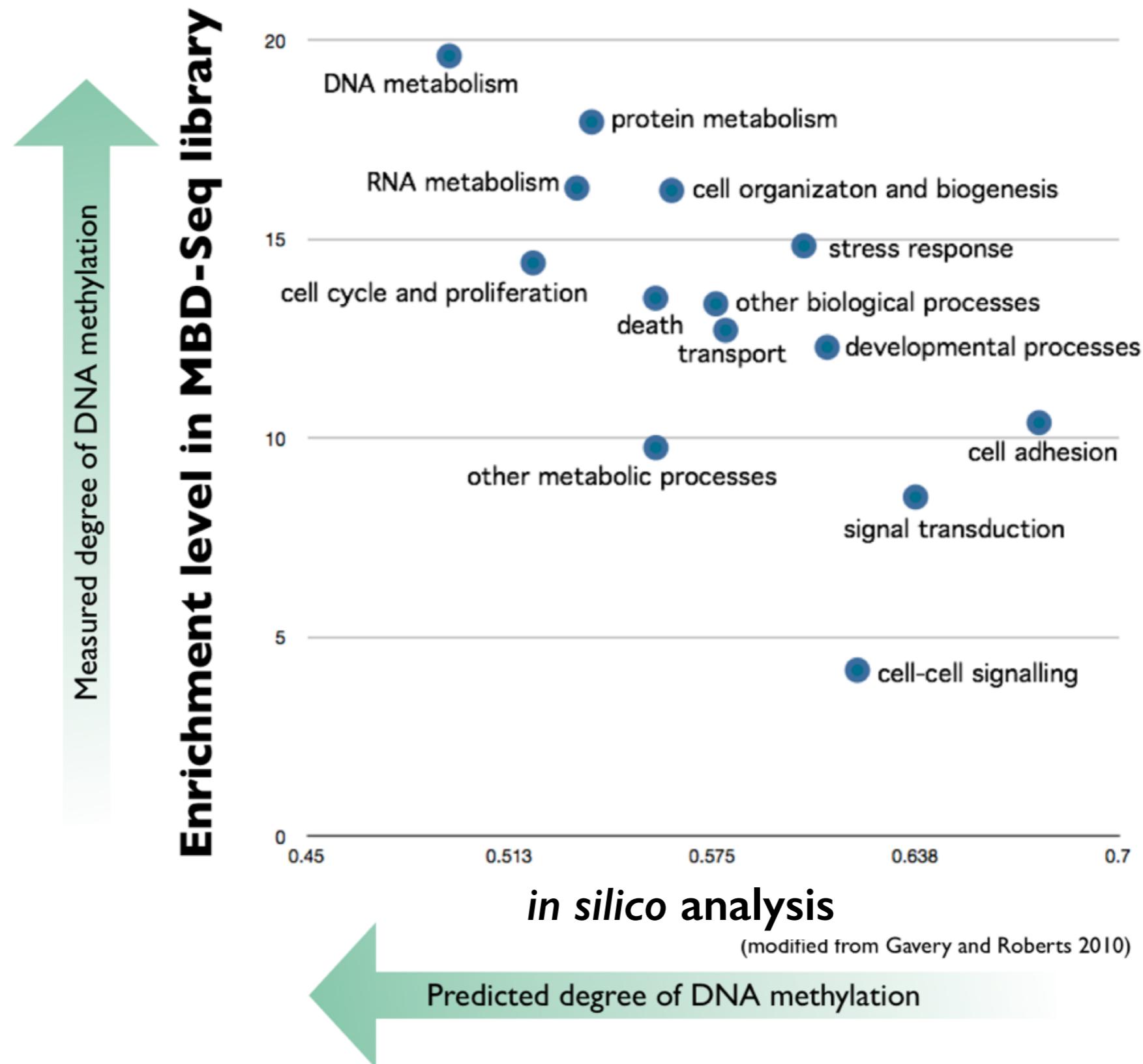
mosaic

associated with gene bodies

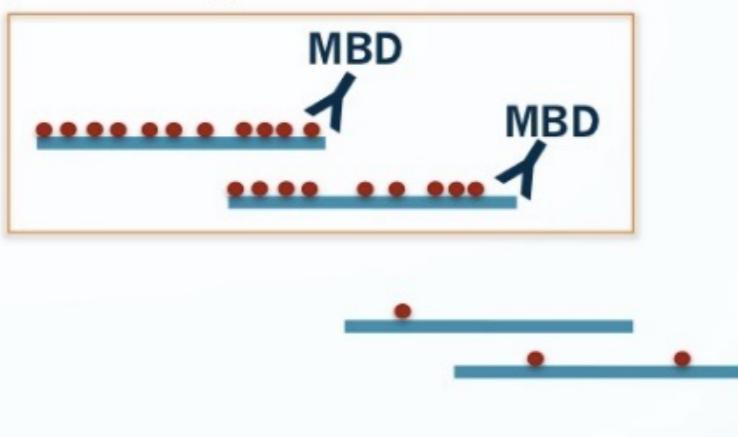




Epigenetic variation **1**

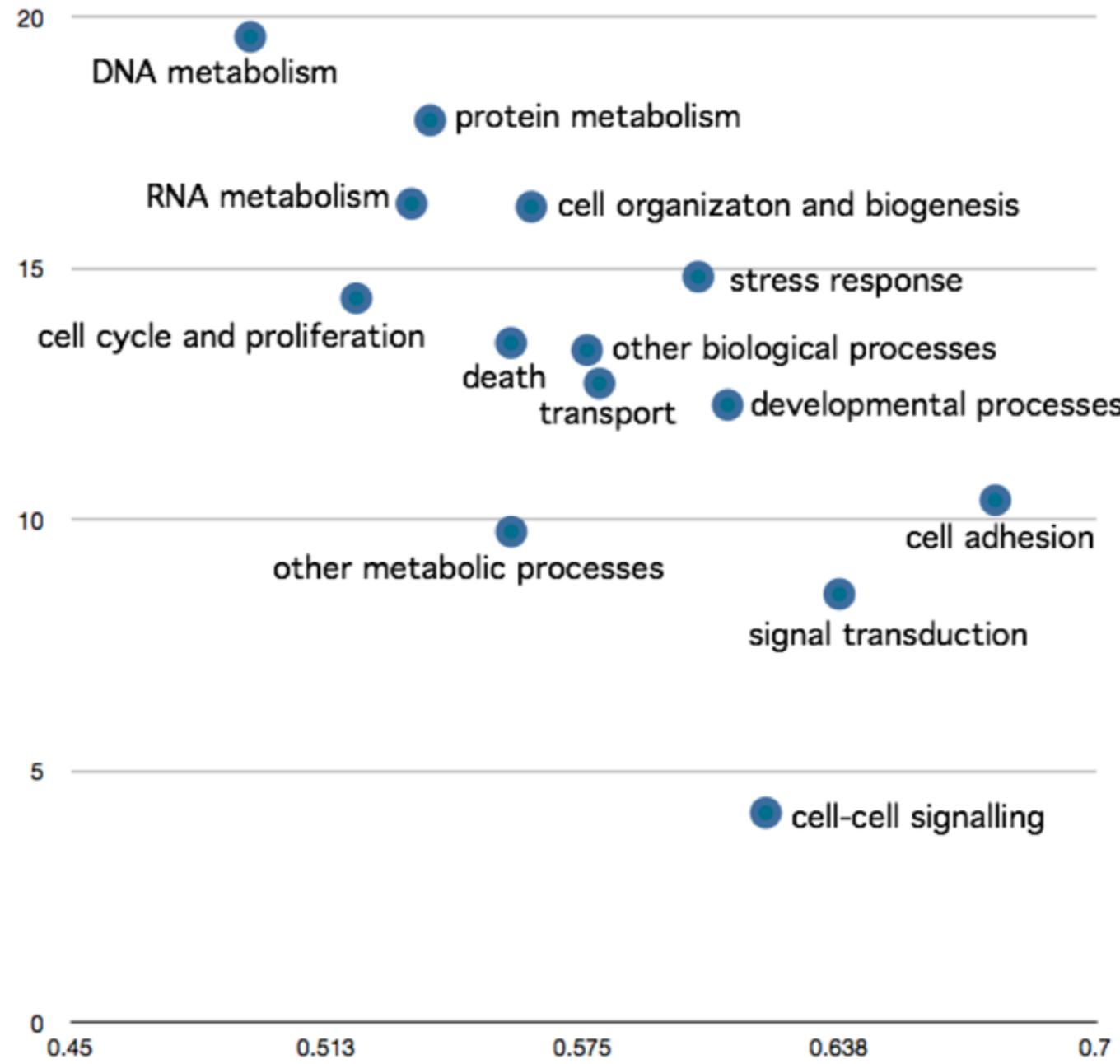


Epigenetic variation 1



Measured degree of DNA methylation

Enrichment level in MBD-Seq library



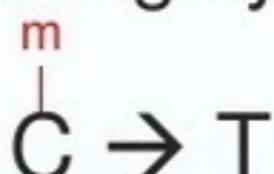
in silico analysis

(modified from Gavery and Roberts 2010)

Predicted degree of DNA methylation

in silico approach

- Principle:
 - Methylated cytosines are highly mutable

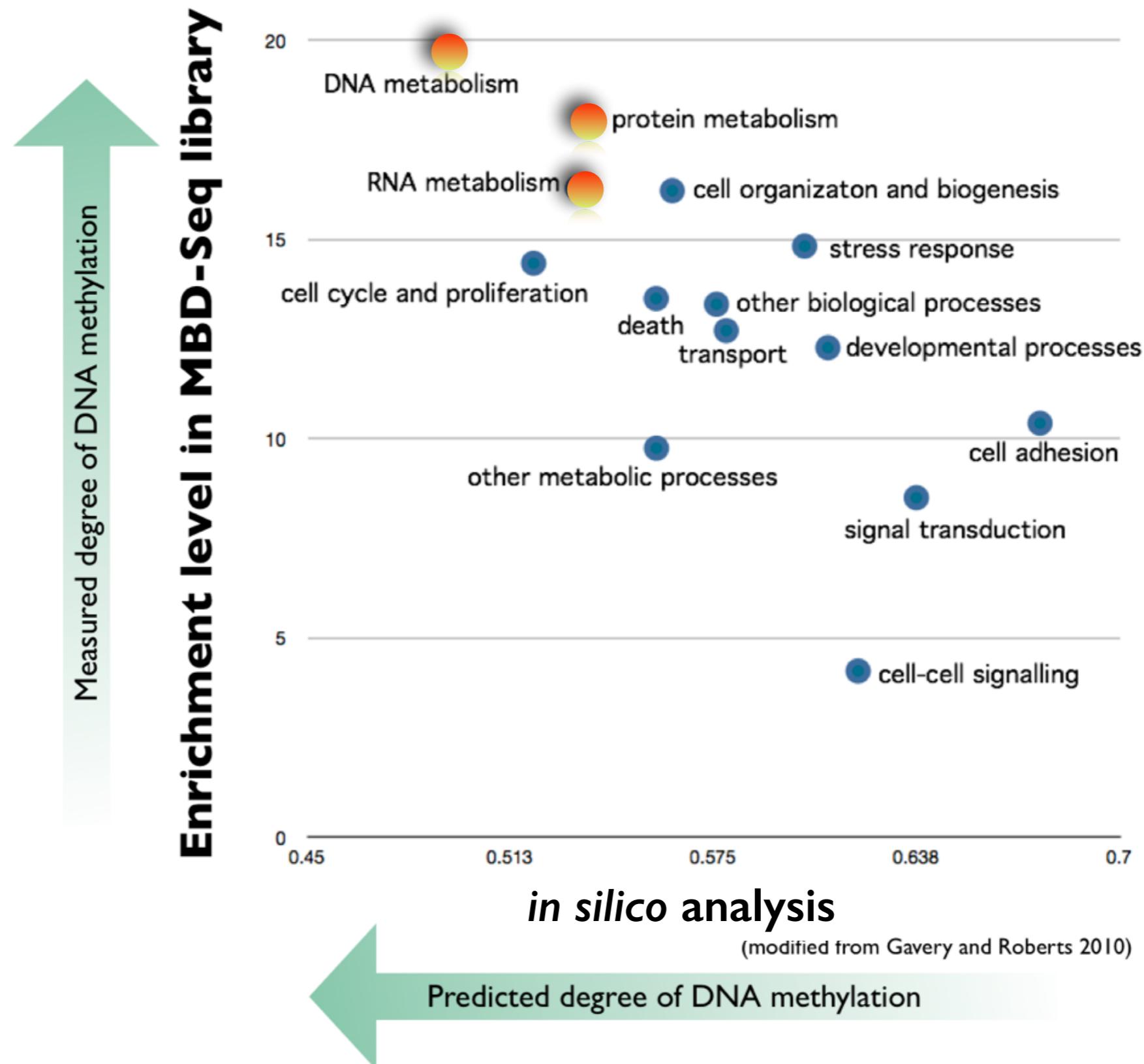


- Methylated regions of DNA are depleted of CpG dinucleotides over evolutionary time (CpG to TpG)

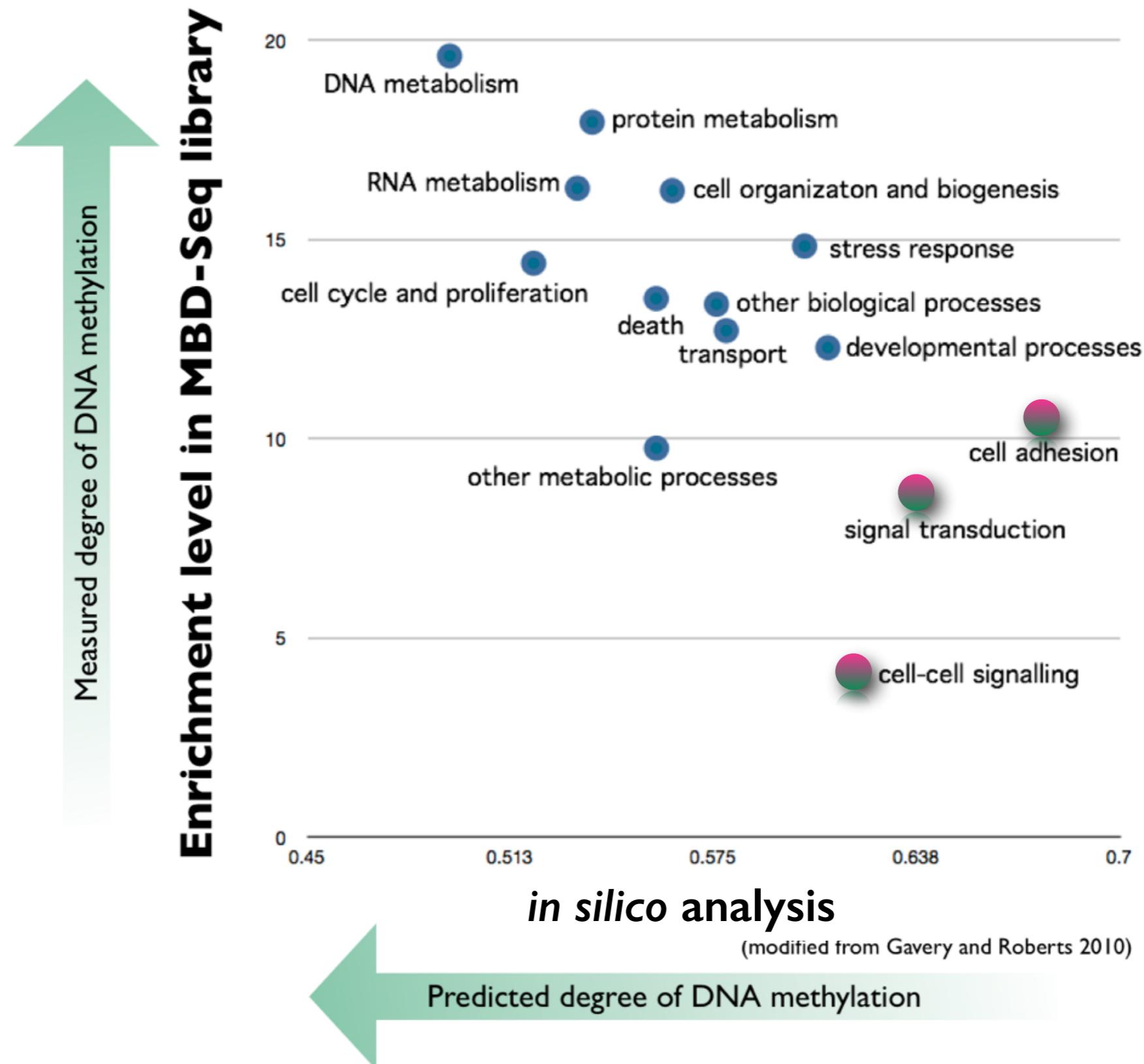
$$\text{CpG O/E} = \frac{\text{CpG observed}}{\text{CpG expected}}$$


