

# Influence of Epigenetic Variation on Marine Invertebrate Physiology

# Steven Roberts



**epigenetics**

latest online genetics weekly DNA live addition includes responses relationship

physiological new research

integrative marine role Mac level

characterizing Highlights adaptive

maintaining Sharing dependent component developed

new view

Research

Mac

level

examine check Lab Ocean

strive page process

providing Data notebooks functional

organismal investigating

members newest

follow

Facebook electronic

protome

Resource

practice

sure

focuses

meetings

nucleotide organisms

environmental

blogs

impacts

core change

methylation

bivalves

Using

Acidification approaches

list context transcription

Meeting Check Plan one lab

## Epigenetics: Background and Fish

# Background

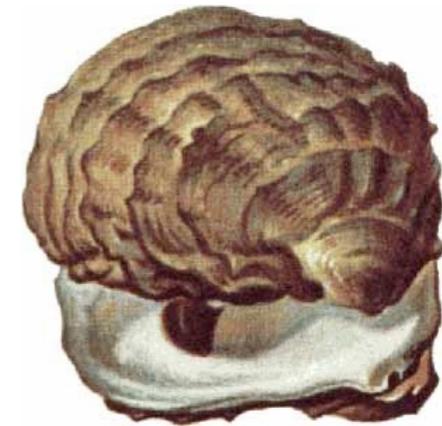
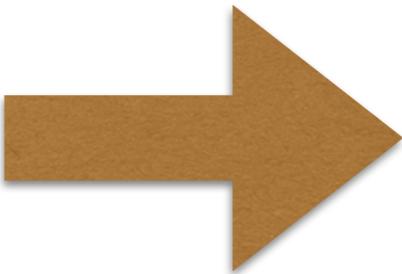
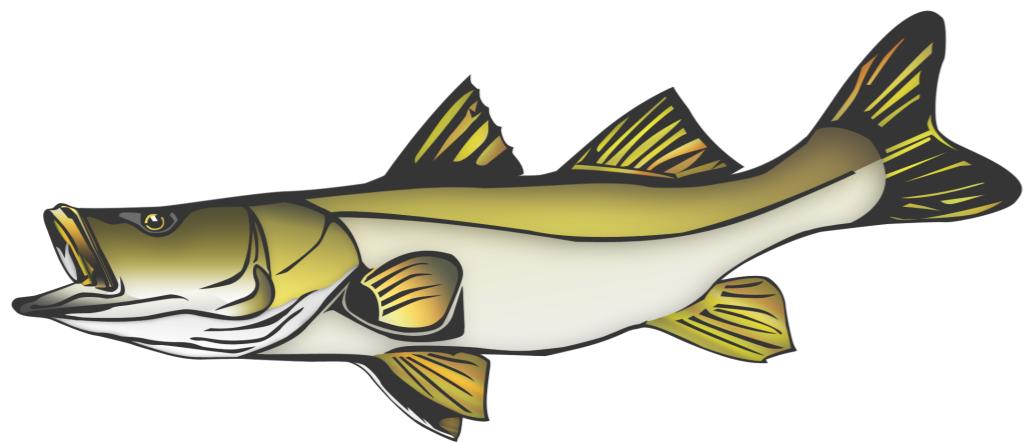
## Physiology

*How fundamental processes work in aquatic species*

# Background

## Physiology

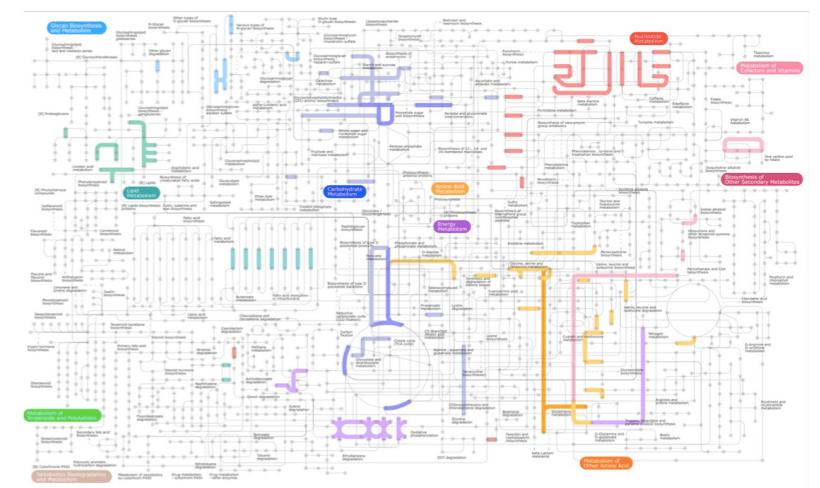
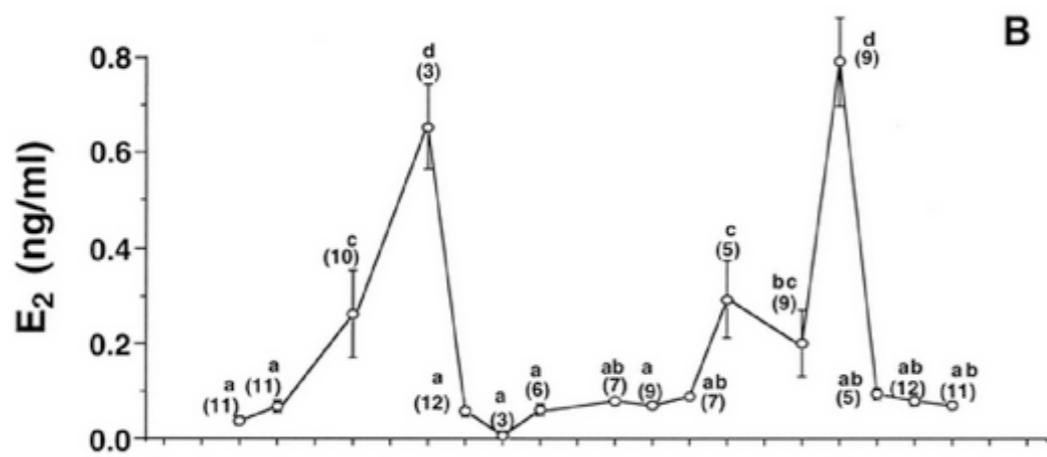
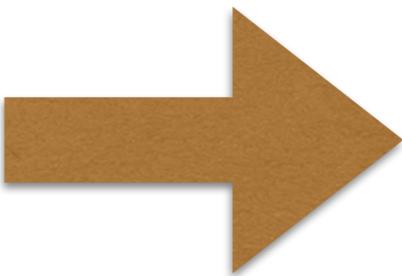
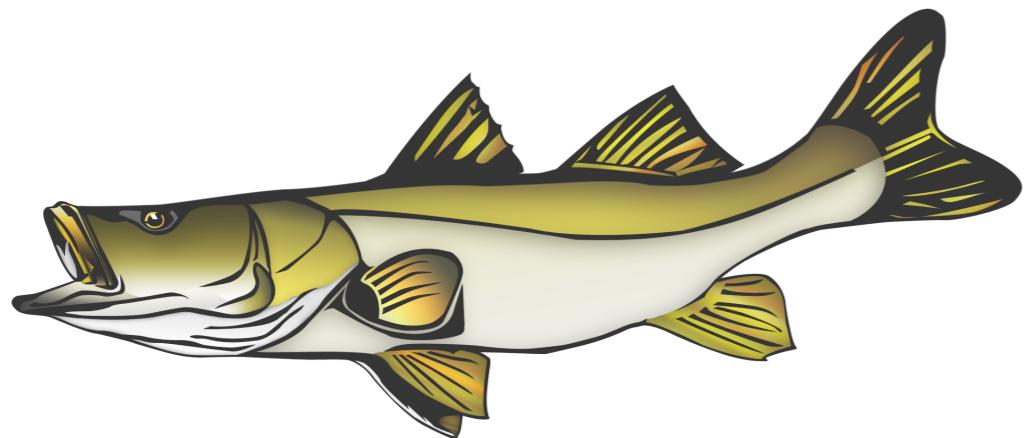
*How fundamental processes work in aquatic species*



# Background

## Physiology

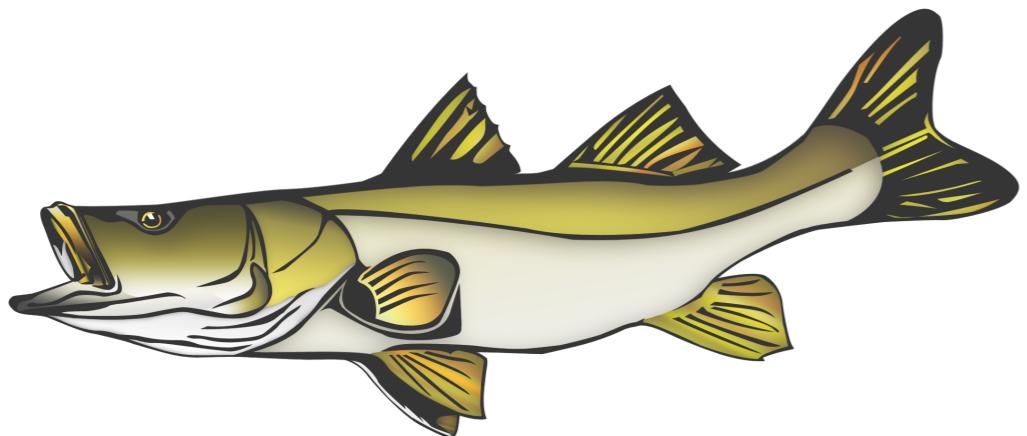
*How fundamental processes work in aquatic species*