high = unmethylated

Epigenetic variation **1**



Epigenetic variation **1**



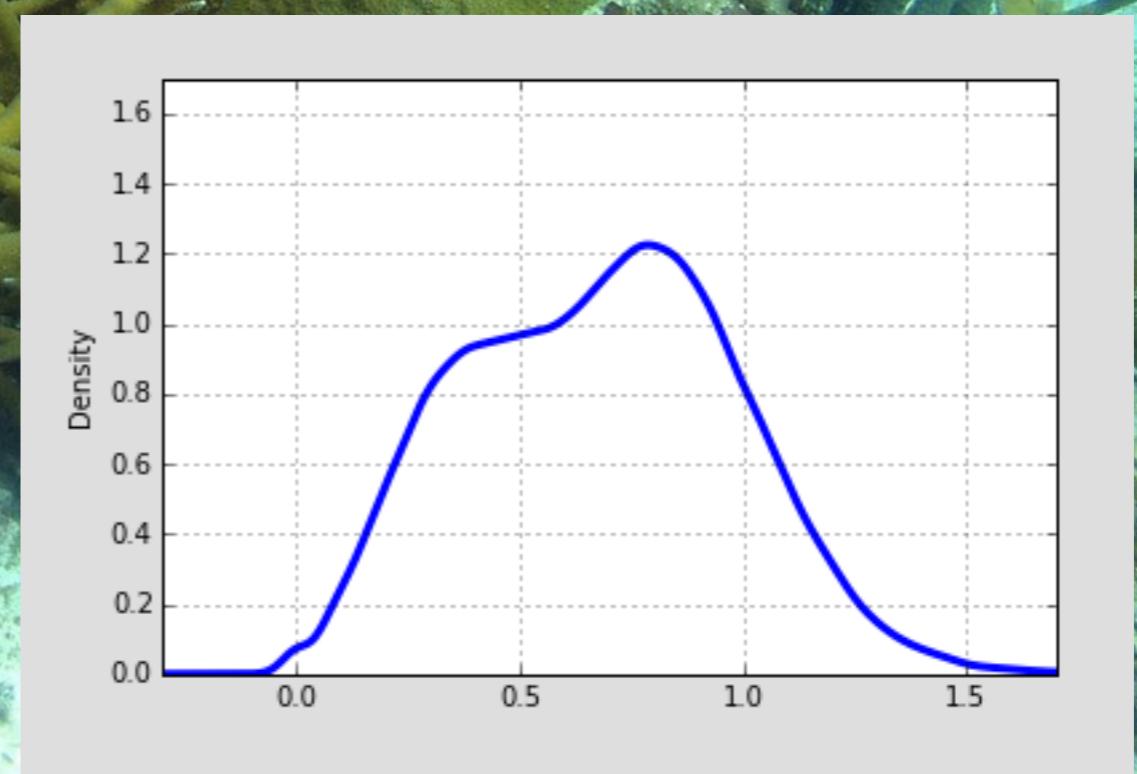
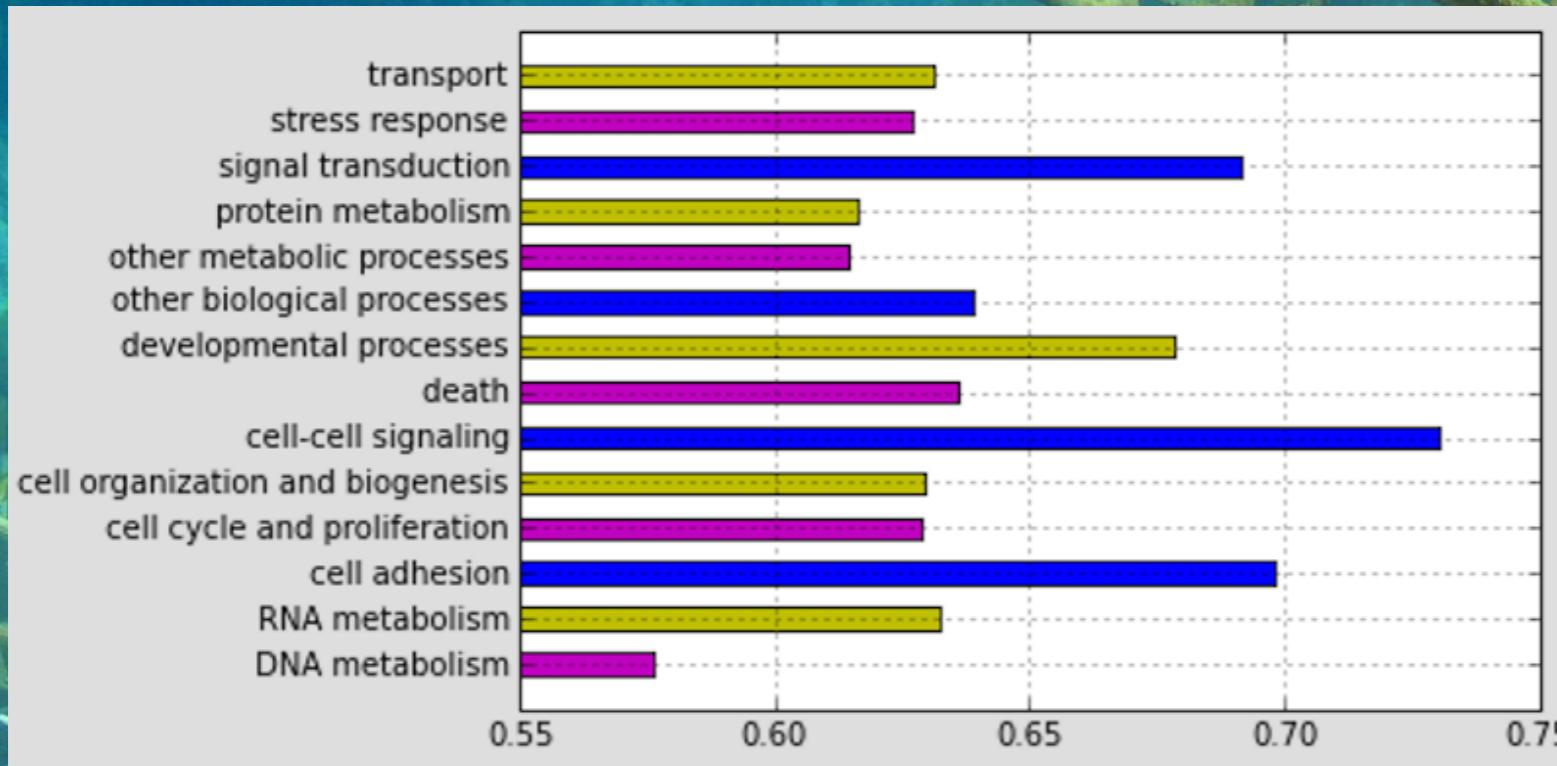
Jay Dimond

Acropora palmata

Acropora cervicornis

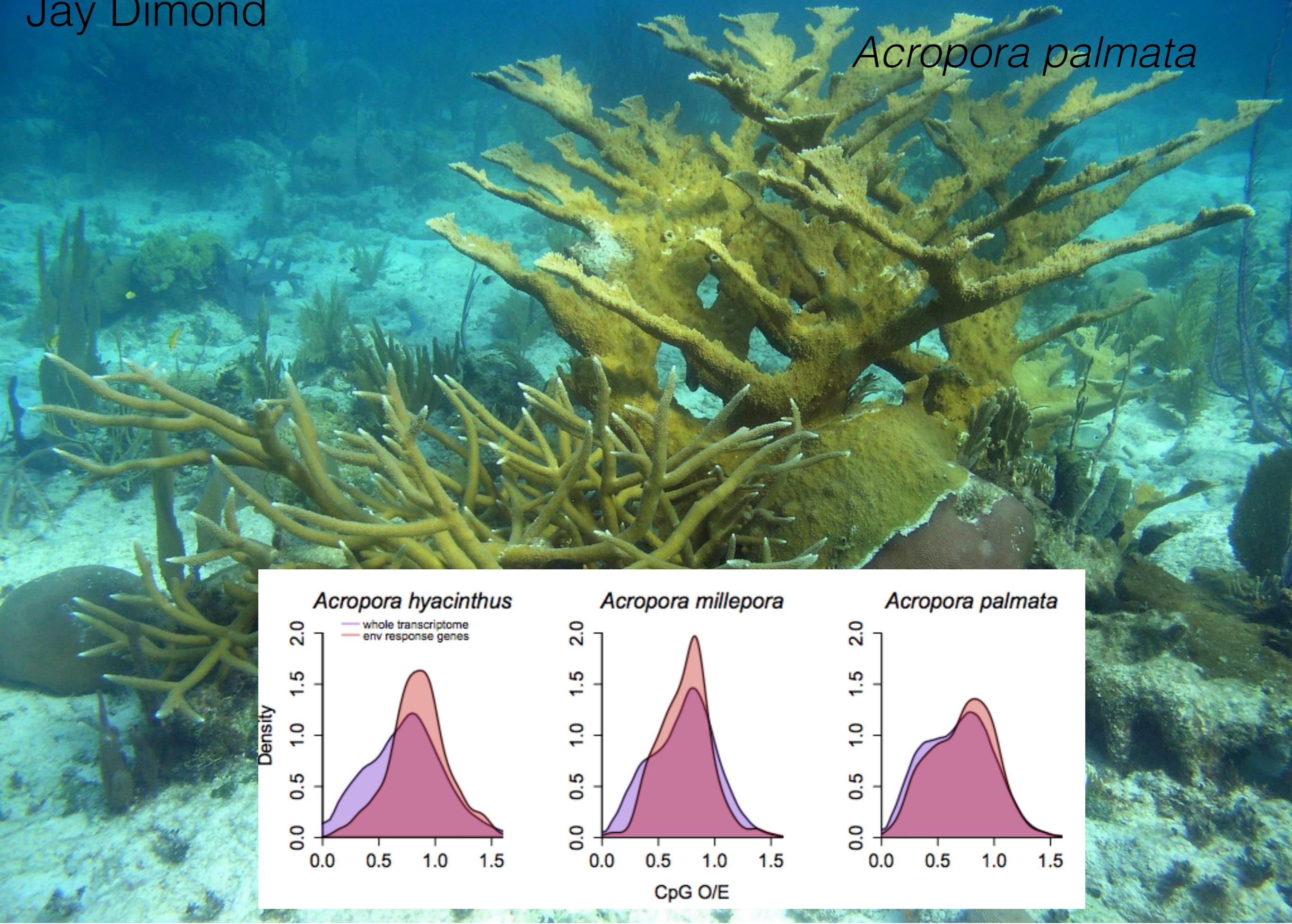
Jay Dimond

Acropora palmata



Jay Dimond

Acropora palmata

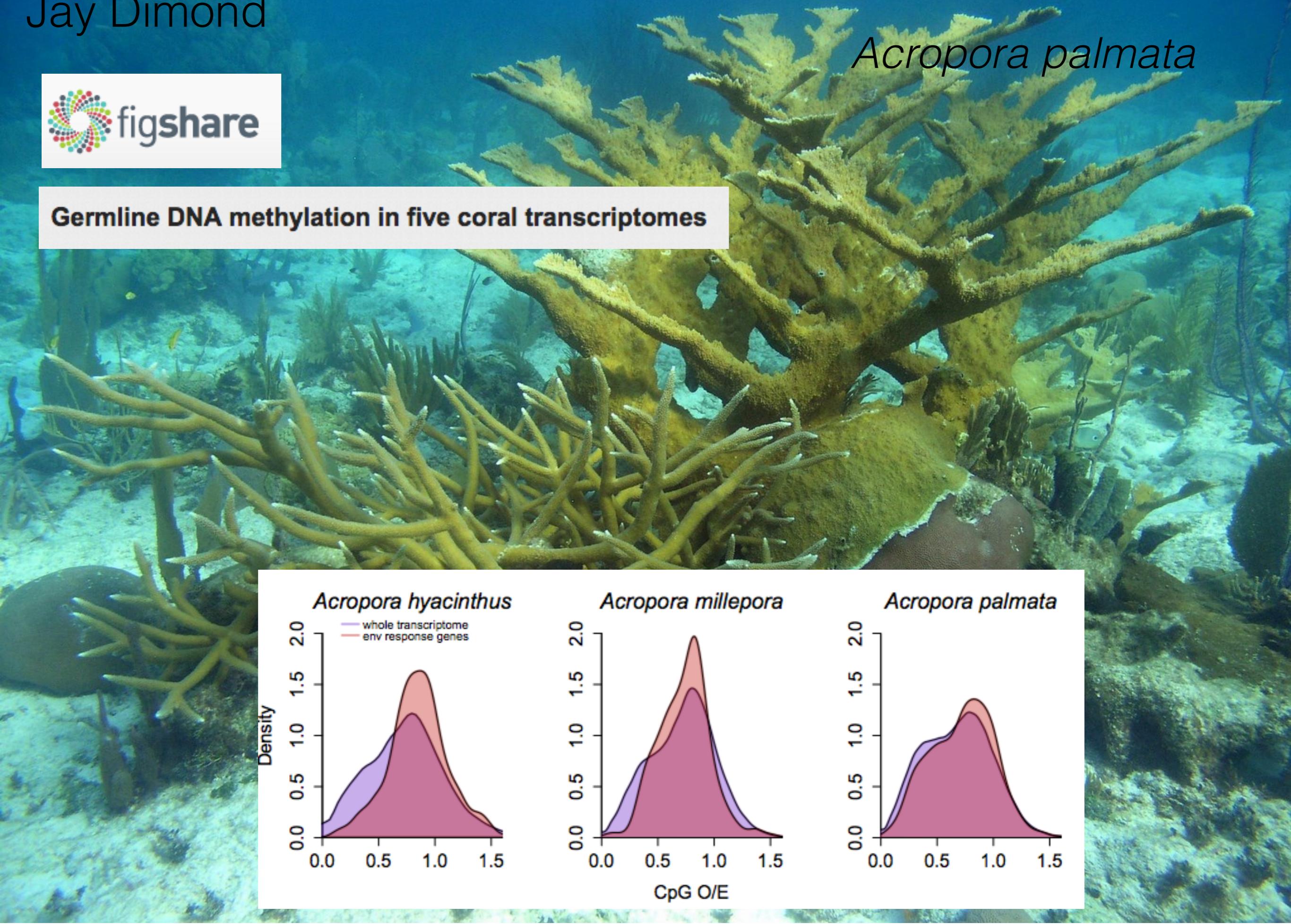


Jay Dimond

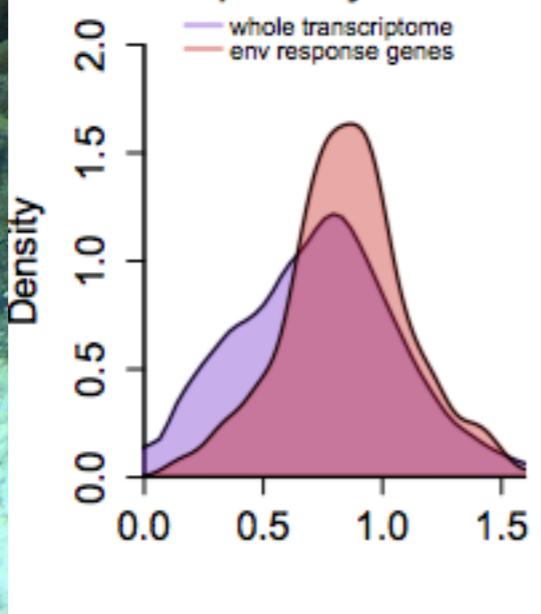
Acropora palmata



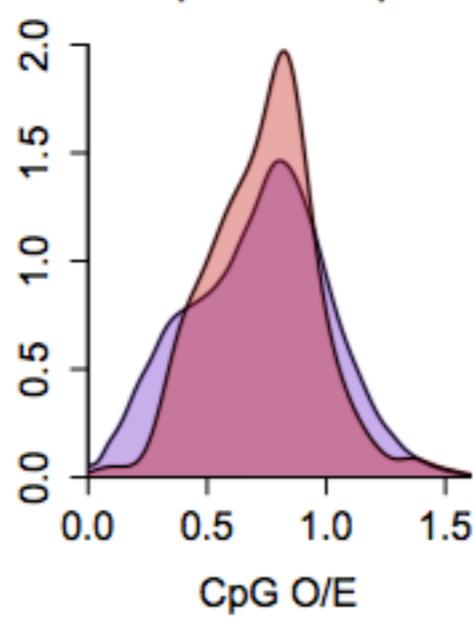
Germline DNA methylation in five coral transcriptomes