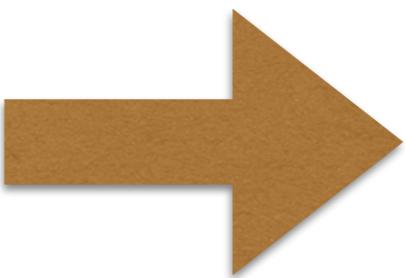
# Background

## Physiology

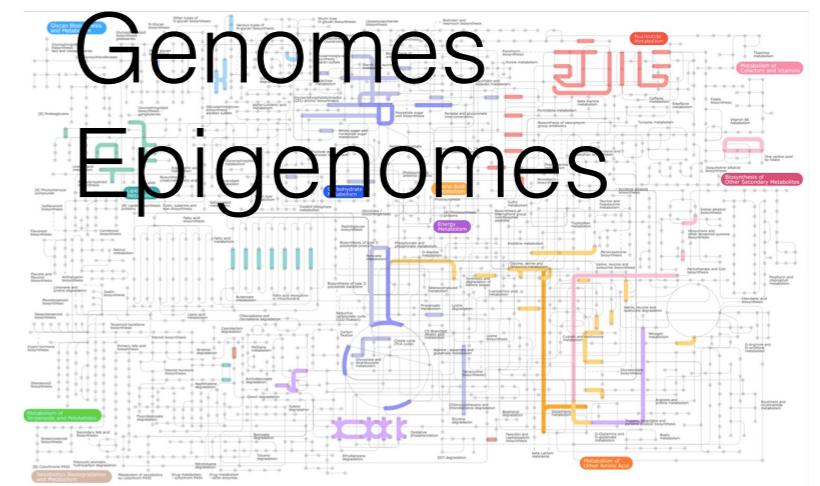
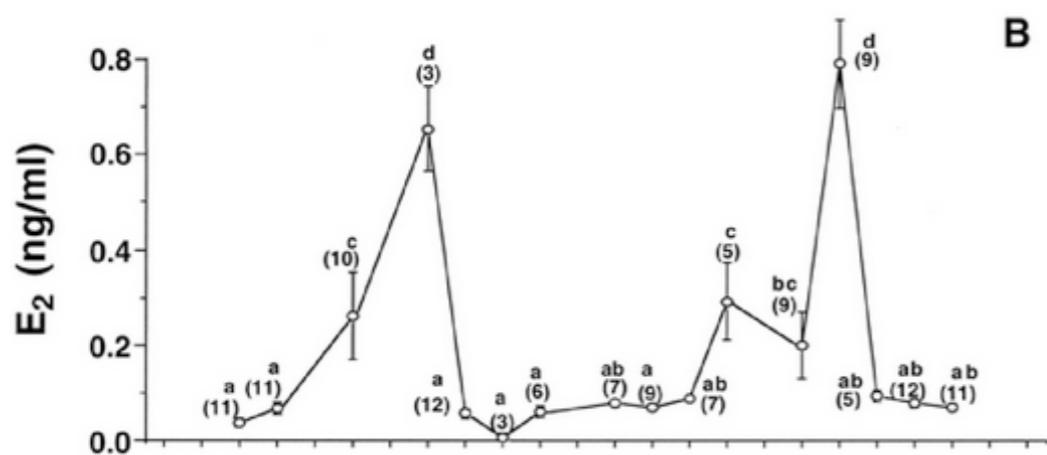
*How fundamental processes work in aquatic species*



Hormones  
Proteins



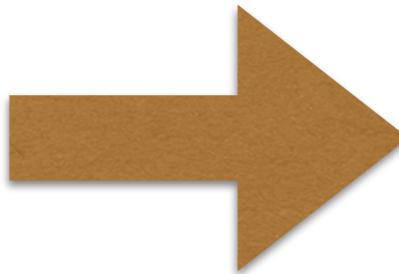
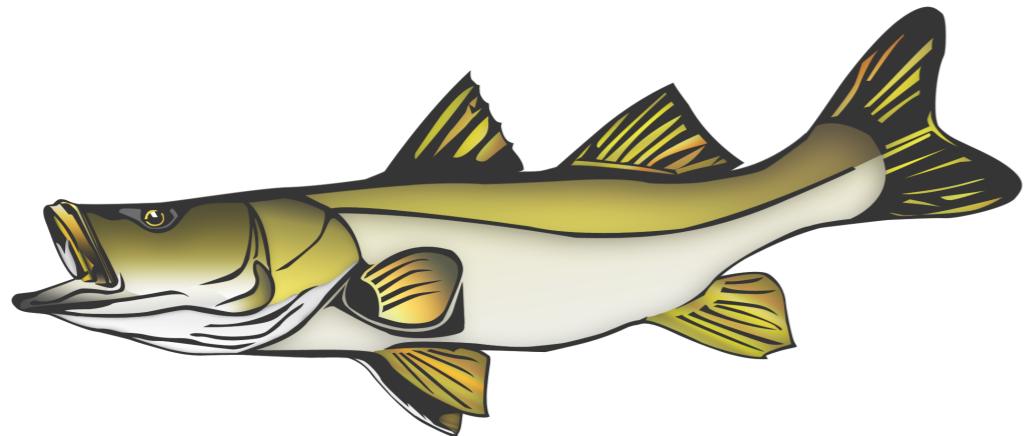
Transcriptomes  
Proteomes  
Genomes  
Epigenomes



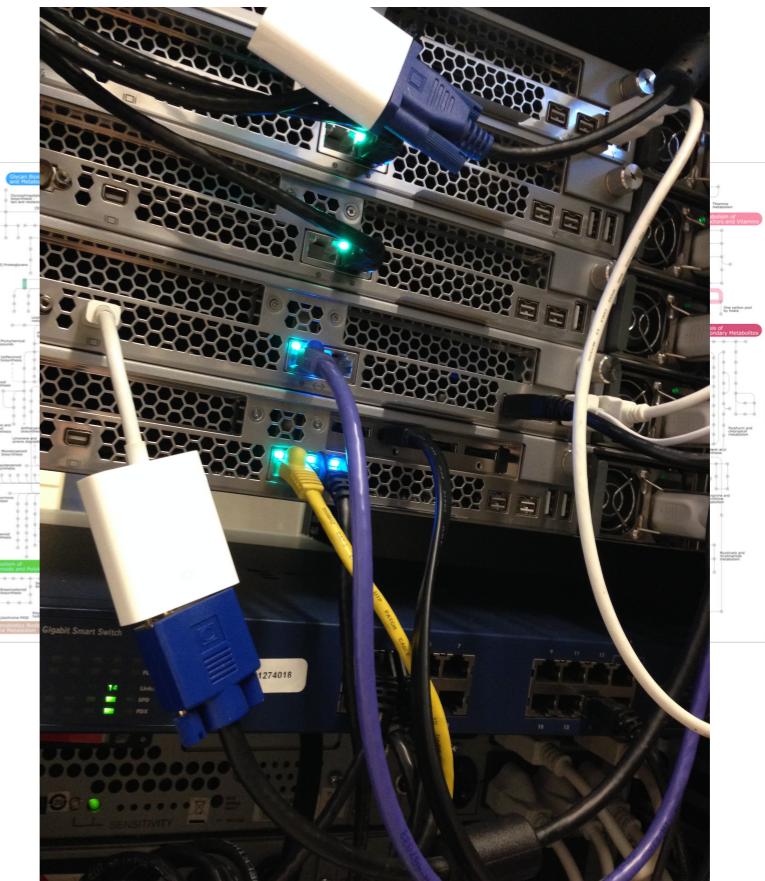
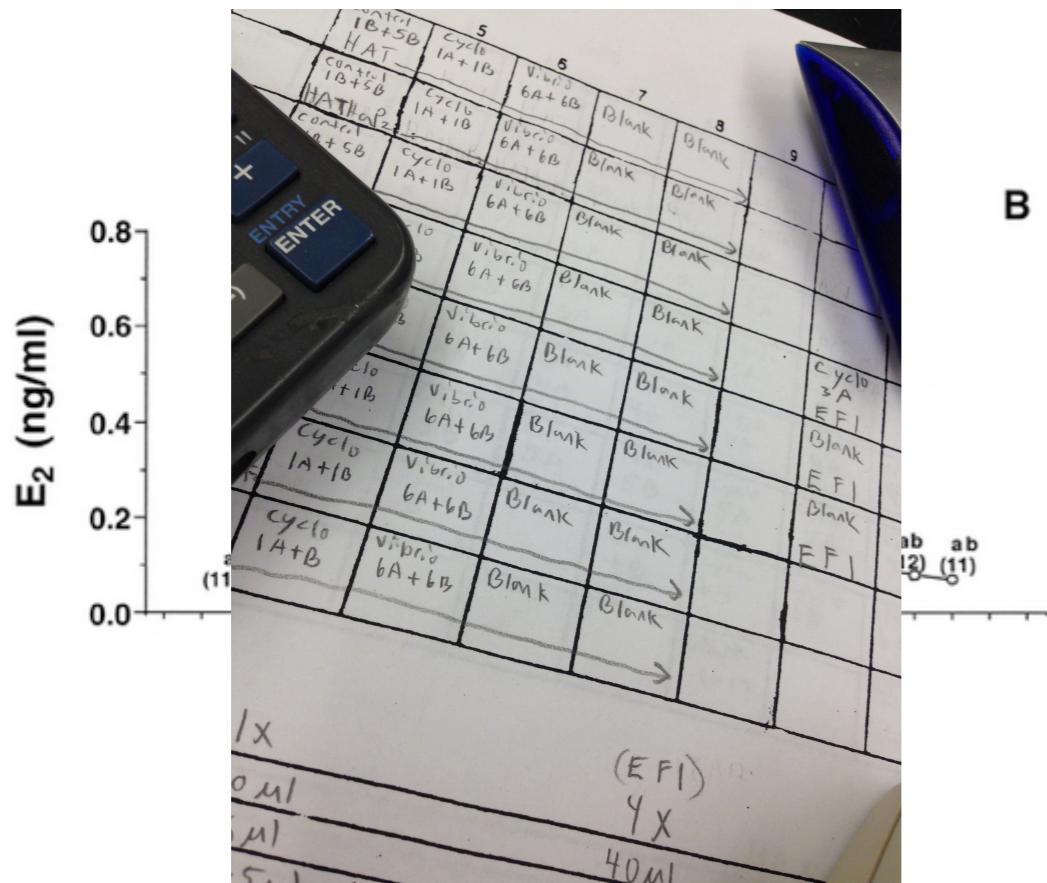
# Background