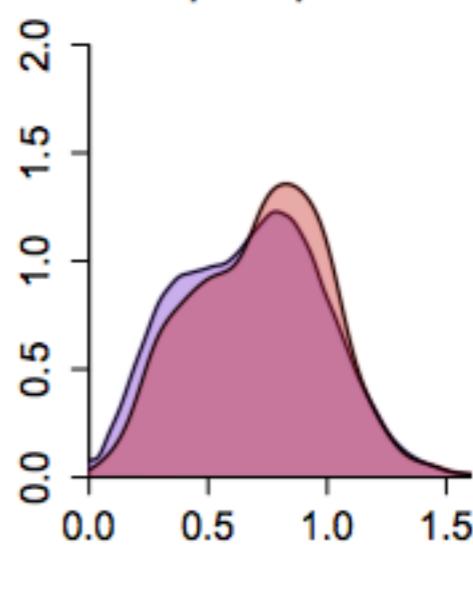
Acropora hyacinthus



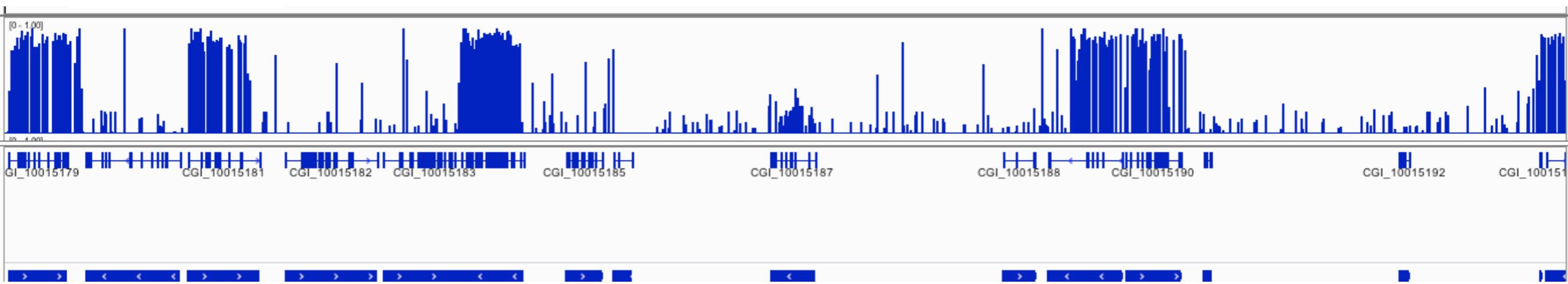
Acropora millepora



Acropora palmata



Epigenetic variation **1**

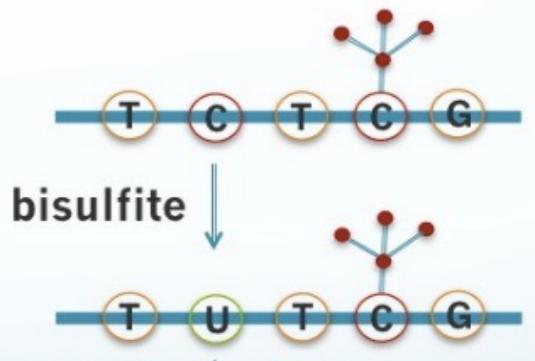


mosaic

associated with gene bodies
based on gene function

Epigenetic variation **1**

Family and Developmental Variation



Sperm &
Larvae
(72h & 120h)



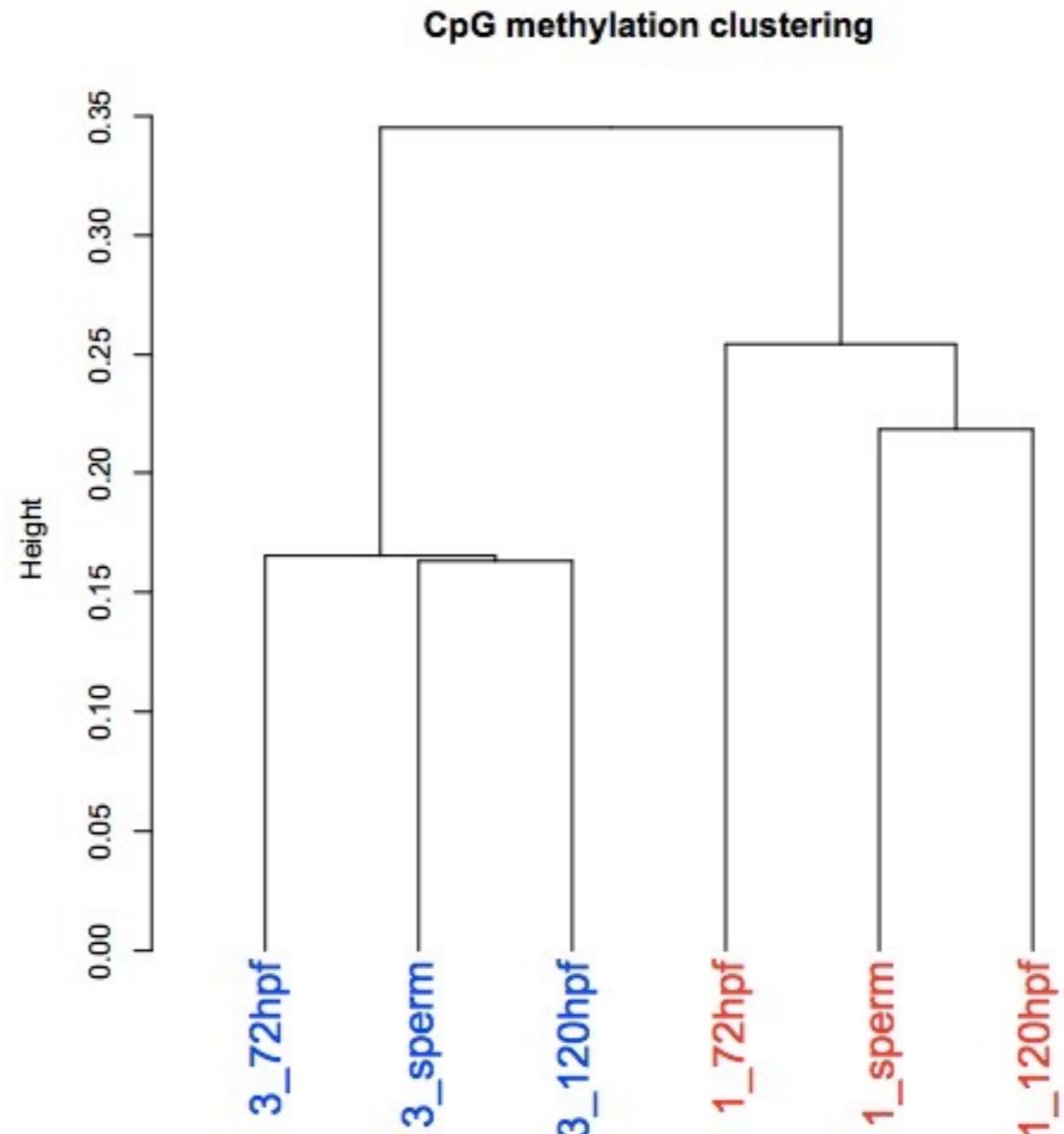
bioRxiv
beta
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New Results

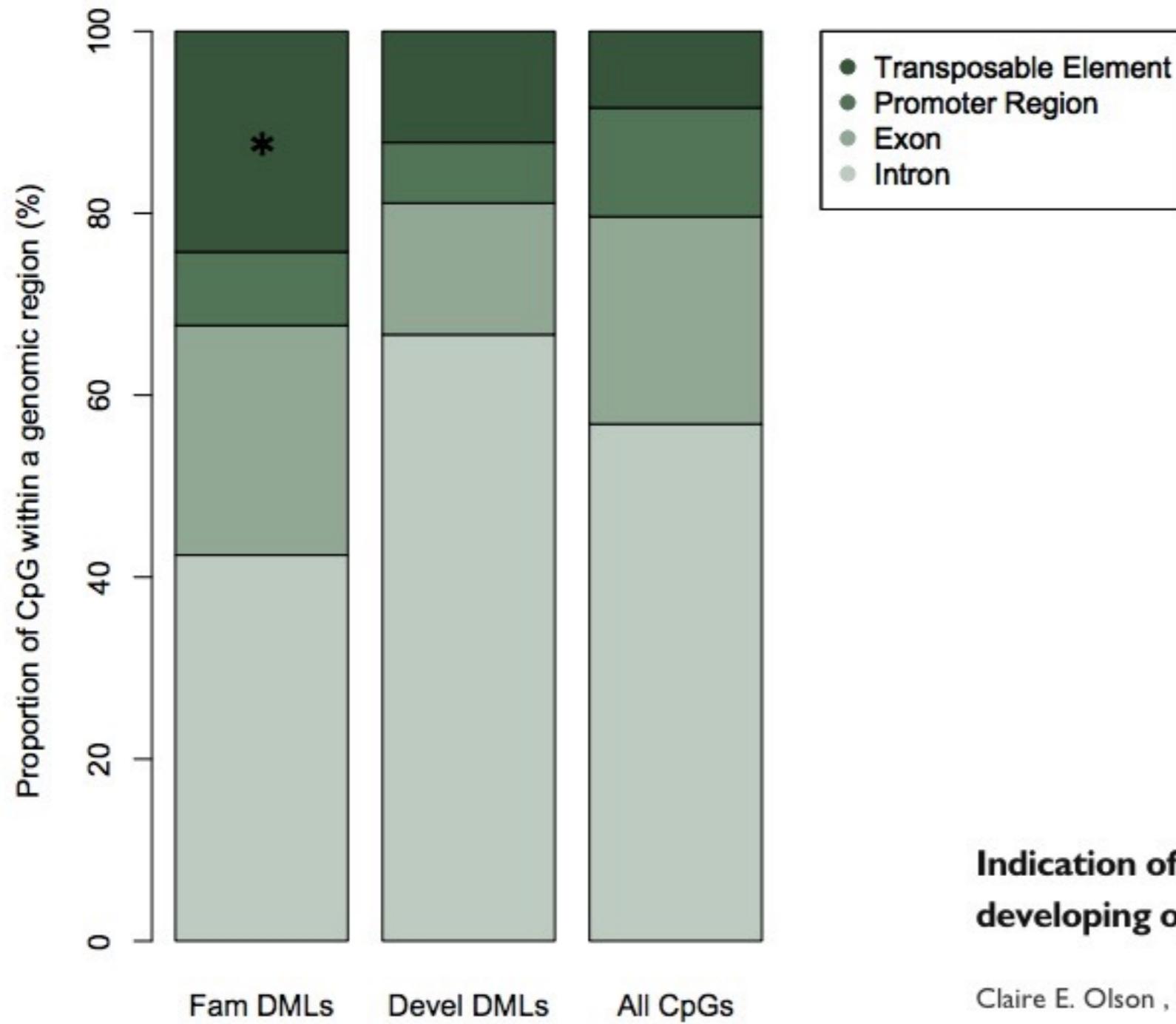
Indication of family-specific DNA methylation patterns in developing oysters

Claire E. Olson , Steven B. Roberts

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



Epigenetic variation **1**

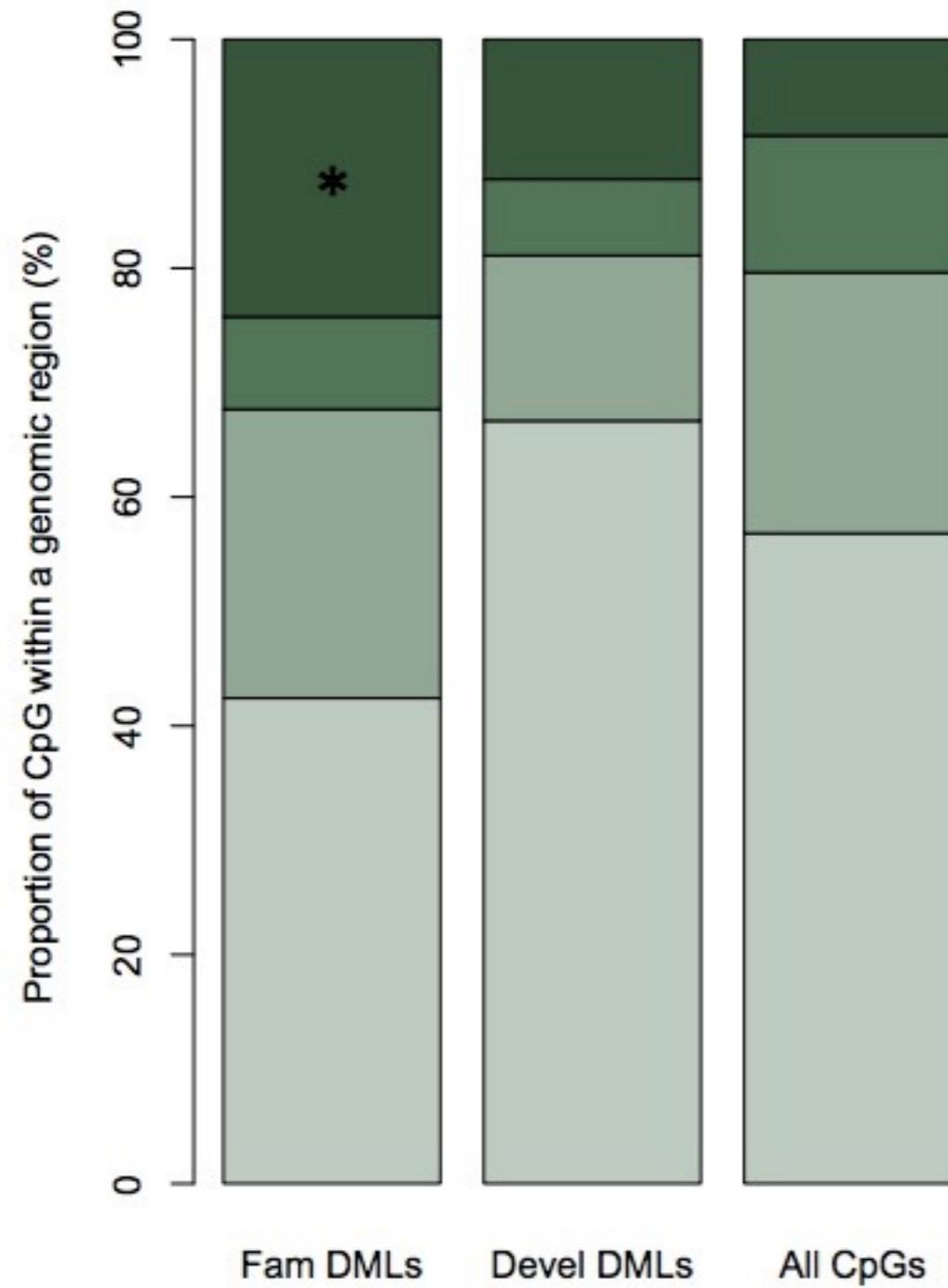


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Epigenetic variation **1**

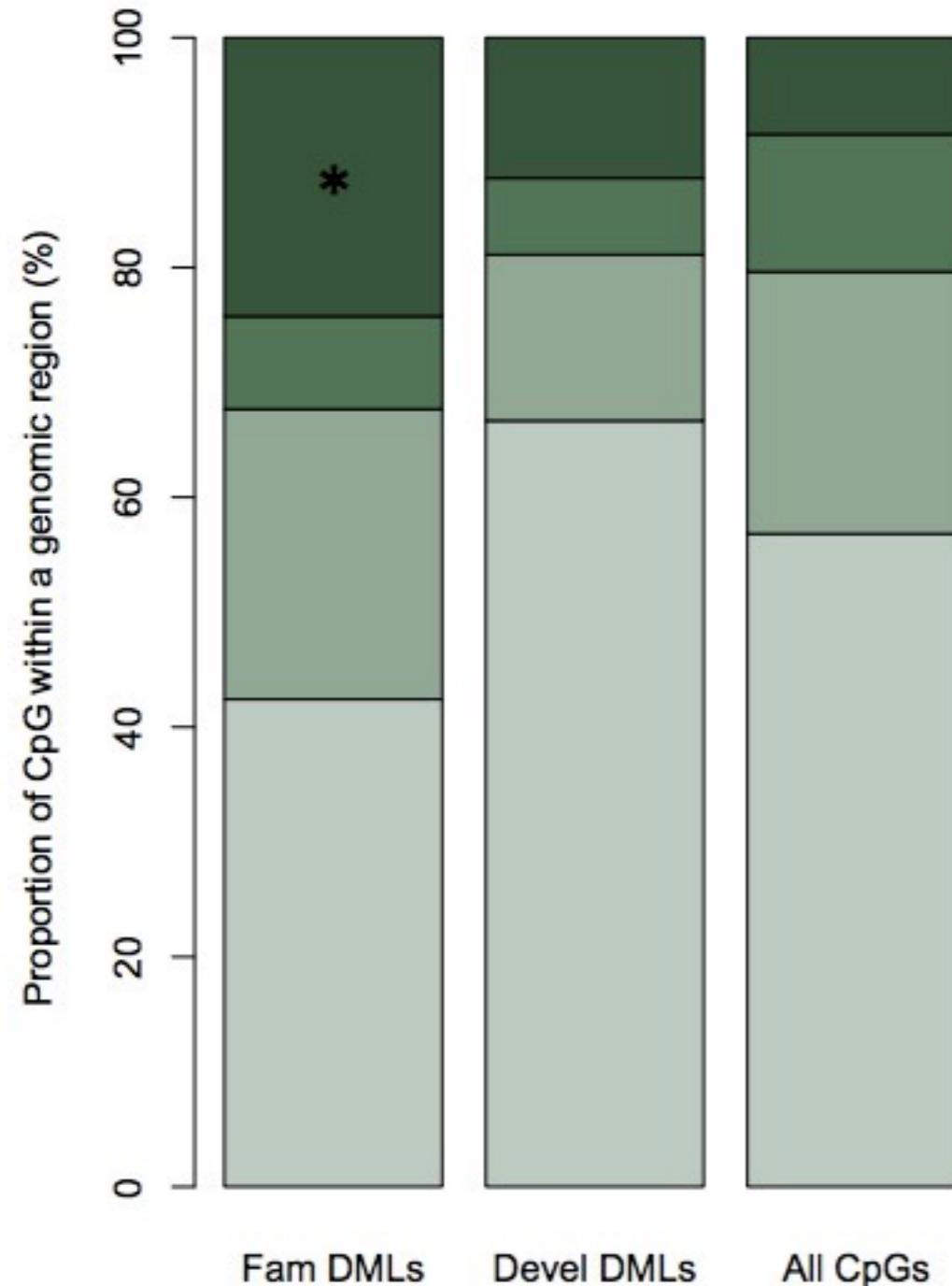


Differentially methylated loci in gene bodies could be lethal or deleterious, as they would alter gene expression.