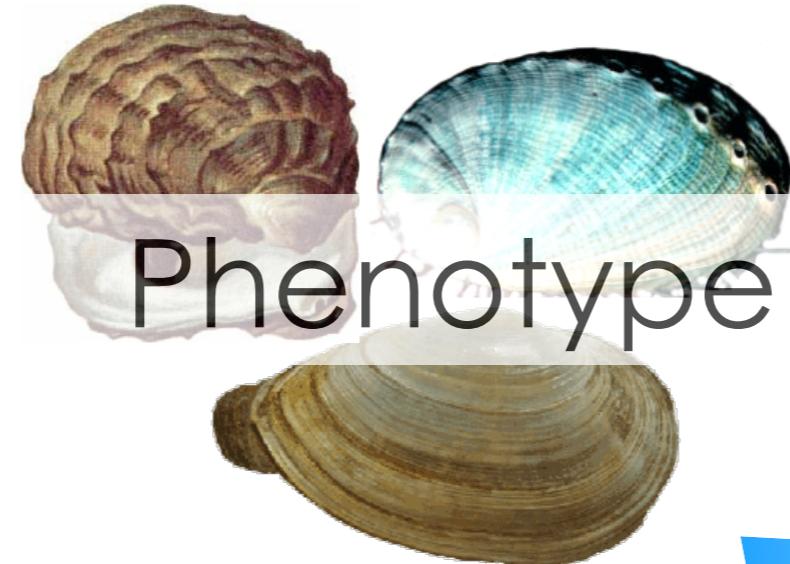
## Physiology

*How fundamental processes work in aquatic species*



B





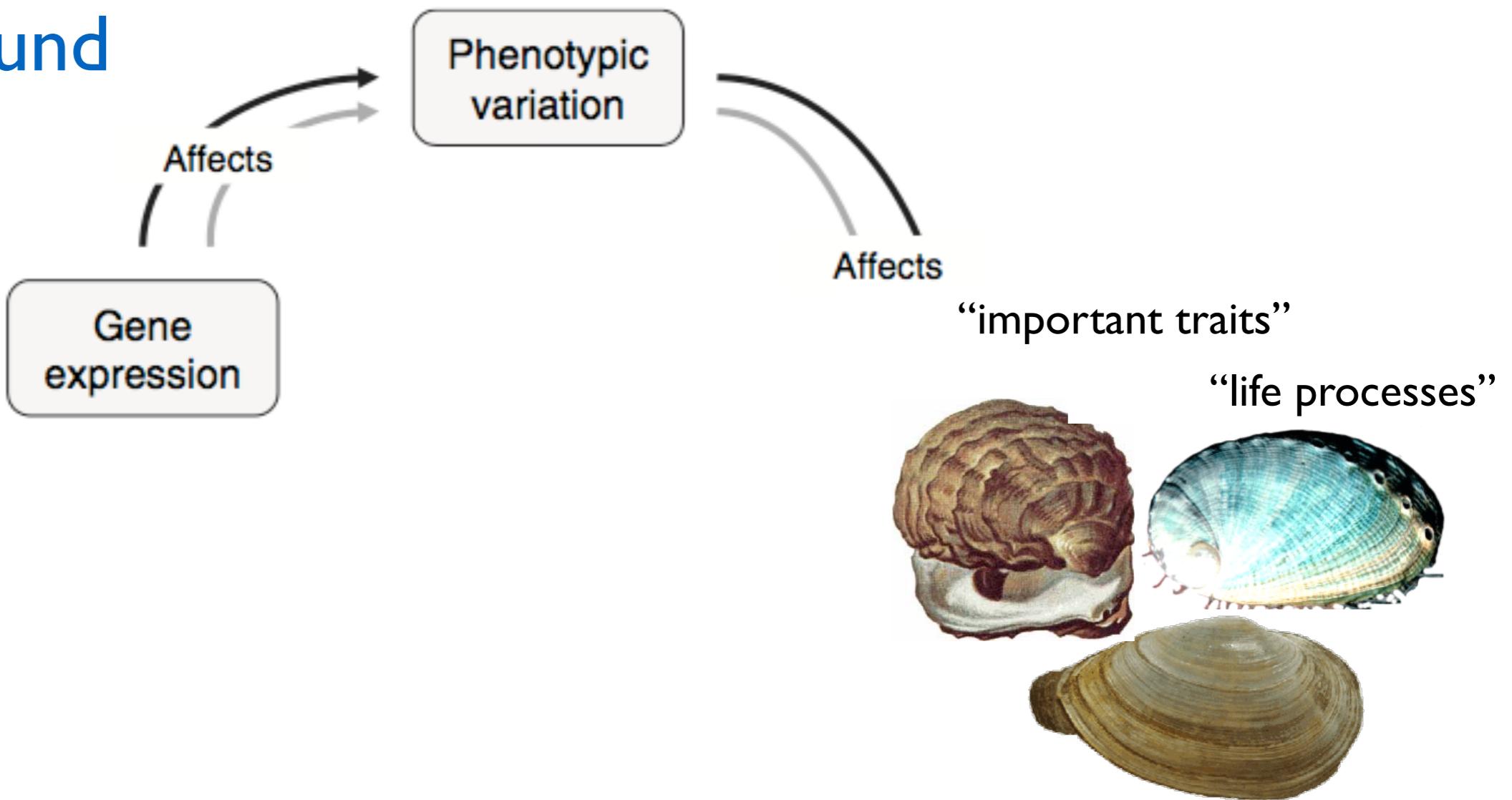
Phenotype

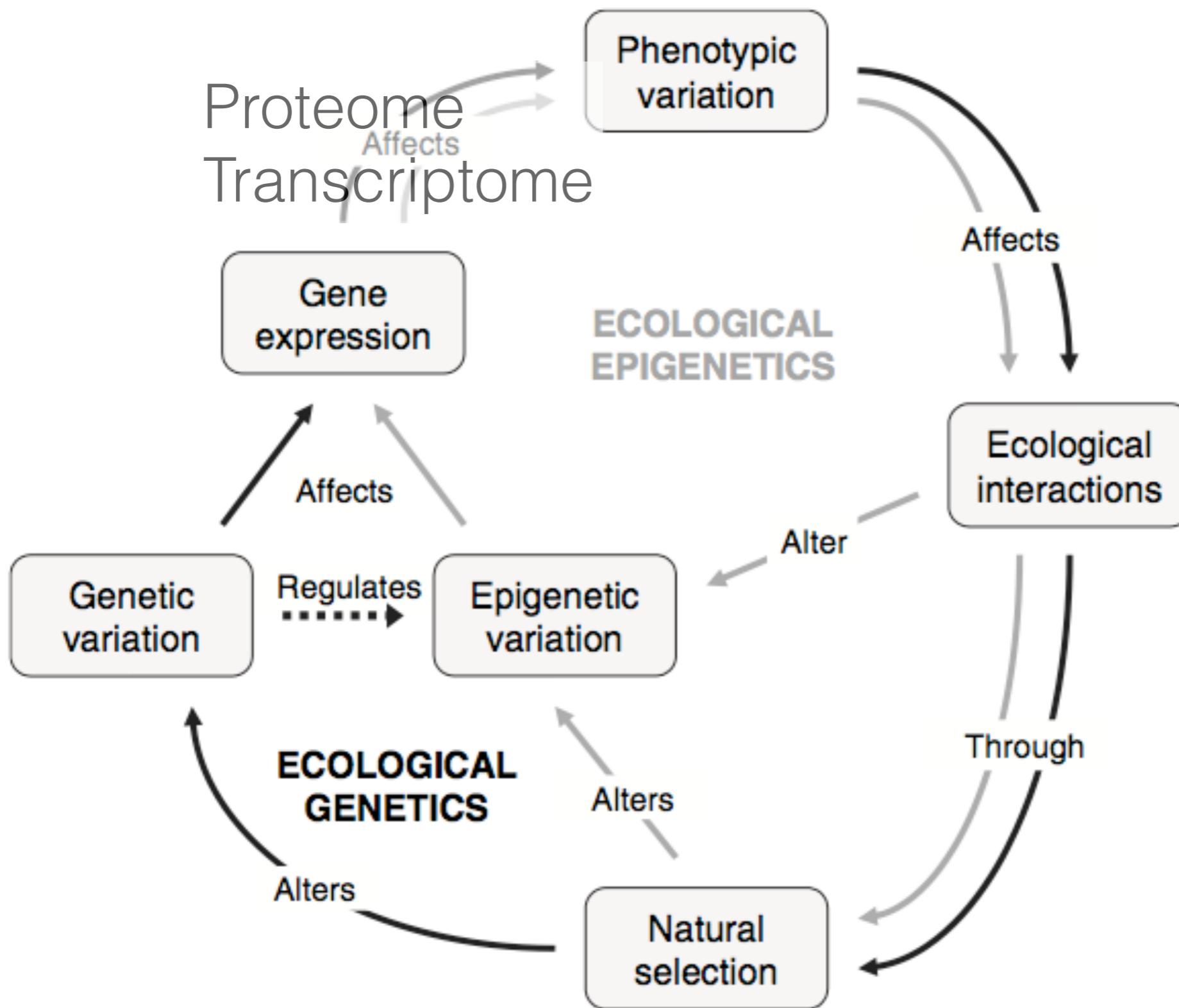


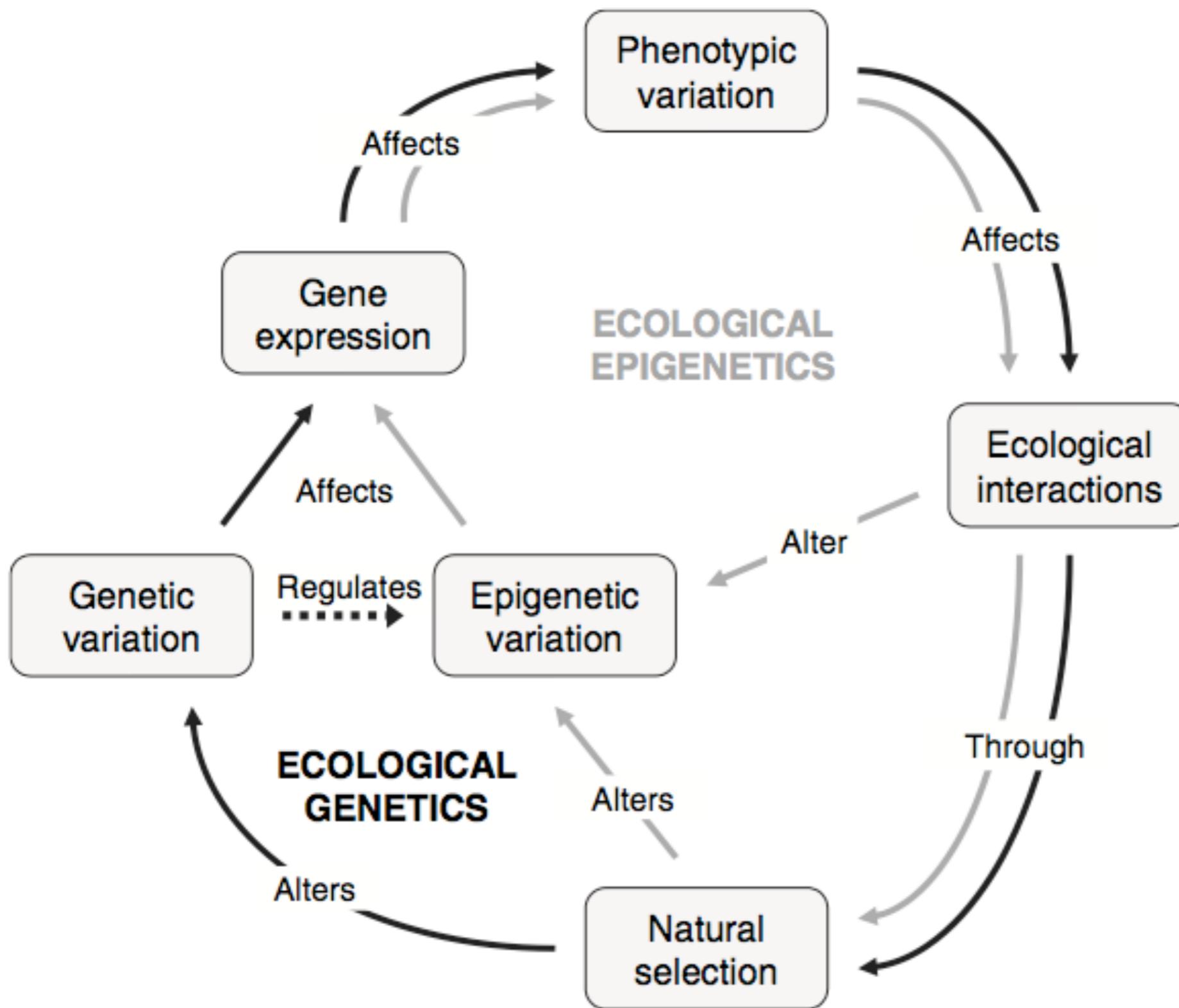
Epigenetics

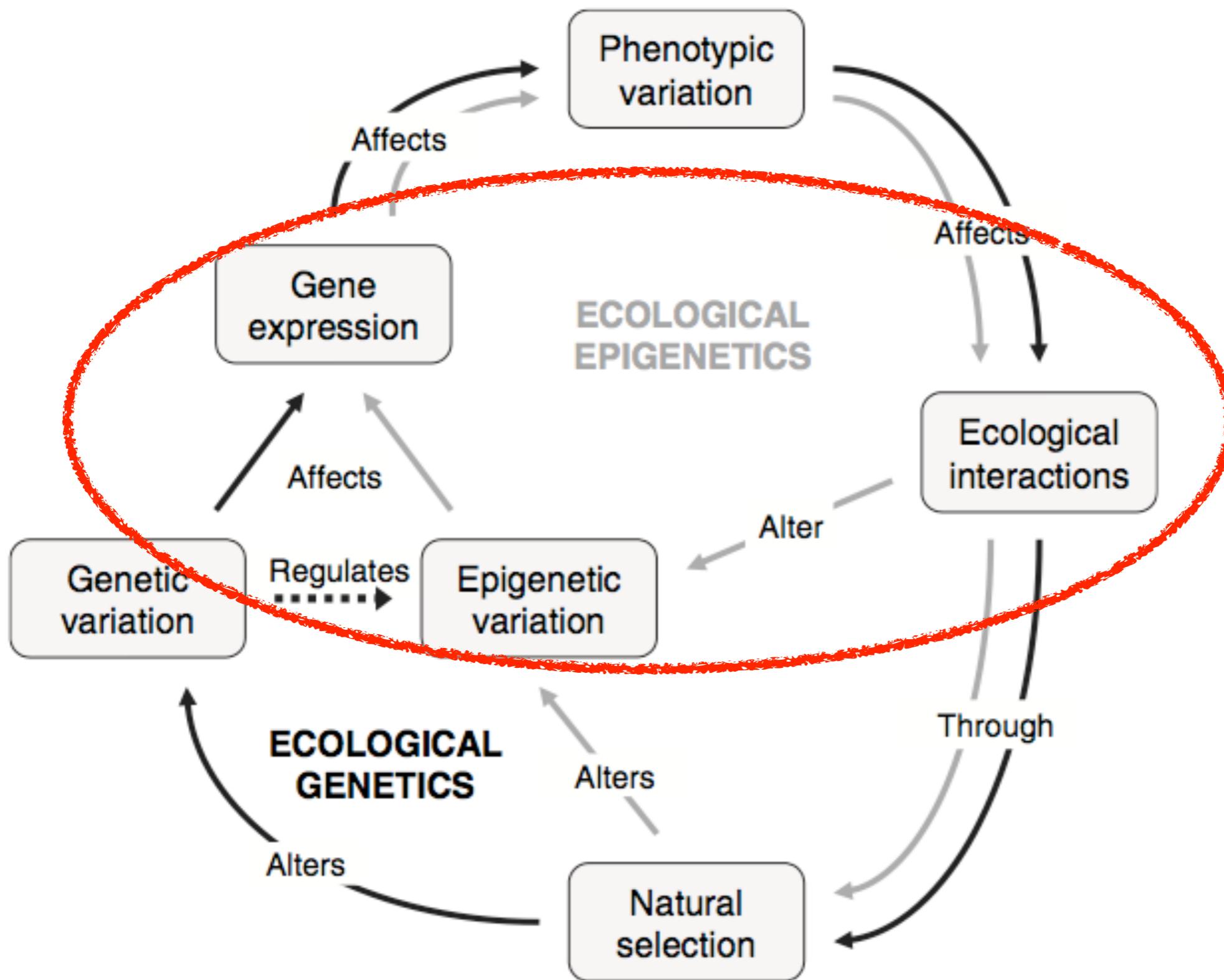


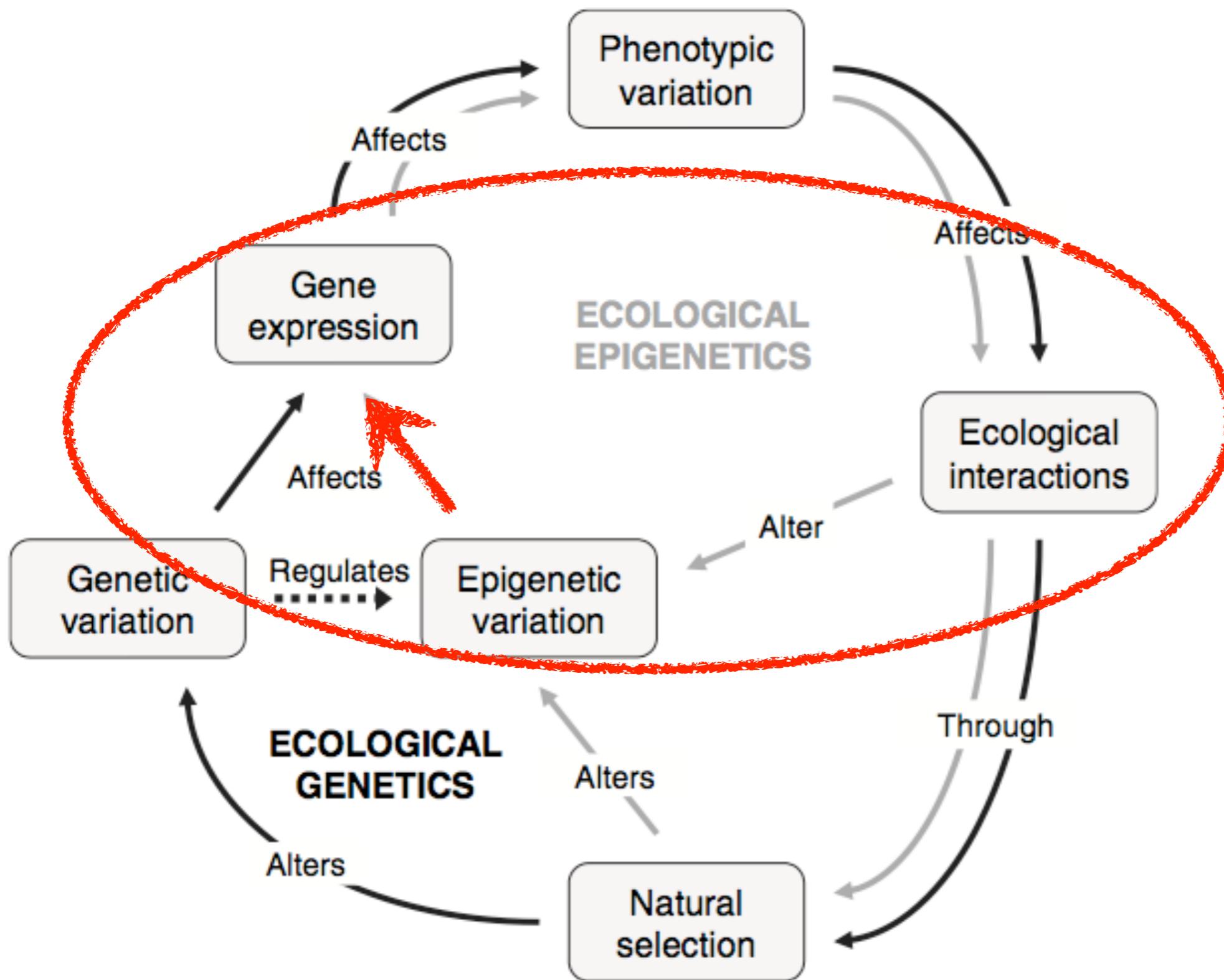
# Background











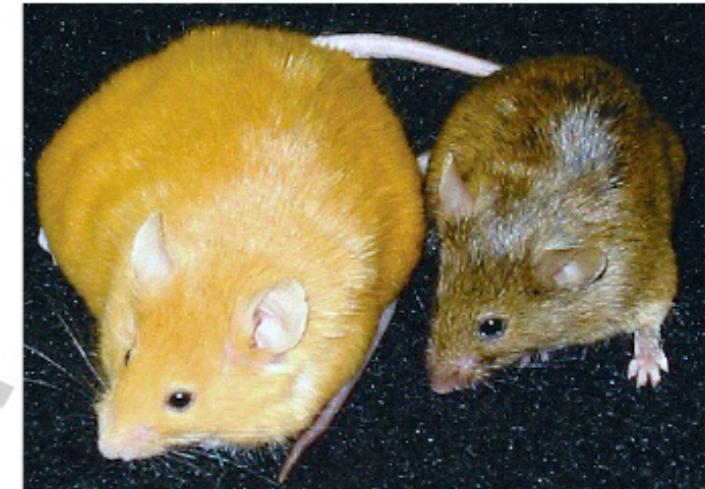