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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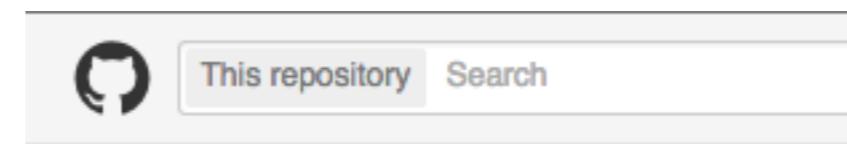
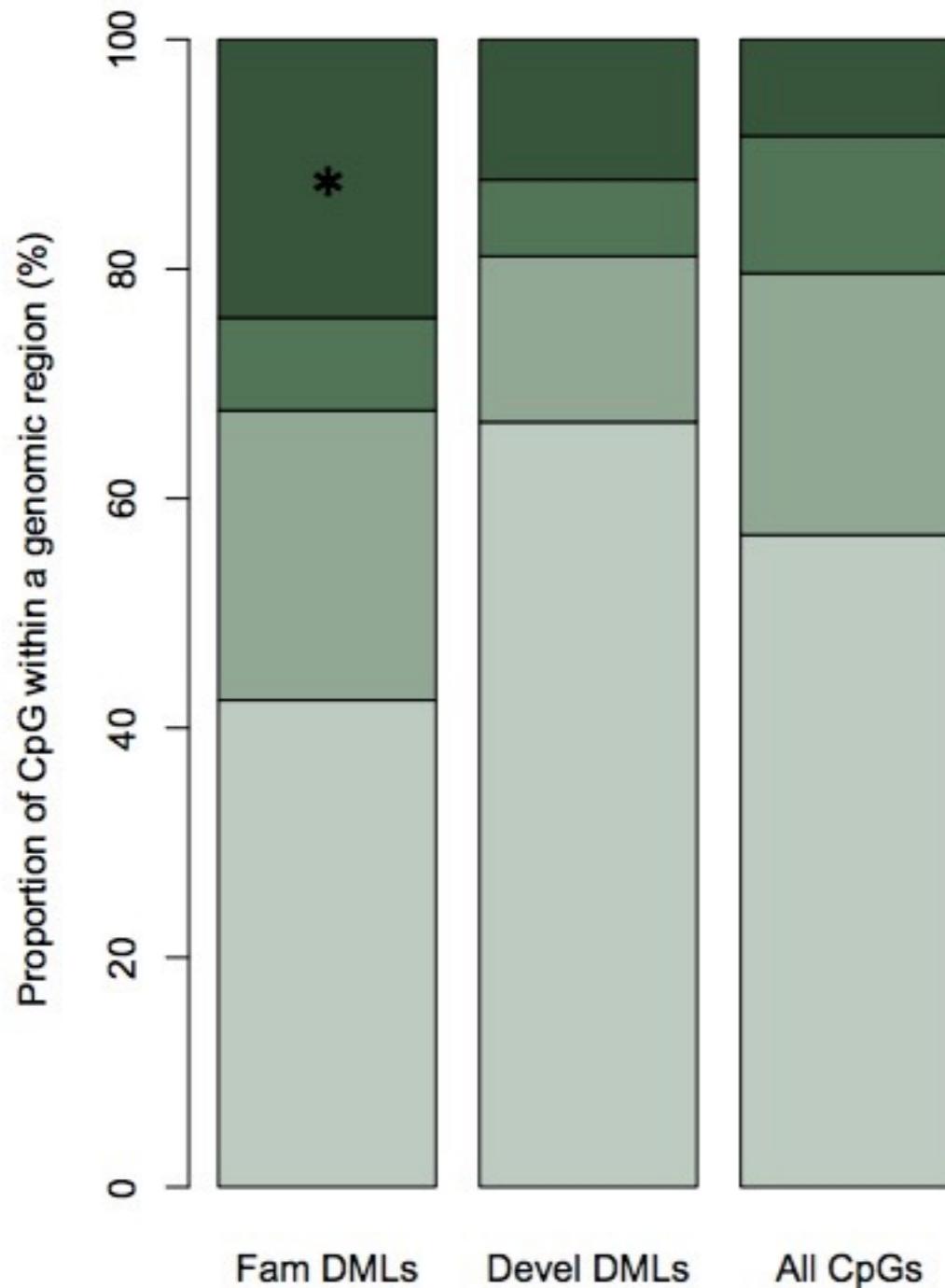


Assumes some form of random process
occurring during gametogenesis?

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



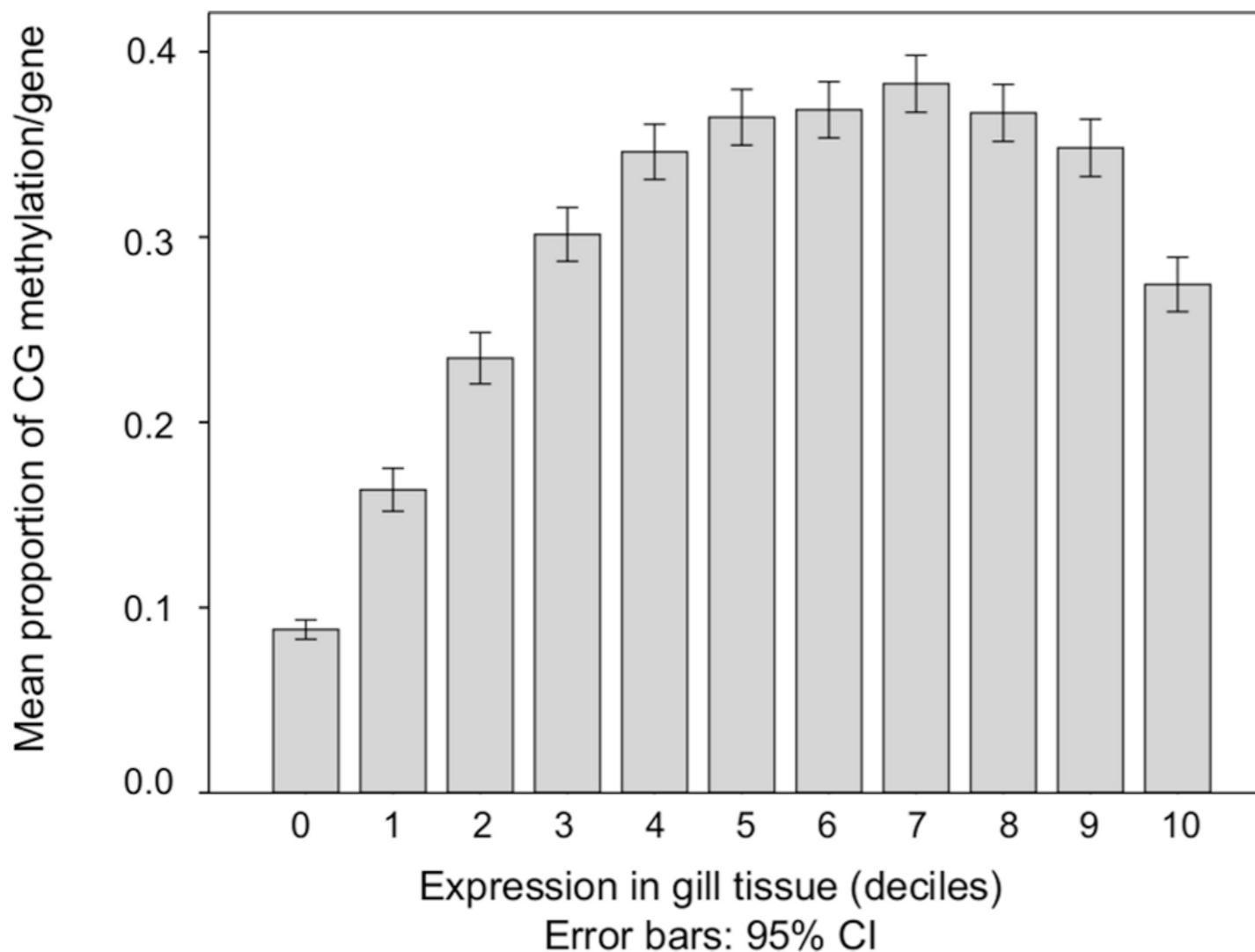
Epigenetic
variation

Function?

Gene expression

2

Epigenetic variation



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

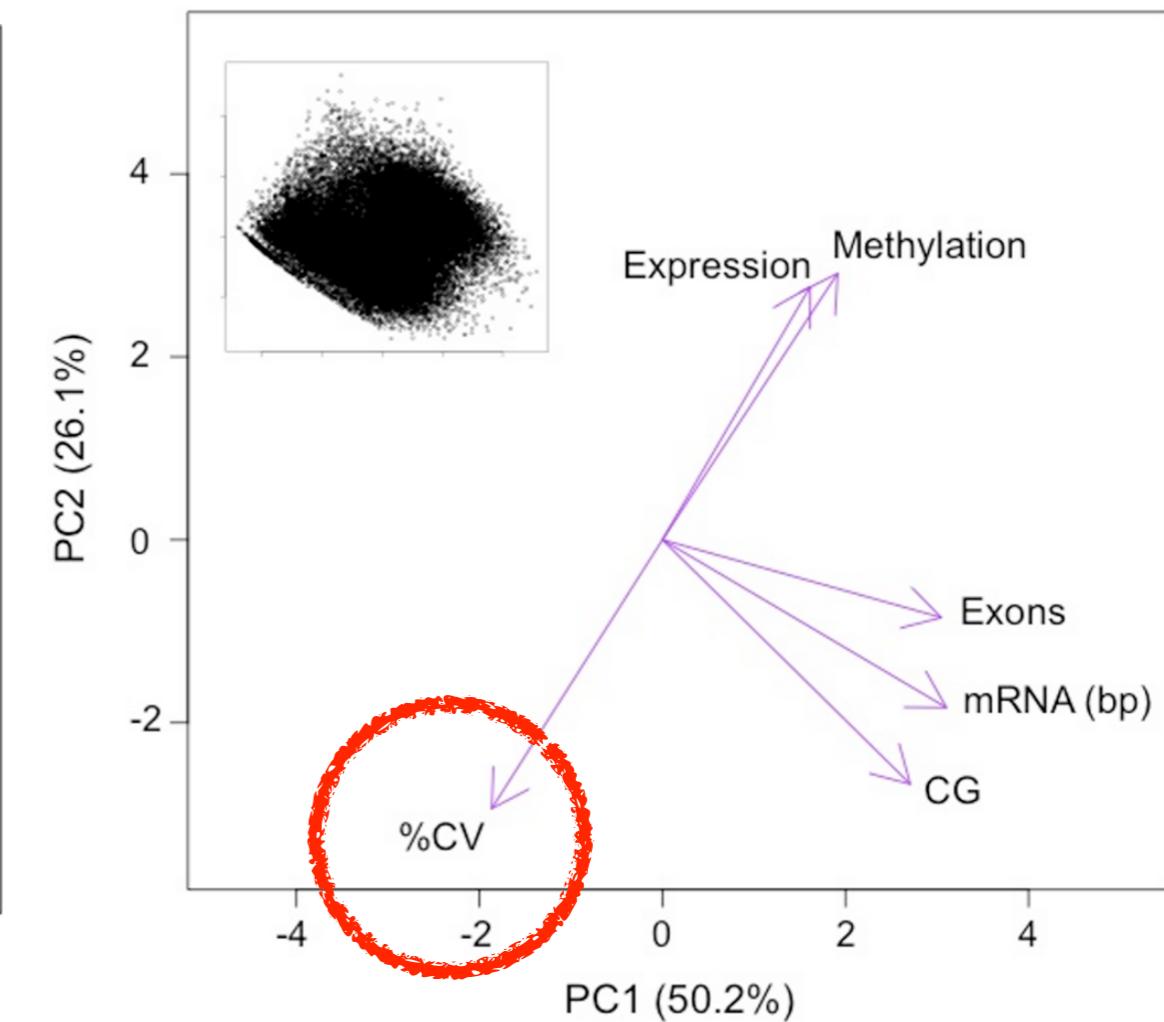
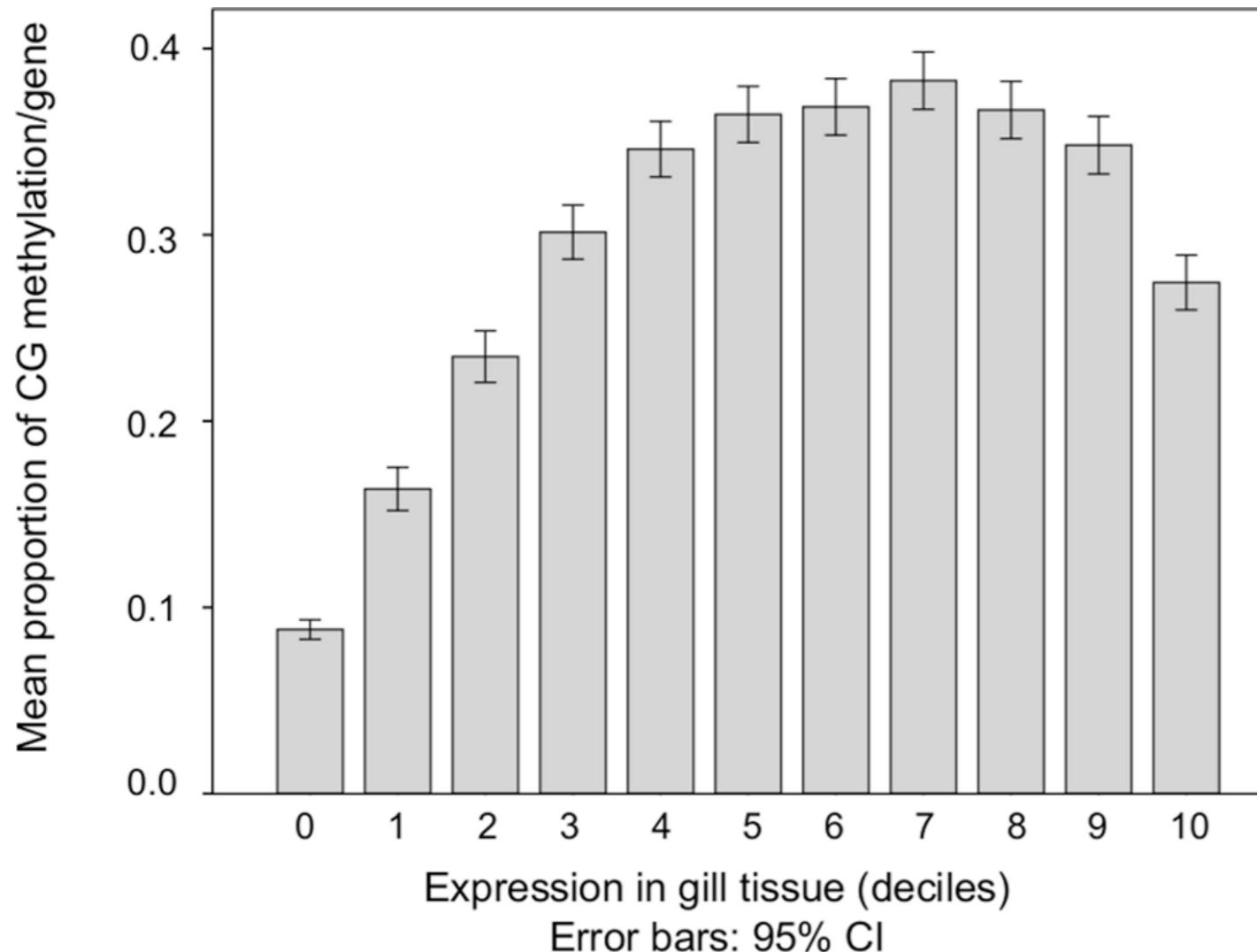
Mackenzie R. Gavery and Steven B. Roberts

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

Gene expression

2

Epigenetic variation



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

Mackenzie R. Gavery and Steven B. Roberts

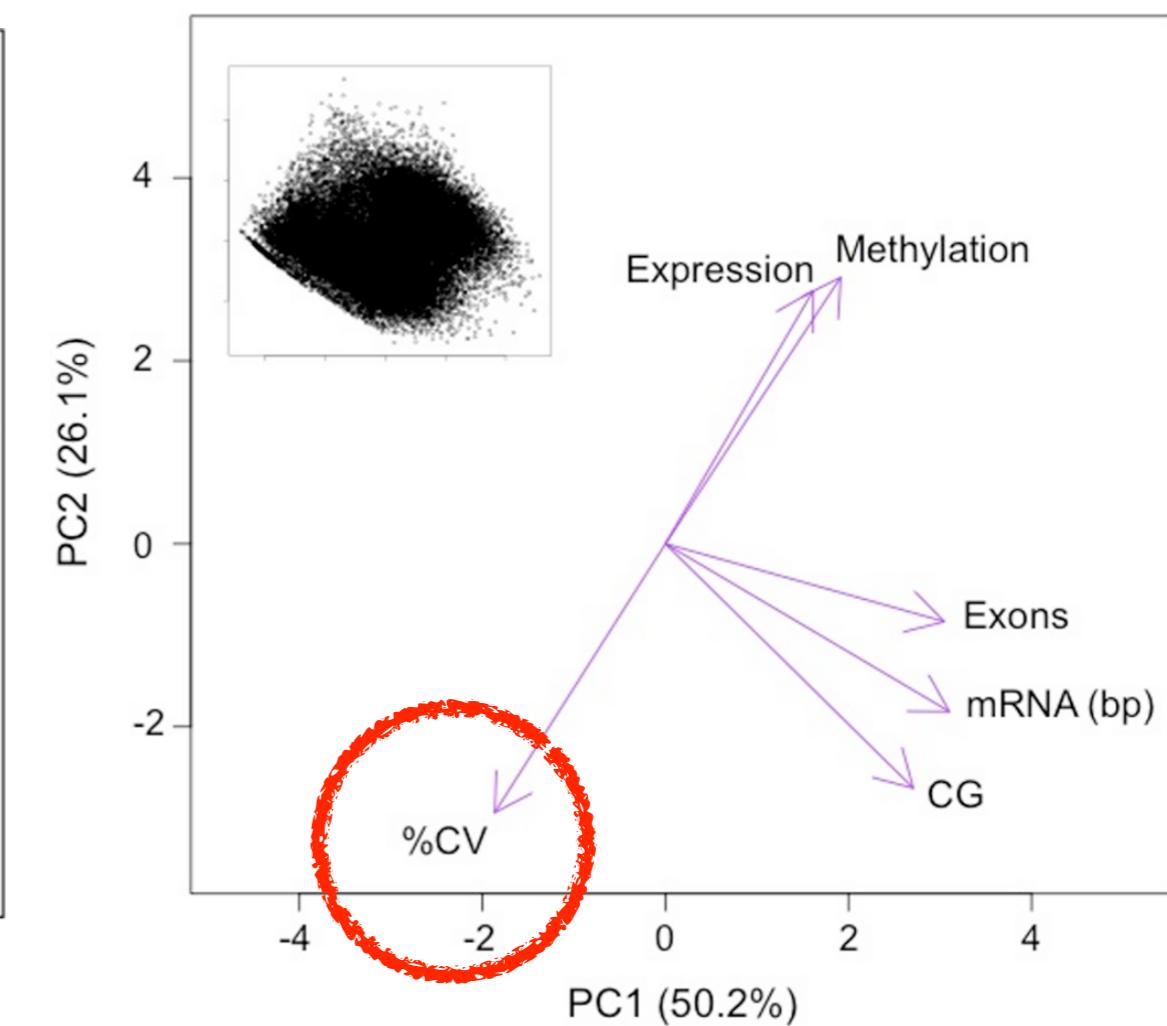
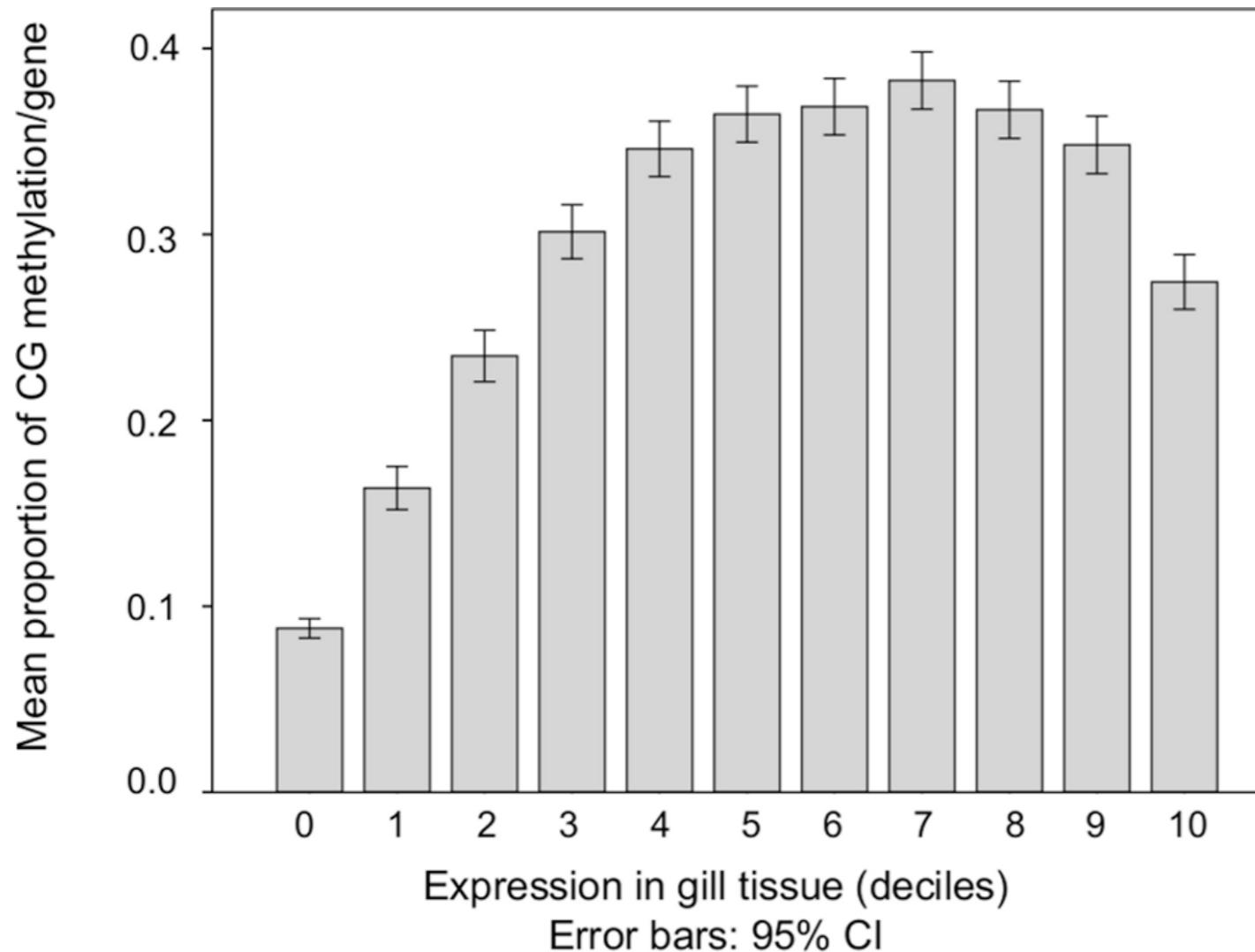
School of Aquatic and Fishery Sciences, University of Washington, Seattle, WA, USA

Gene expression

2

Epigenetic variation

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



What?

A context dependent role for DNA methylation in bivalves

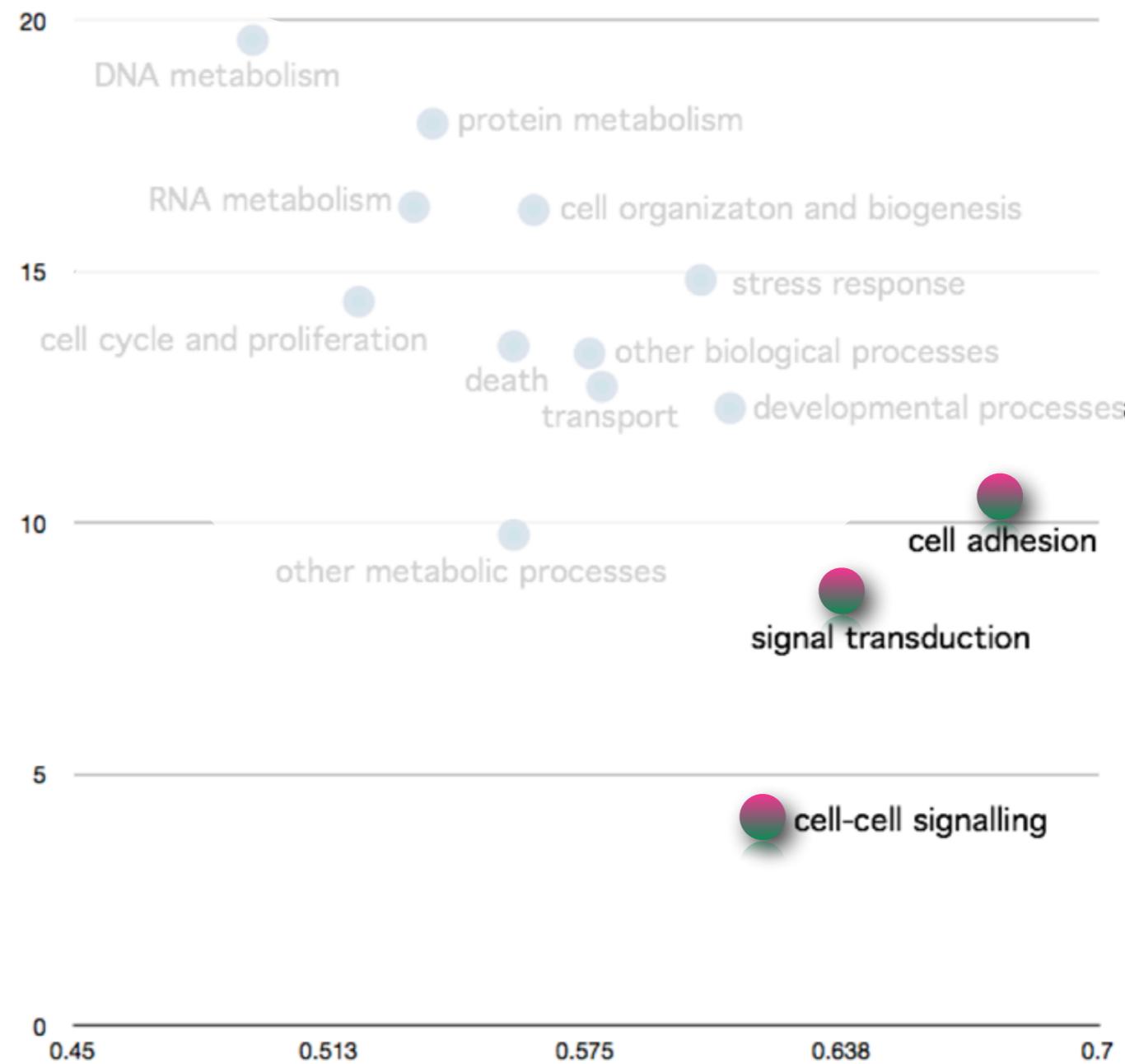
Mackenzie R. Gavery and Steven B. Roberts