# Epigenetics

A high-magnification fluorescence microscopy image showing dark, irregular shapes representing epigenetic marks (such as DNA methylation) scattered across a light-colored, textured background that represents the underlying chromatin structure.

Photo credit: Flickr, Creative Commons, he-boden



# Epigenetics



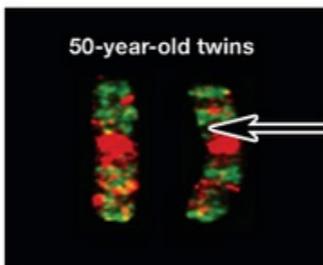
## Nature AND Nurture

### 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.

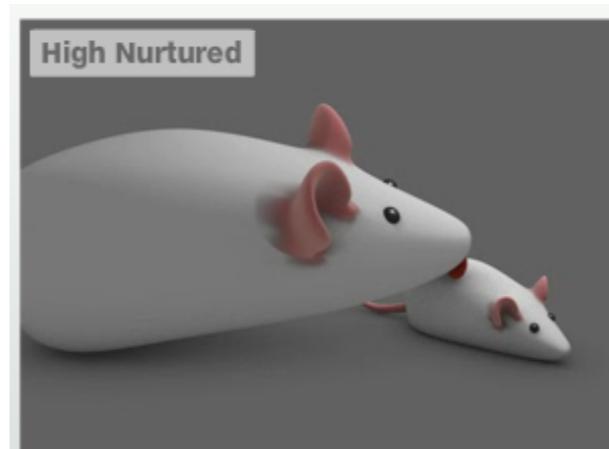