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

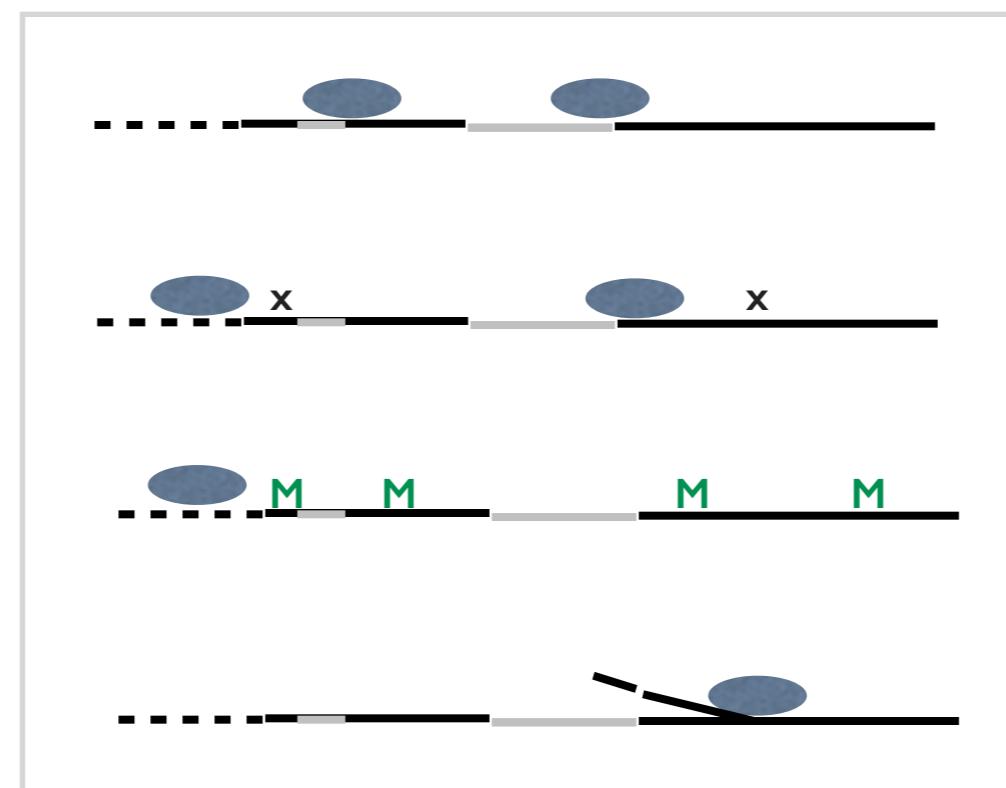
signal transduction

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



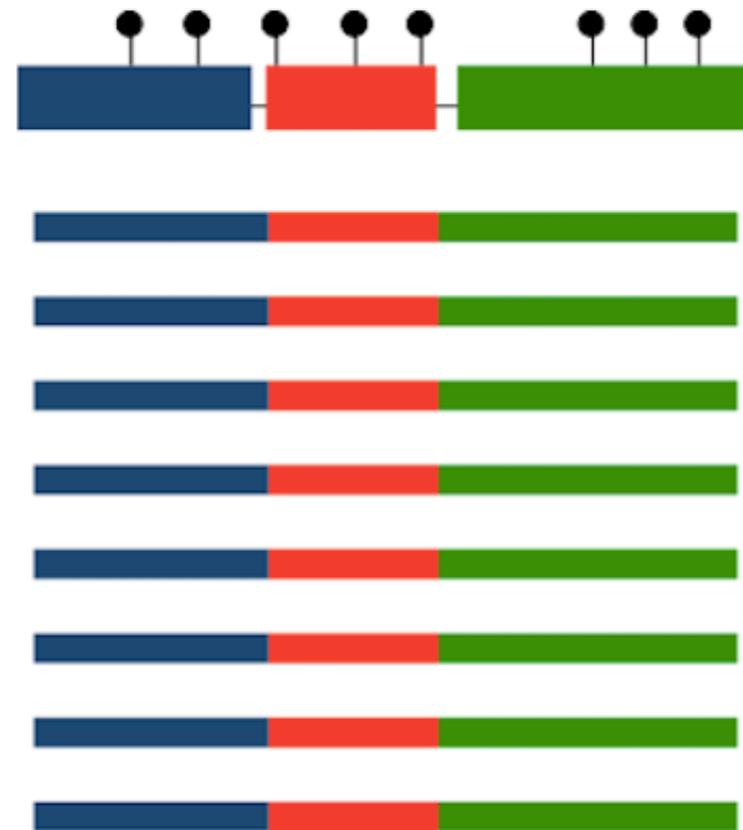
germline methylation

*ubiquitously expressed,
critical genes*

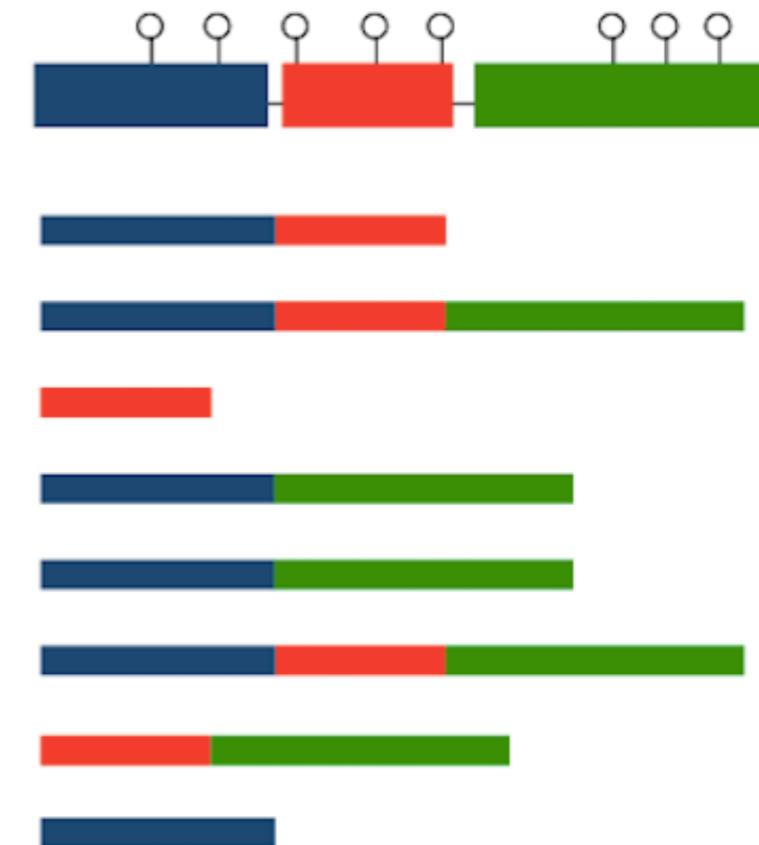
Transcriptional opportunities



conventional transcription
5' UTR promotor



housekeeping



response to
change

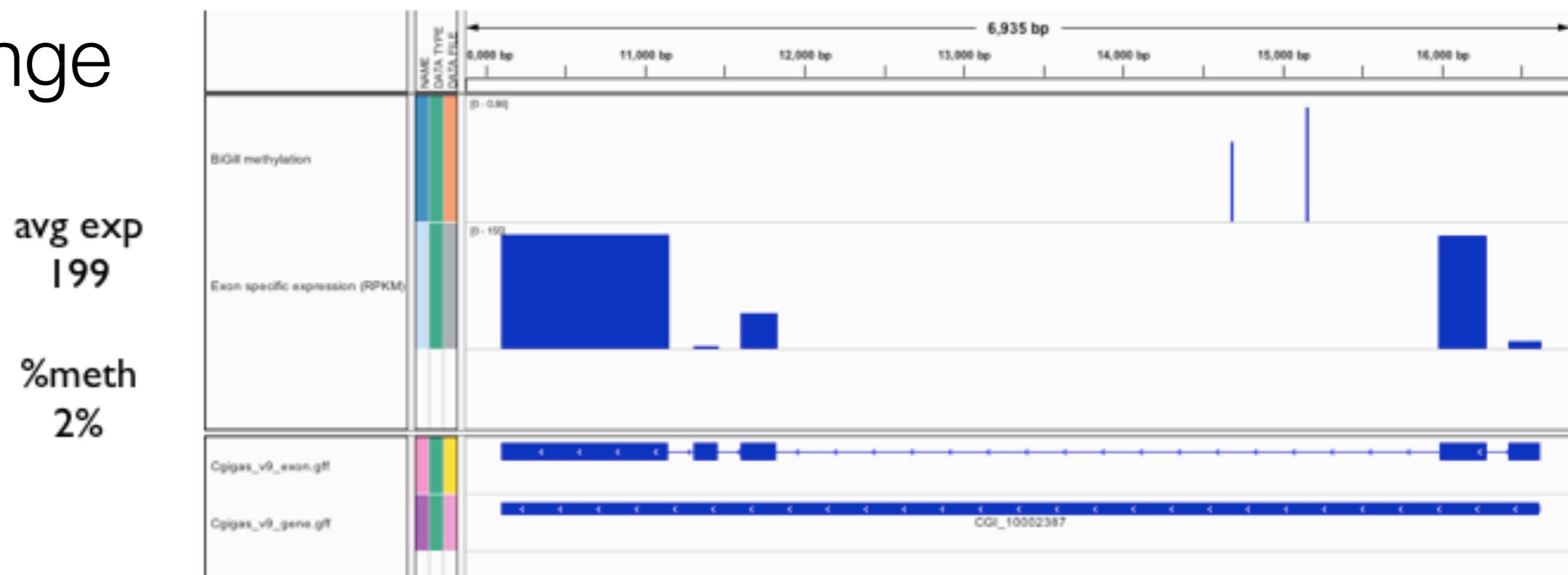
A context dependent role for DNA methylation in bivalves

Mackenzie R. Gavery and Steven B. Roberts

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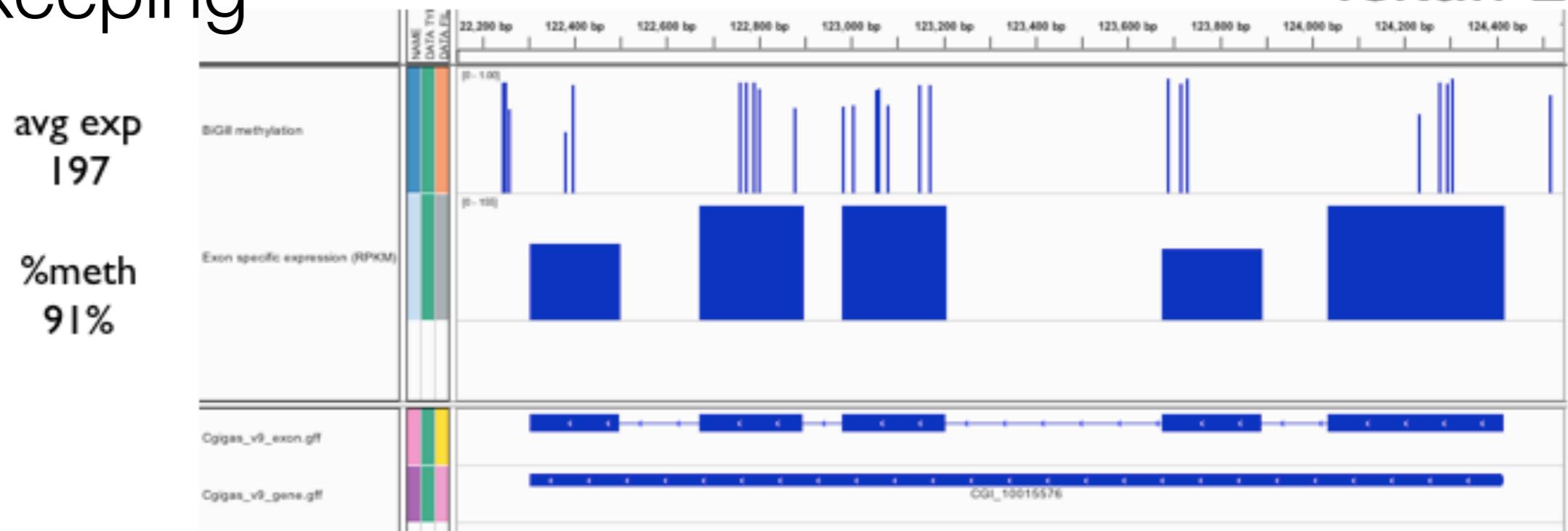
response to
change

Heat shock 70 kDa protein 12A



housekeeping

Tektin-2



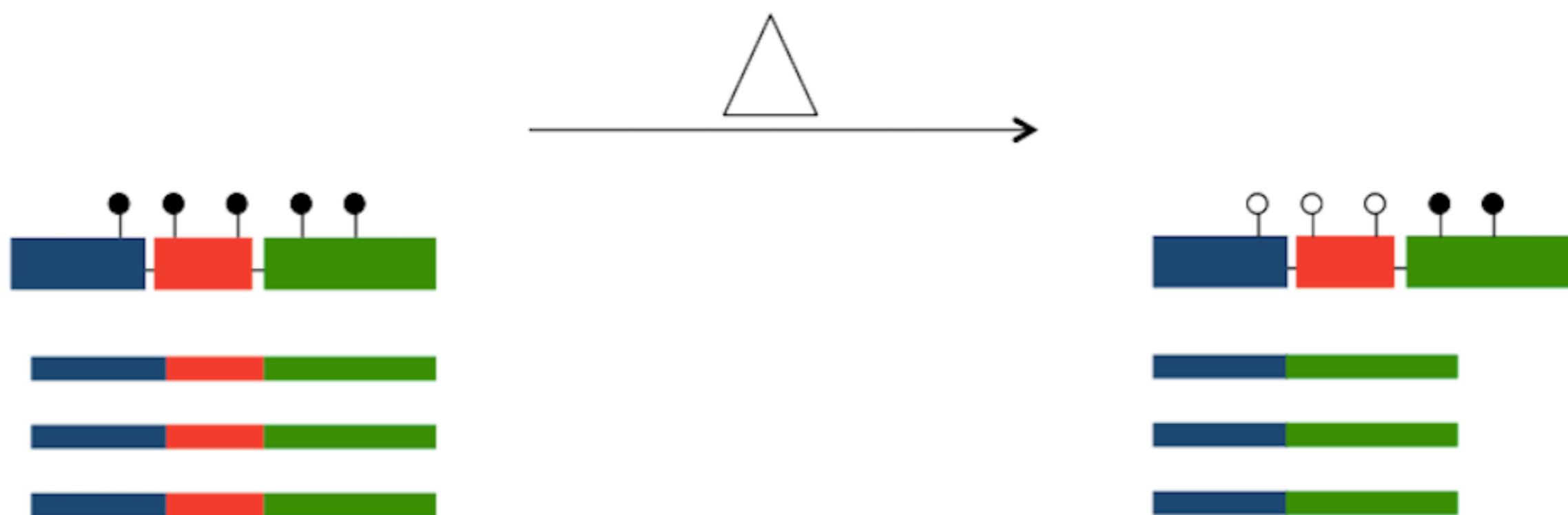


Targeted Regulation

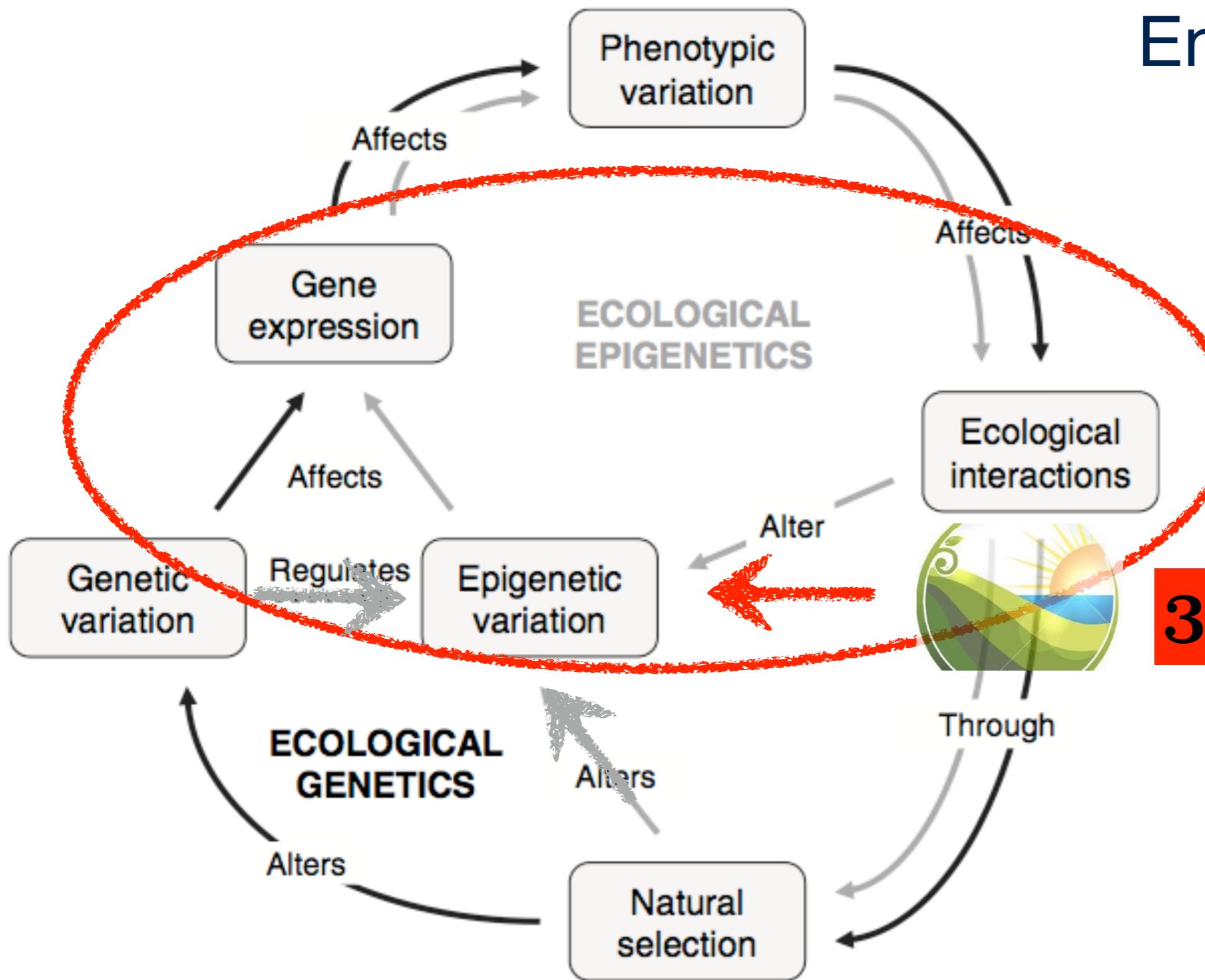
A context dependent role for DNA methylation in bivalves

Mackenzie R. Gavery and Steven B. Roberts

Advance Access publication date 7 January 2014



Environmental Influence



Ecology Letters, (2008) 11: 106–115

doi: 10.1111/j.1461-0248.2007.01130.x

modified from

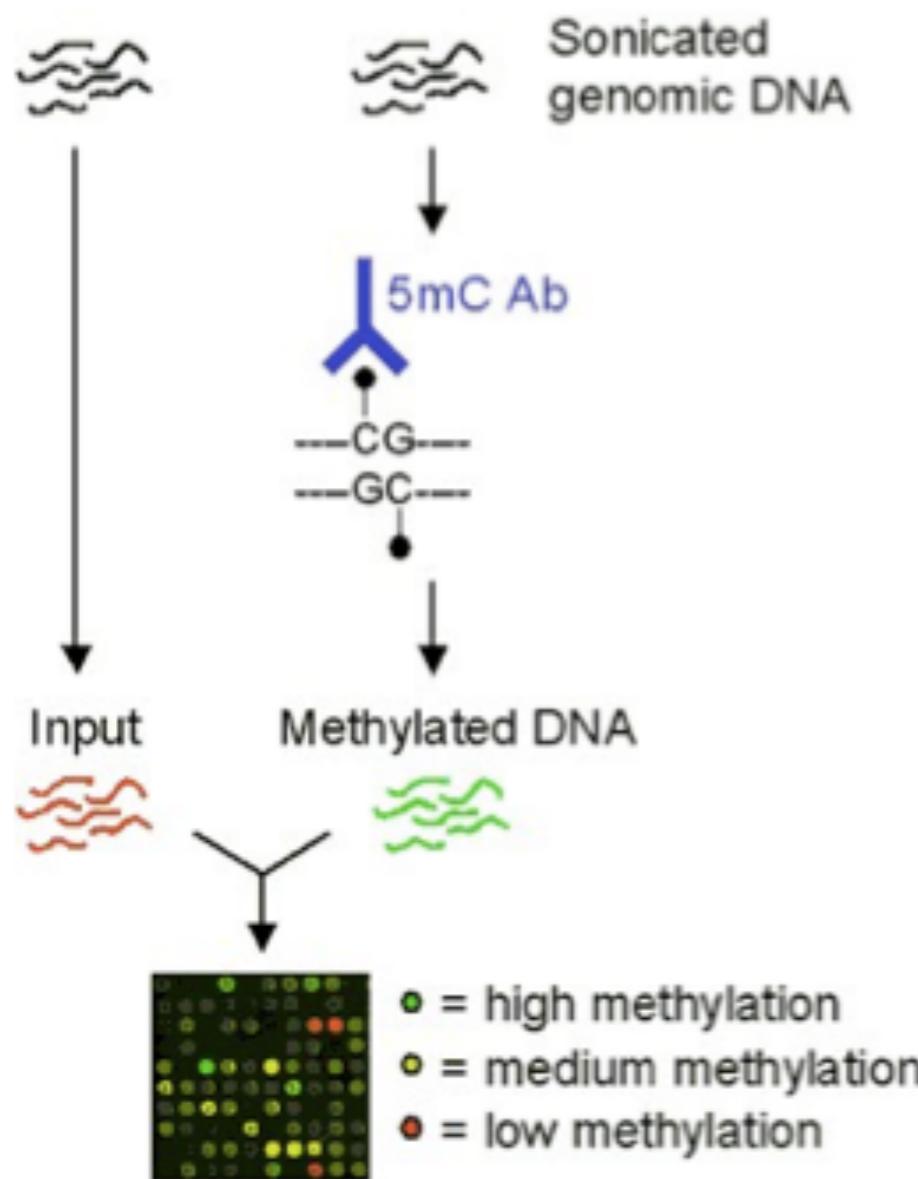
IDEA AND
PERSPECTIVE

Epigenetics for ecologists

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

Very new data

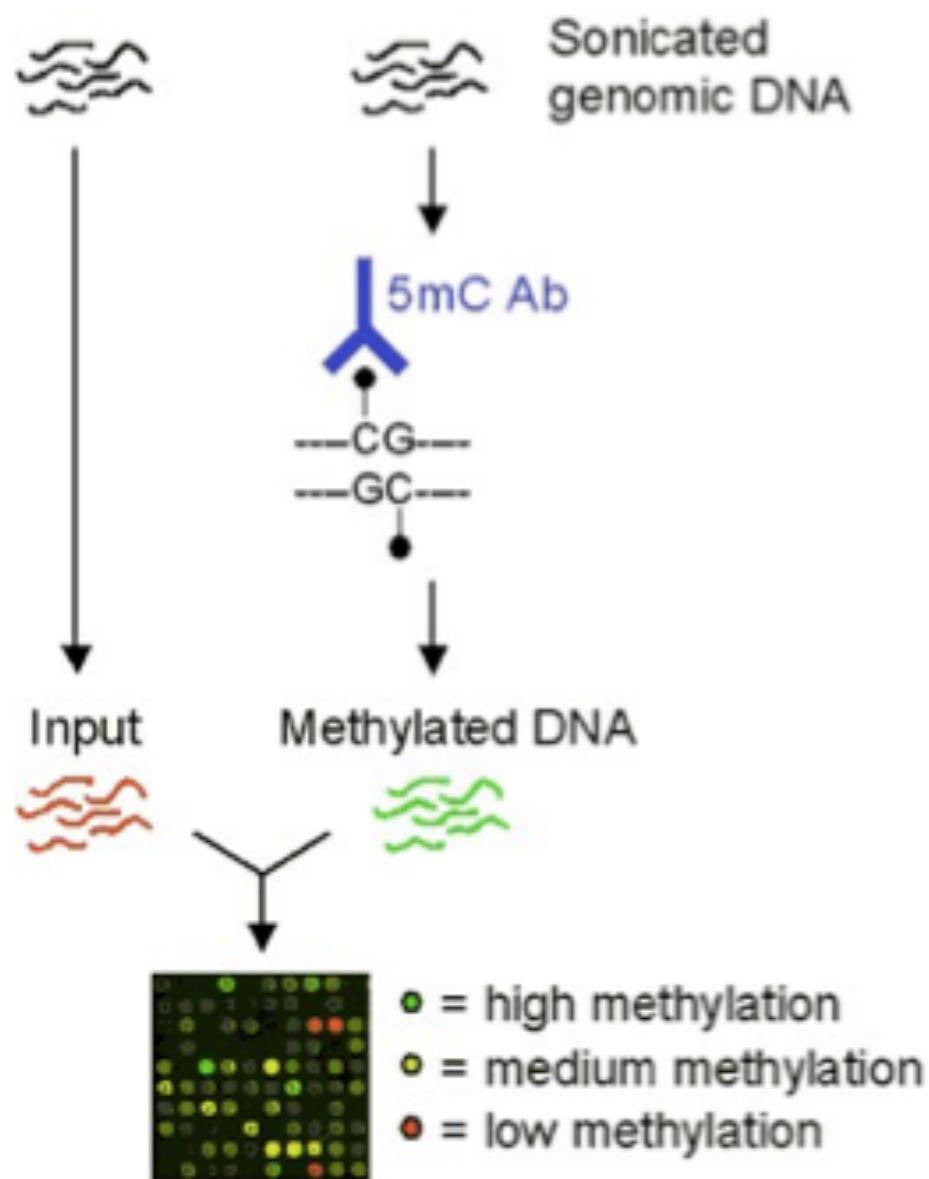
Environmental impact (Estrogens)



- 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

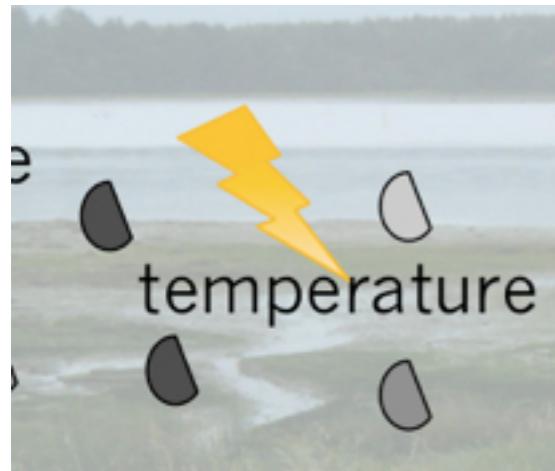
Environmental impact (Estrogens)



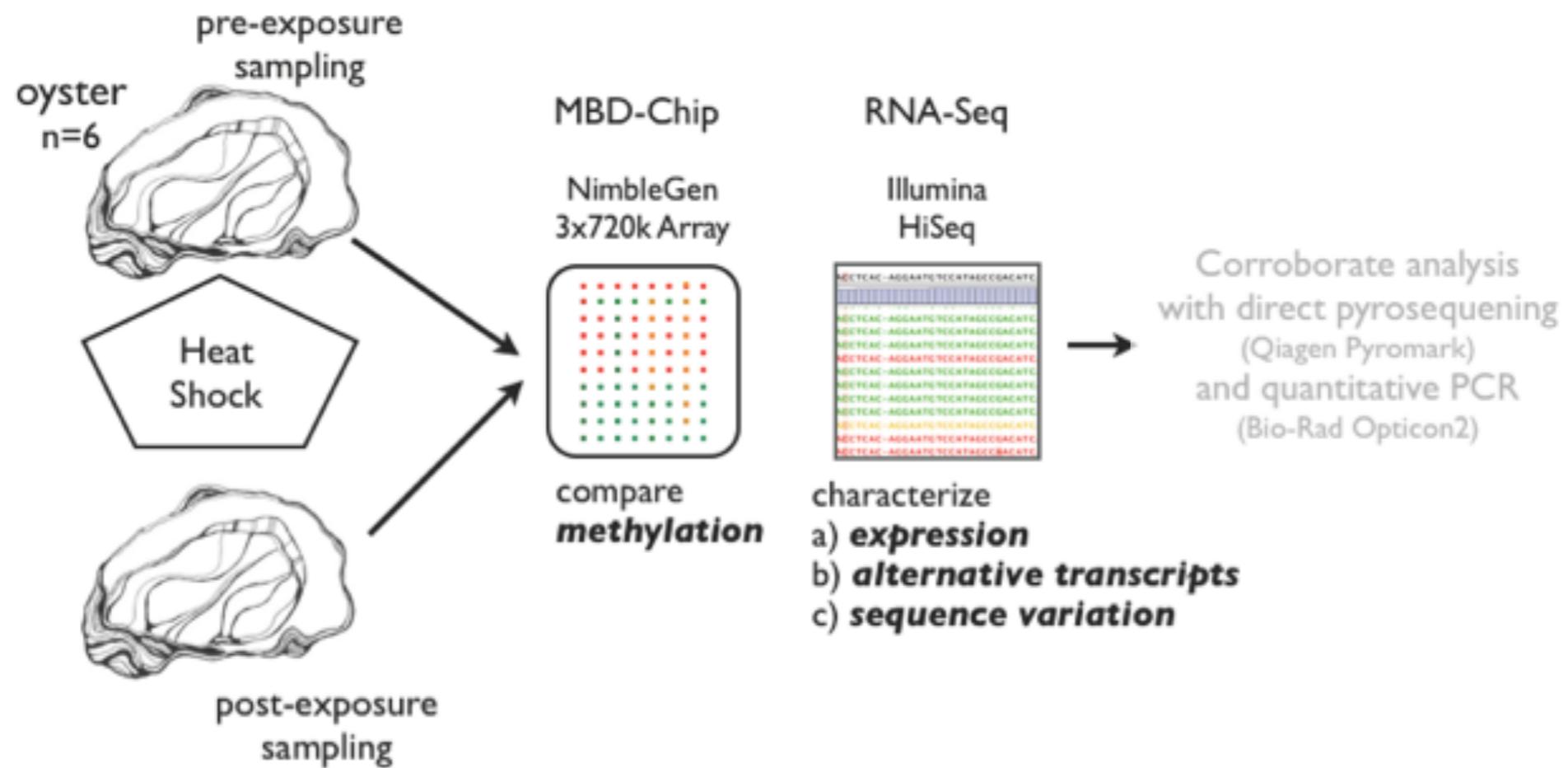
Exposure results in significant hypomethylation

Very new data

Environment and gene expression

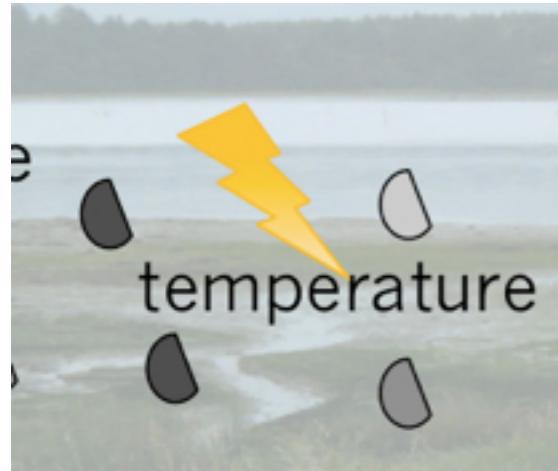


stochastic or targeted?



Very new data

Environment and gene expression

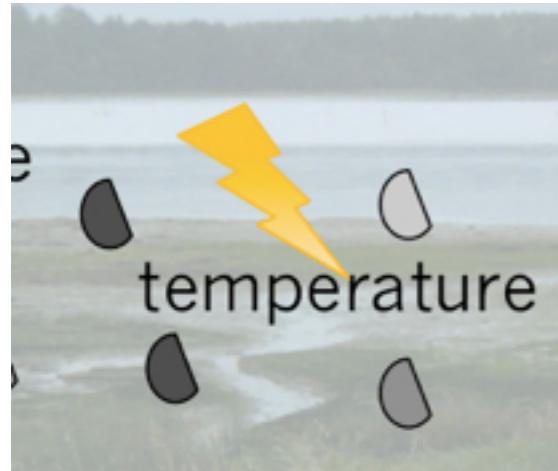


stochastic or targeted?

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

Very new data

Environment and gene expression



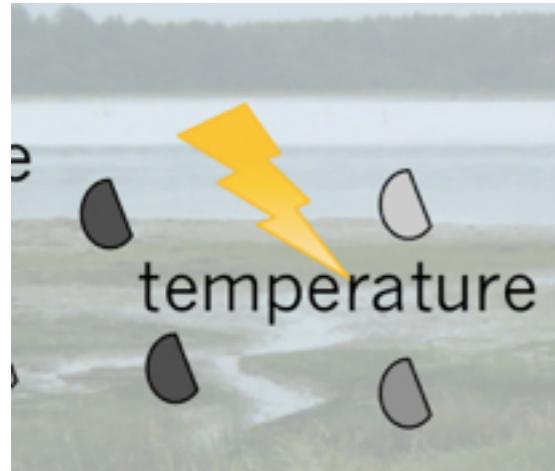
stochastic or targeted?

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

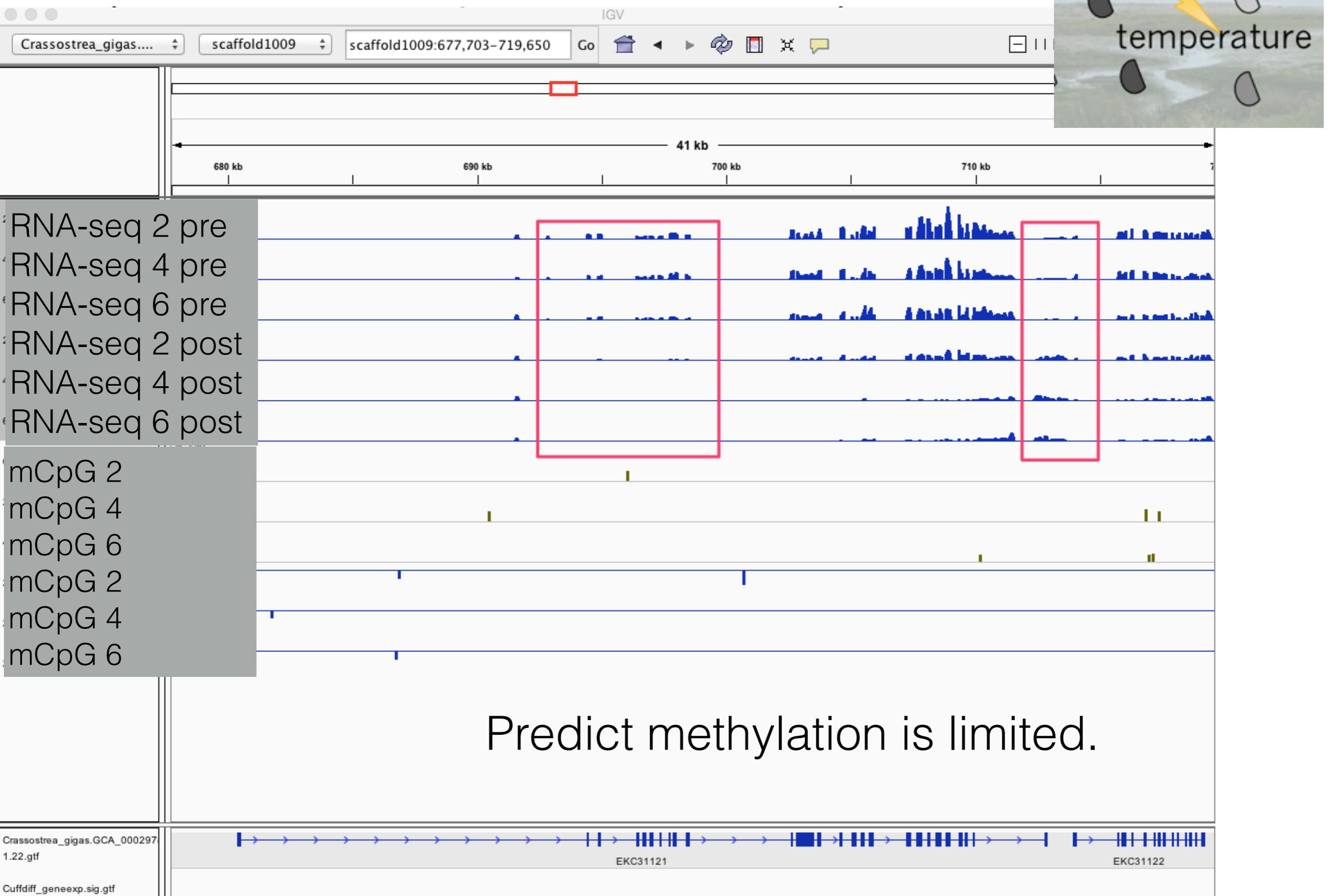


stochastic or targeted?

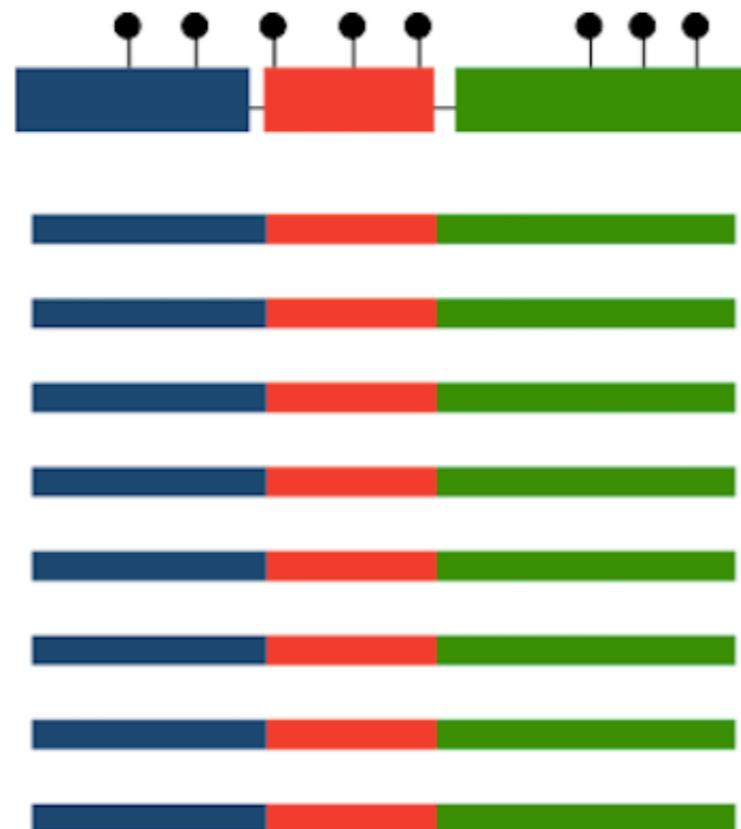
Oyster	Hypo-methylated	Hyper-methylated
2	7224	2803
4	6560	3587
6	7645	4044

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

Very new data



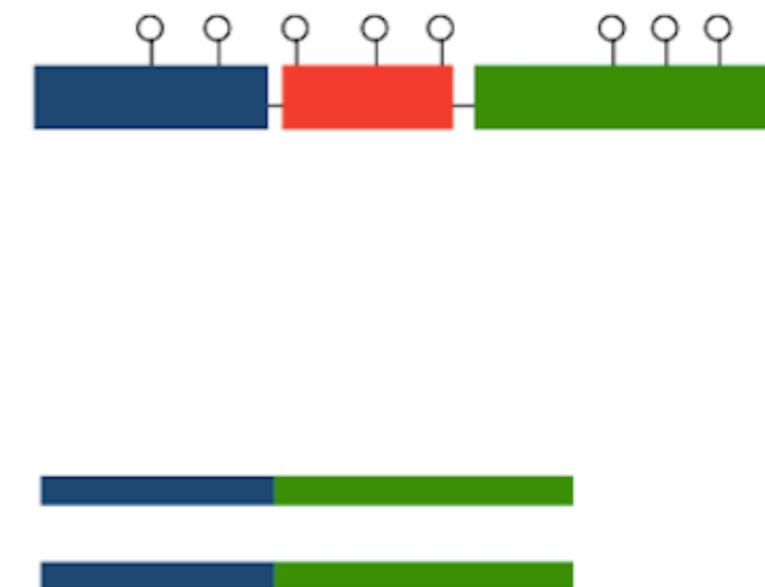
2



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more questions....