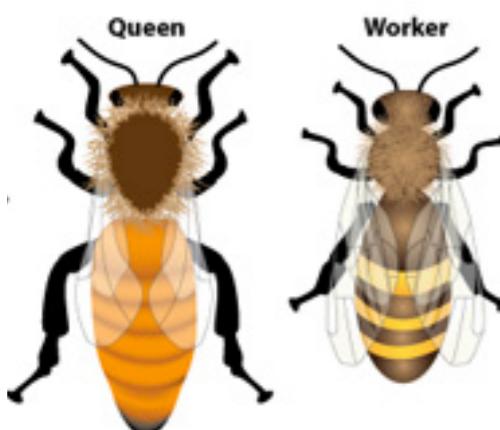
While pregnant, both of their mothers were fed Bisphenol A (BPA) but DIFFERENT DIETS:

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



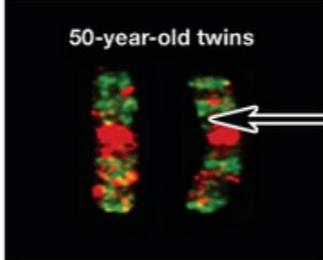
## Nature AND Nurture

### Chromosome 3 Pairs

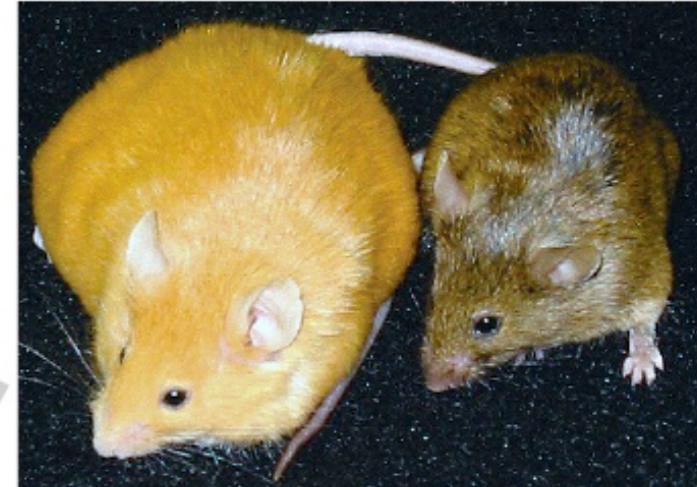
3-year old twins vs. 50-year-old twins



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.