~~Very new data~~
Heritability
Plasticity
Local Adaptation

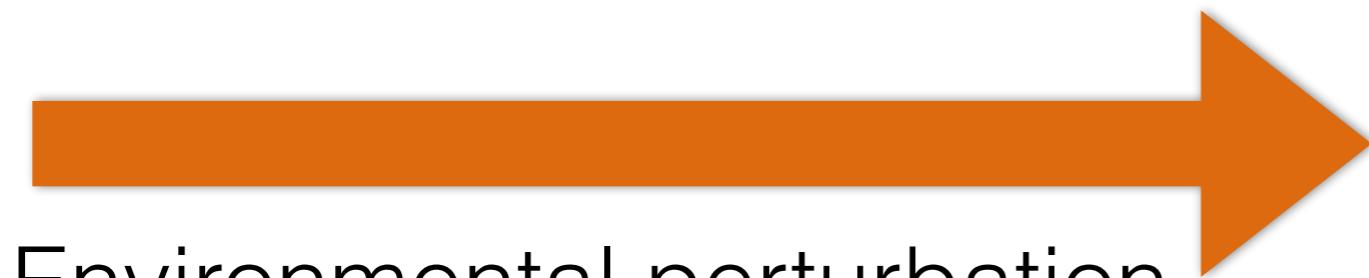
*Genetics
versus
Epigenetics*



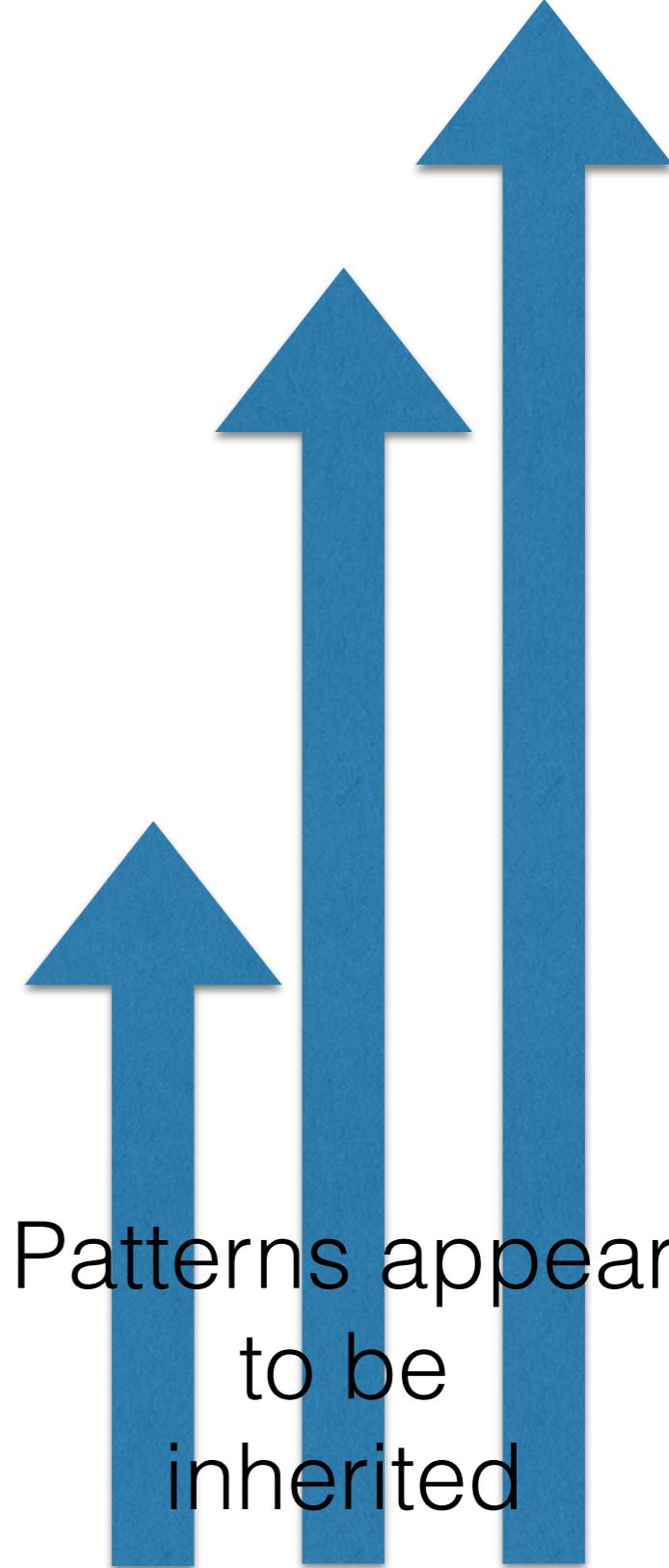
Common Garden Experiment



Considerations



Environmental perturbation
impacts DNA methylation
(predominantly demethylation)



Patterns appear
to be
inherited



Germline methylation encoded with a pattern
product of evolutionary forces

Considerations

Lifespan
or less?

Environmental perturbation
impacts DNA methylation
(predominantly demethylation)

Possibly incorporated
into germline

Germline methylation encoded with a pattern

Patterns appear
to be
inherited

Consideration

Could this provide a “memory”
for subsequent exposure?

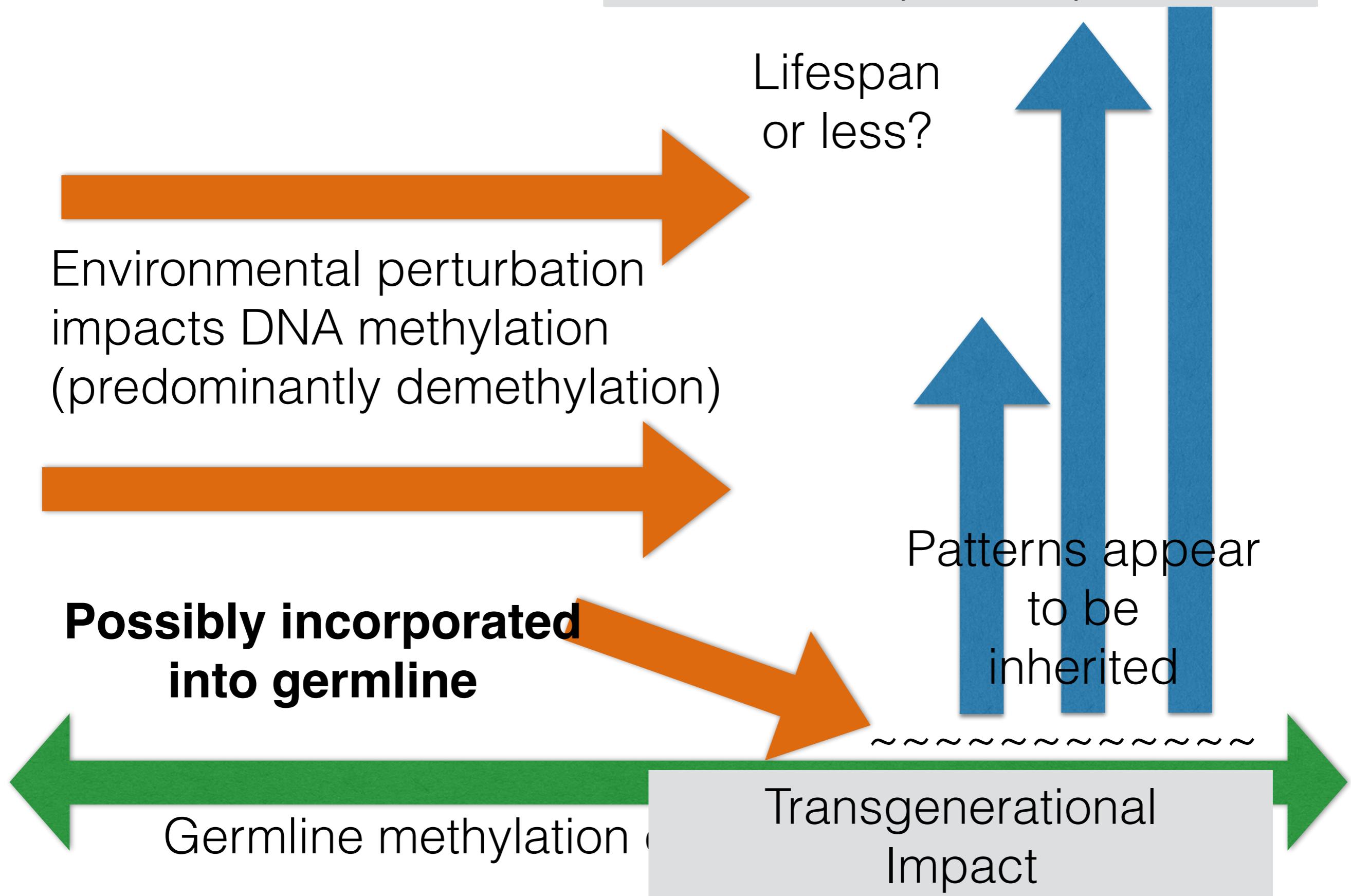




Photo credit: Flickr, Creative Commons, csestums



Change how we consider...
**population structure
adaptation
resilience**

Photo credit: Flickr, Creative Commons, csesums

Next Steps

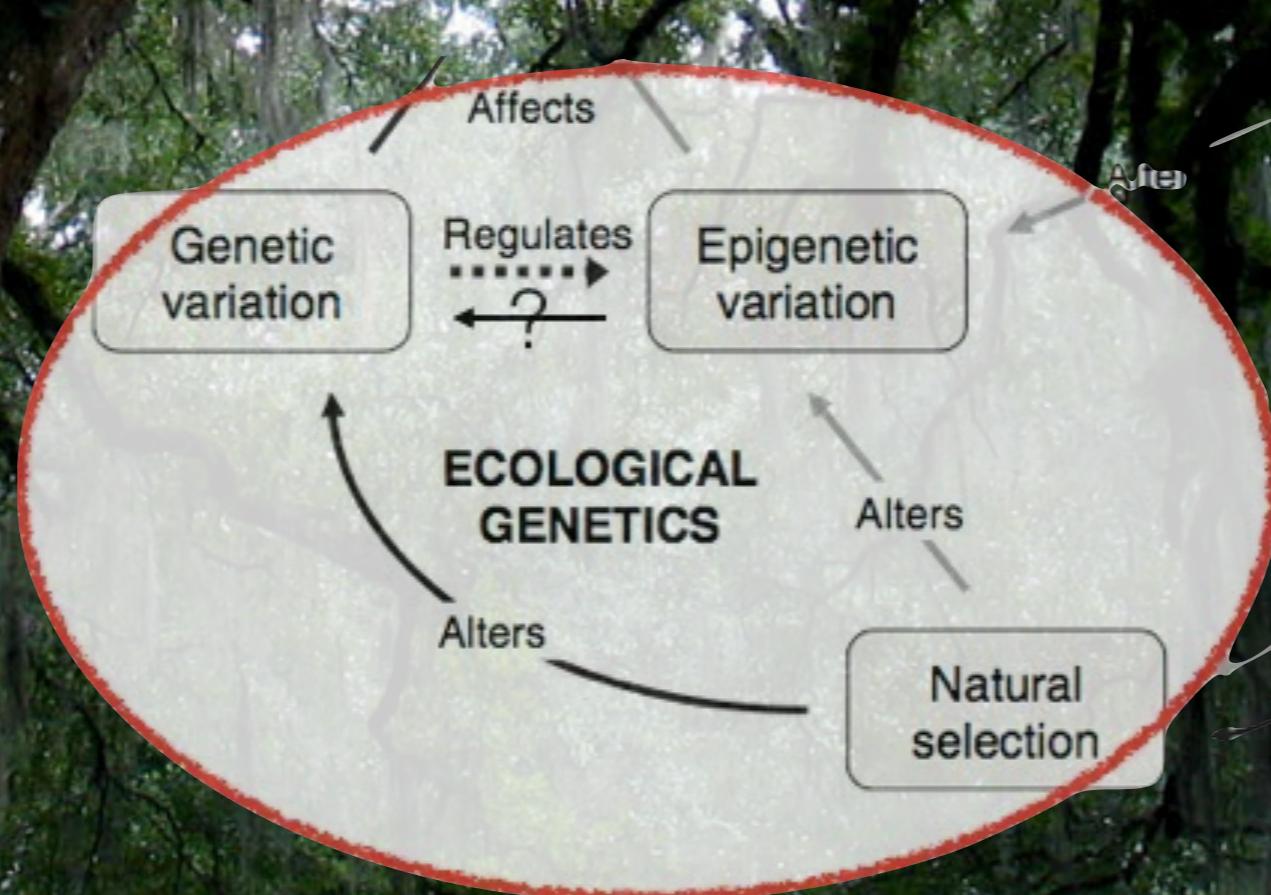


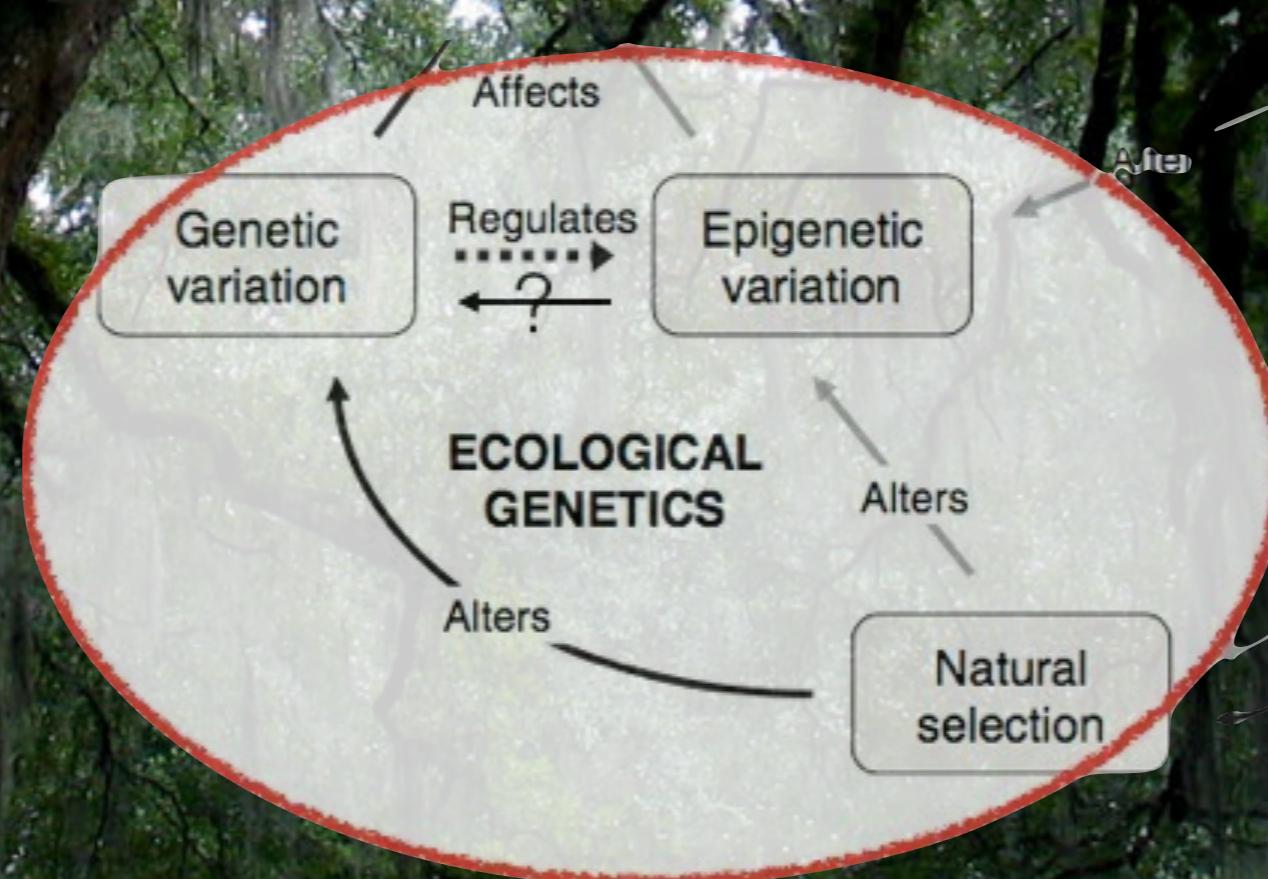
Photo credit: Flickr, Creative Commons, csessums

Next Steps

Other processes
- Histone Mods

Transposable
Elements

“Memory”



Acknowledgements

Mackenzie Gavery
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Bill Howe
Dan Halperin



slides, data & more @ robertslab.info