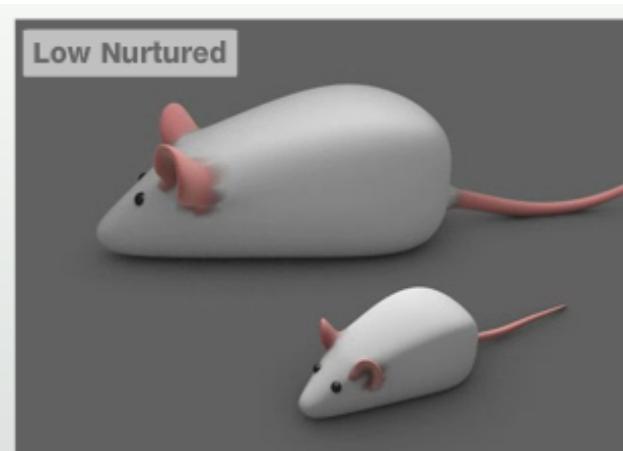
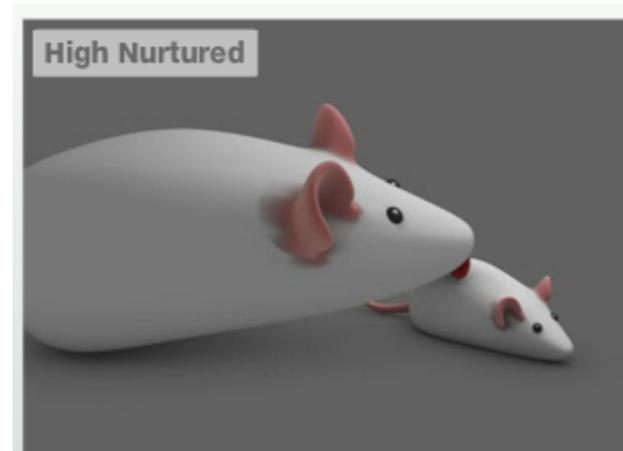
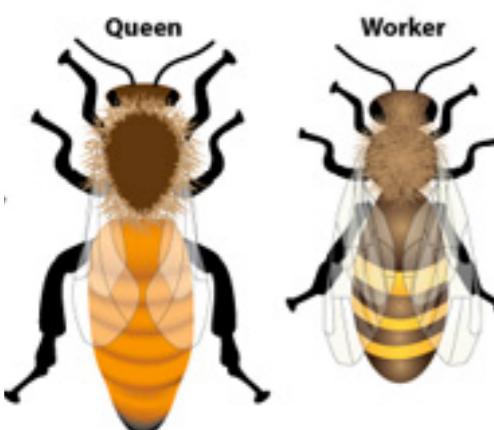
While pregnant, both of their mothers were fed Bisphenol A (BPA) but DIFFERENT DIETS:

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



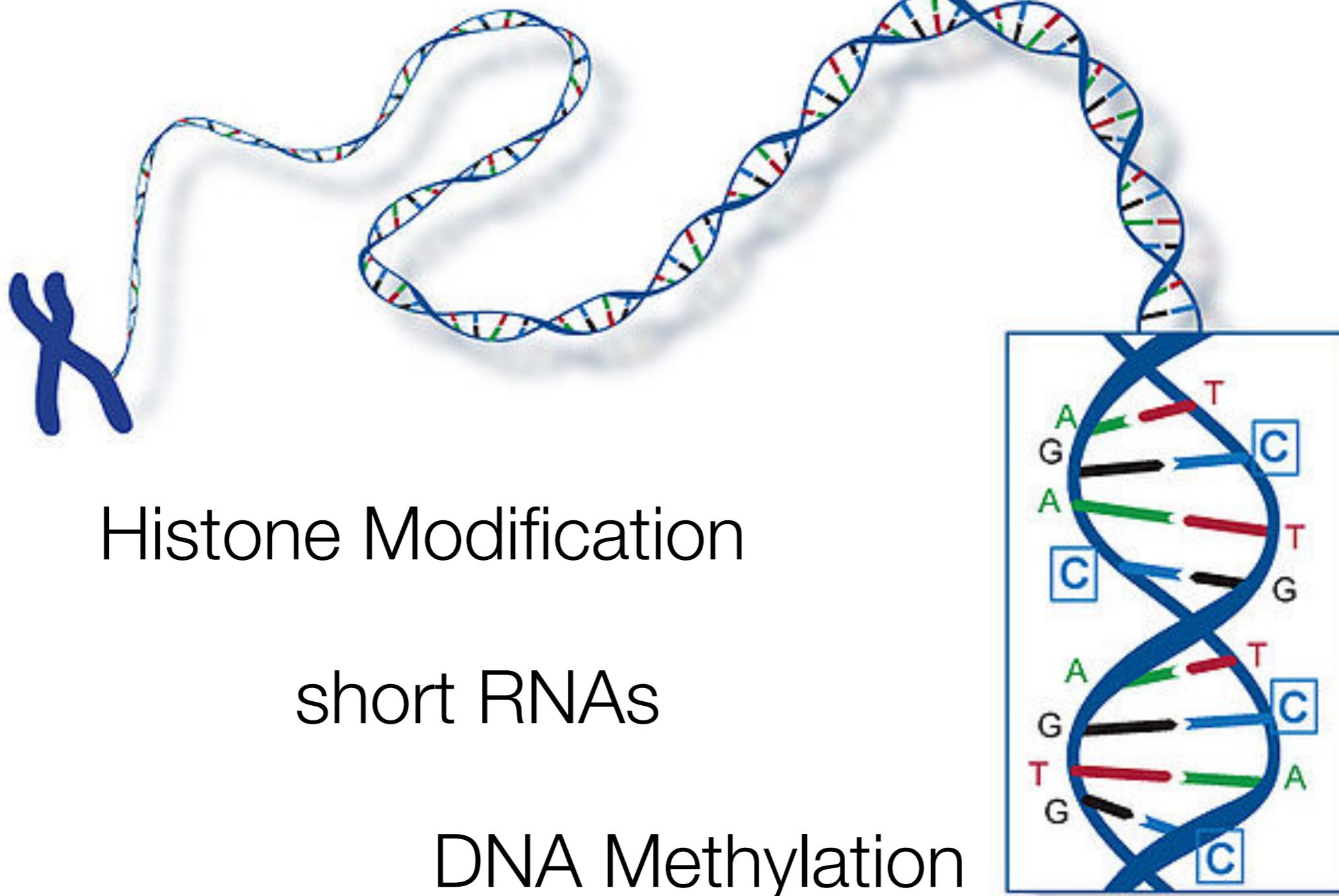
Queen Bee Larvae: Queens are raised in specially constructed cells called "queen cups," which are filled with royal jelly.



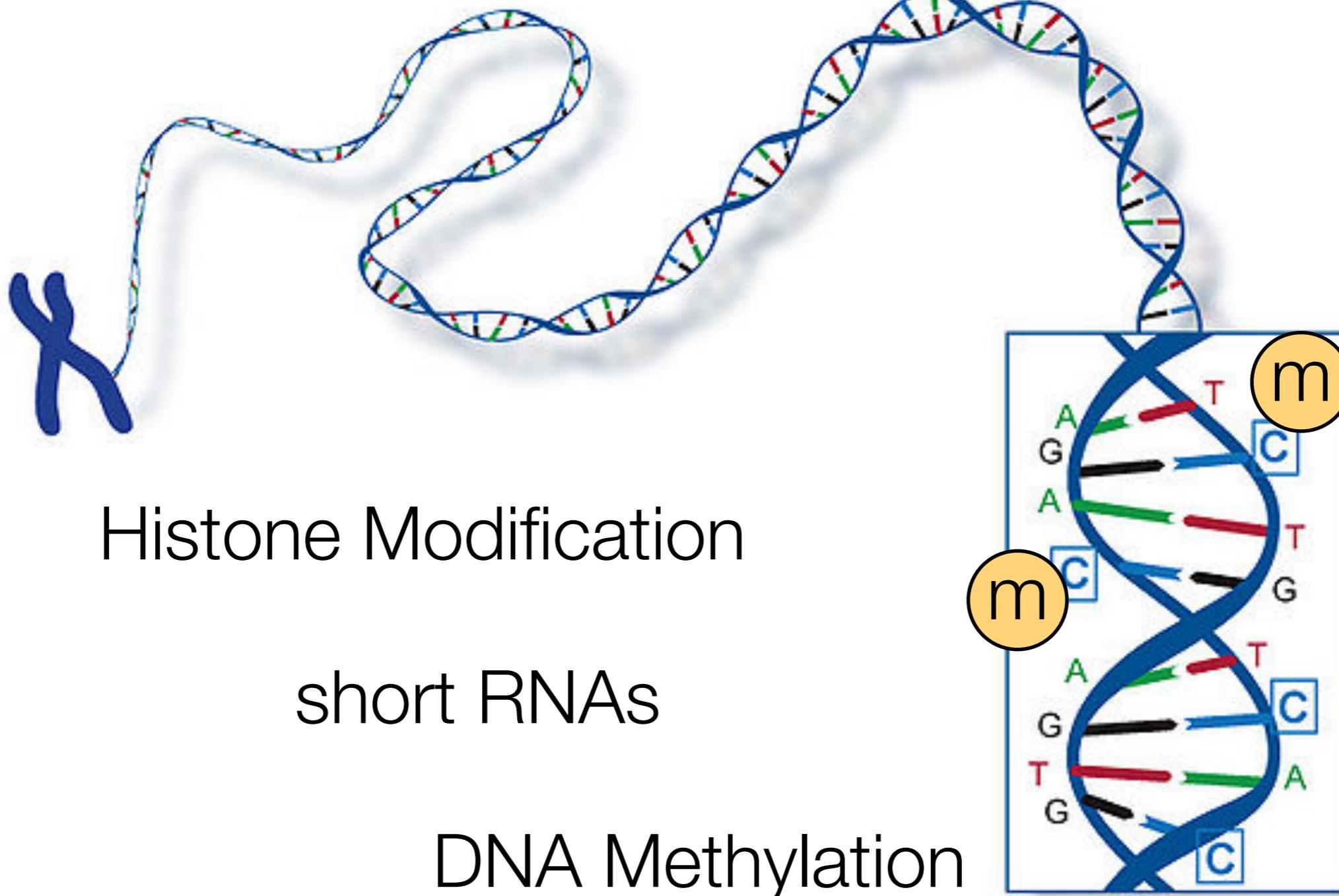
These mothers come from a long line of inbred rats, so their genomes are highly similar. But they care for their pups very differently.

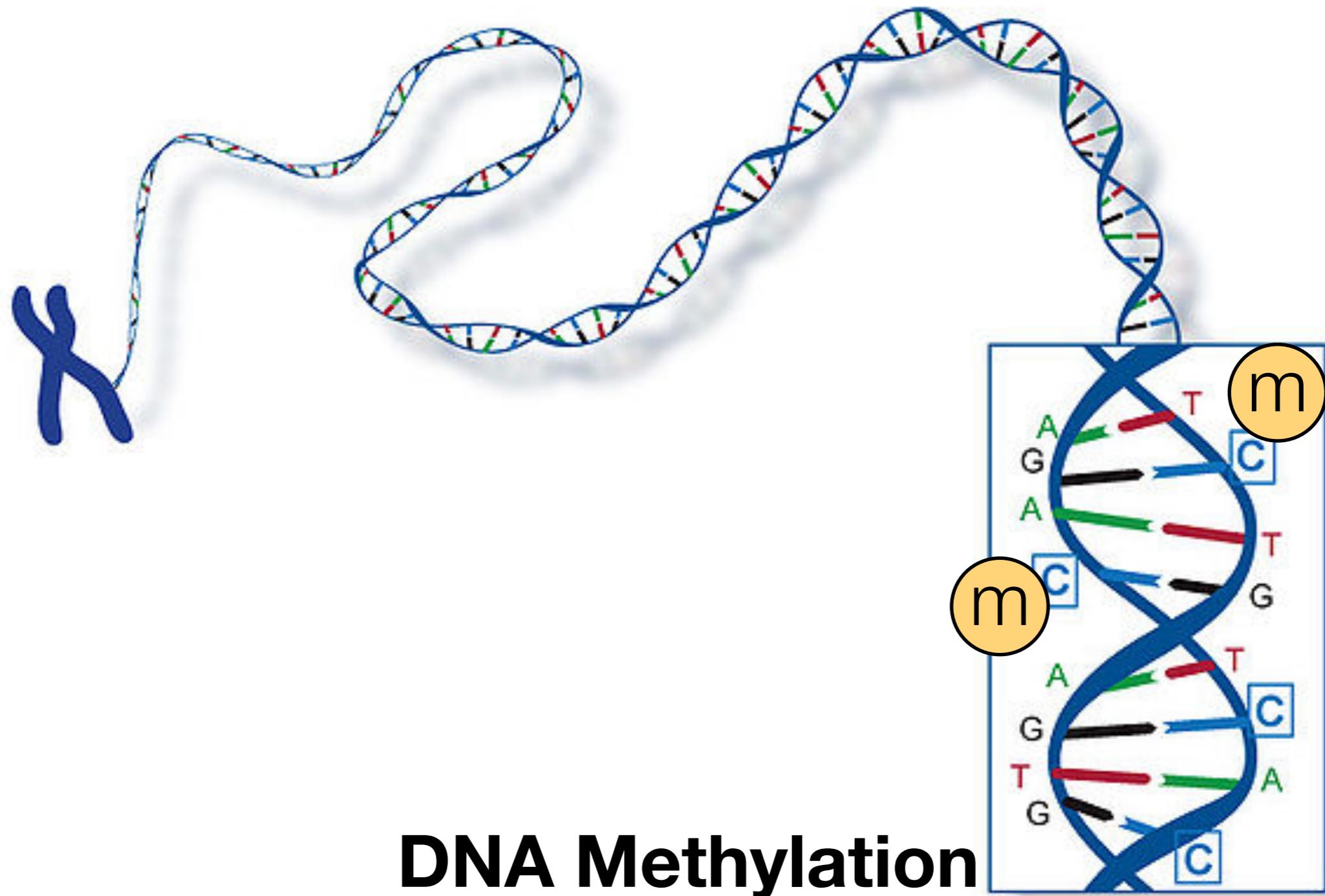
AUDIO

# Epigenetics



# Epigenetics

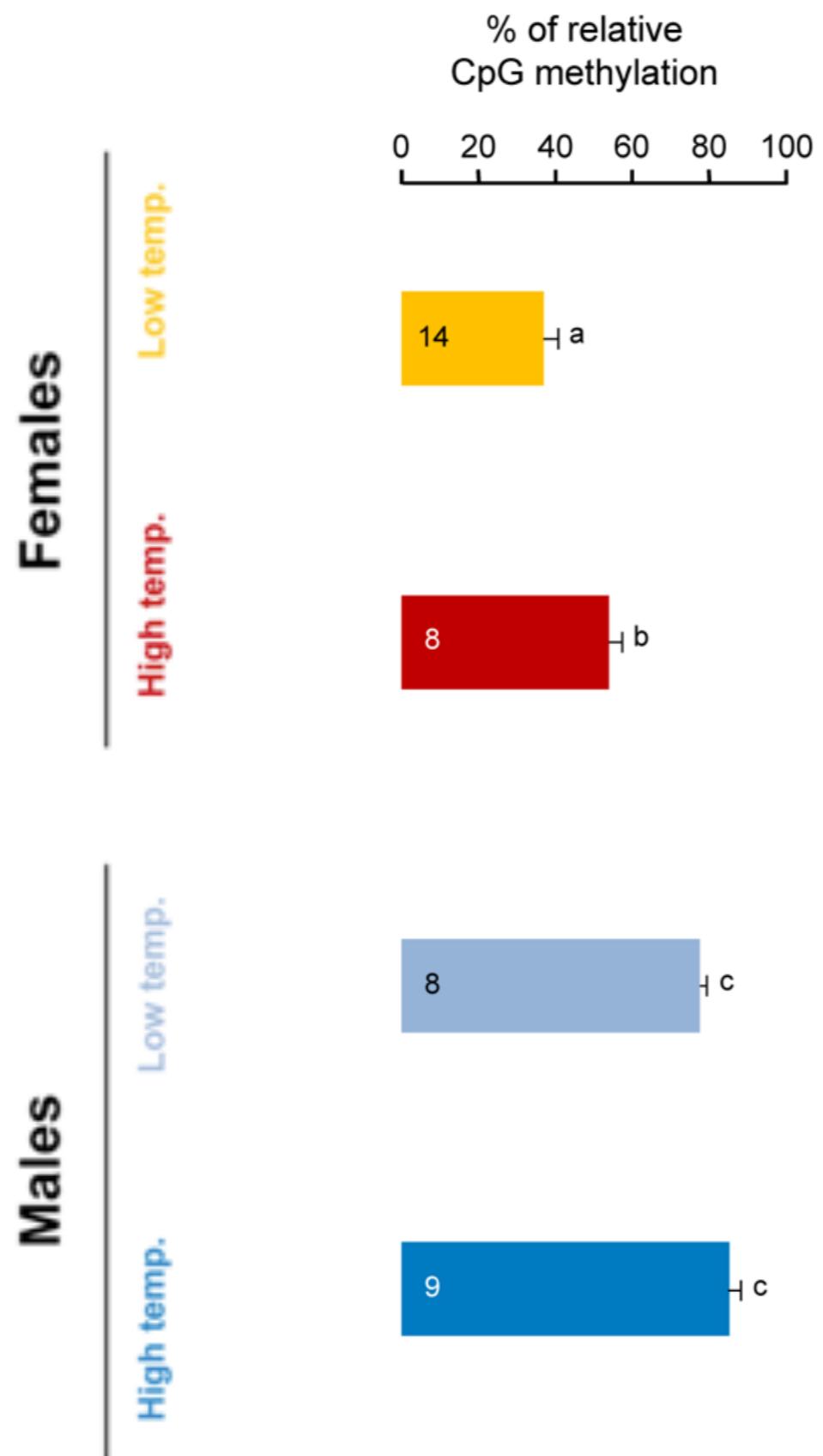




# Function?

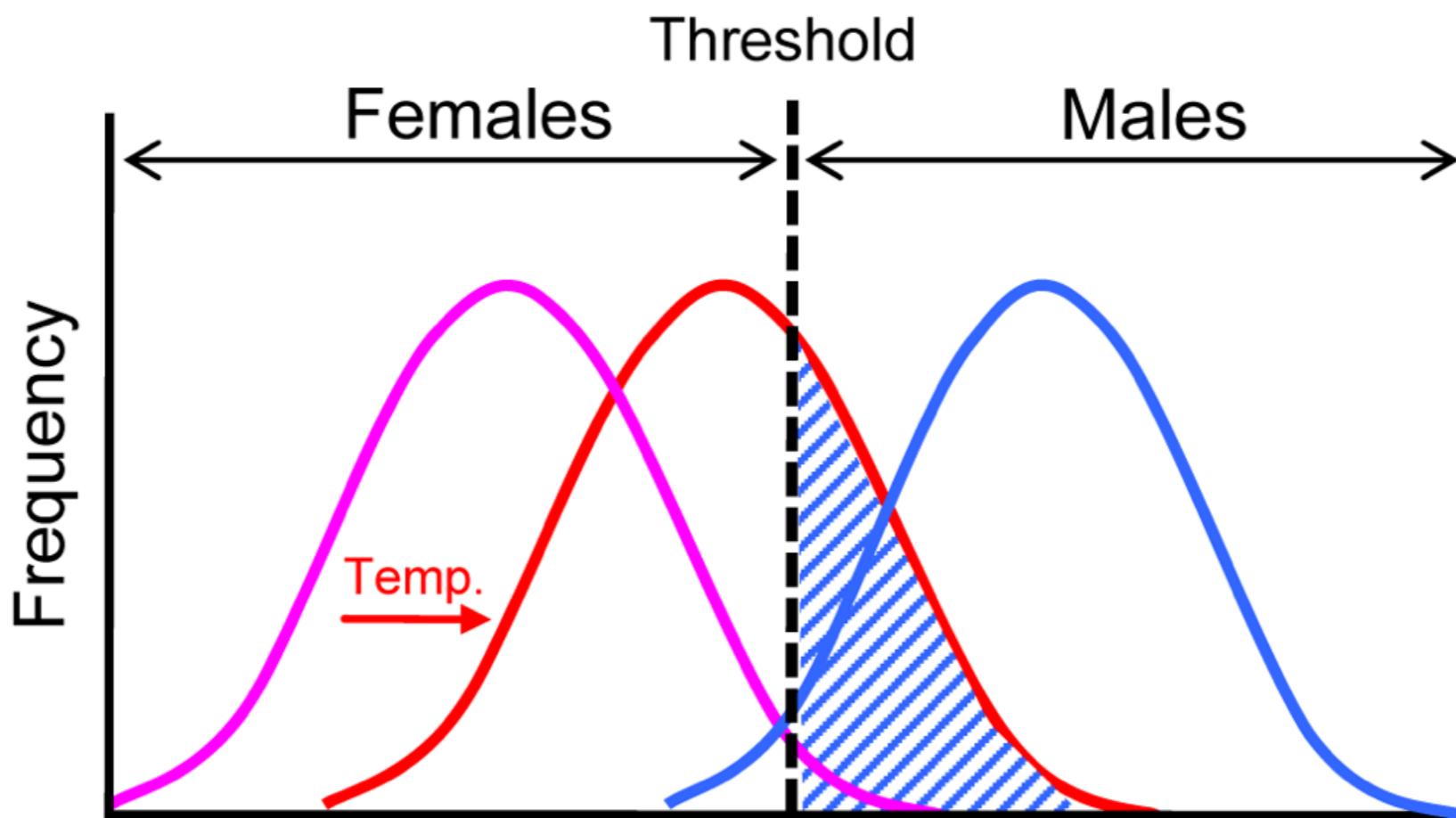
# DNA Methylation of the Gonadal Aromatase (*cyp19a*) Promoter Is Involved in Temperature-Dependent Sex Ratio Shifts in the European Sea Bass

Laia Navarro-Martín, Jordi Viñas, Laia Ribas, Noelia Díaz, Arantxa Gutiérrez, Luciano Di Croce, Francesc Piferrer 



## DNA Methylation of the Gonadal Aromatase (*cyp19a*) Promoter Is Involved in Temperature-Dependent Sex Ratio Shifts in the European Sea Bass

Laia Navarro-Martín, Jordi Viñas, Laia Ribas, Noelia Díaz, Arantxa Gutiérrez, Luciano Di Croce, Francesc Piferrer



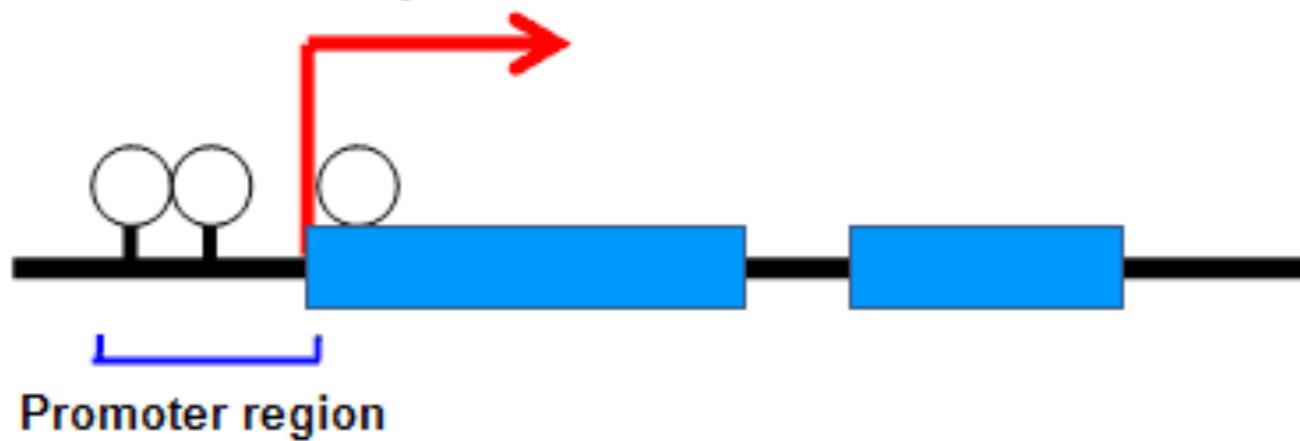
*cyp19a* promoter methylation level

- Low temperature females
- High temperature females
- Males

DNA Methylation of the Gonadal Aromatase (*cyp19a*) Promoter Is Involved in Temperature-Dependent Sex Ratio Shifts in the European Sea Bass

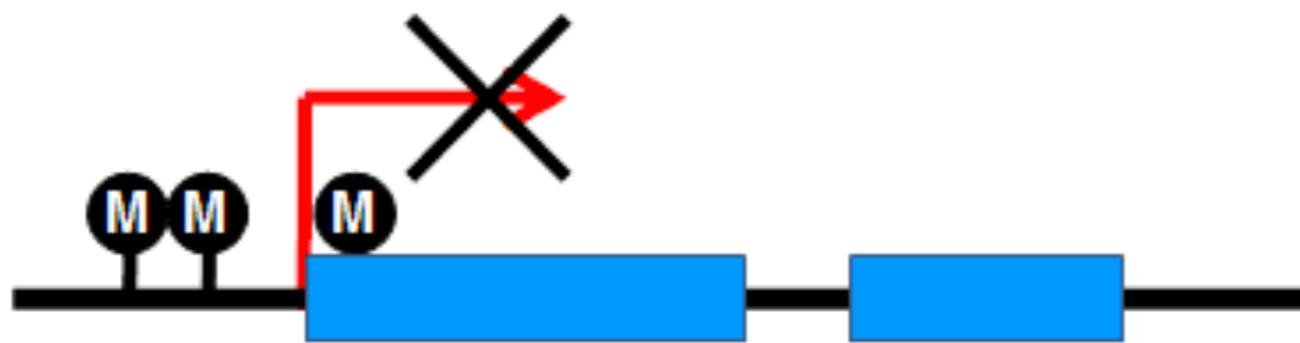
Low temp.

### Genes that can be expressed



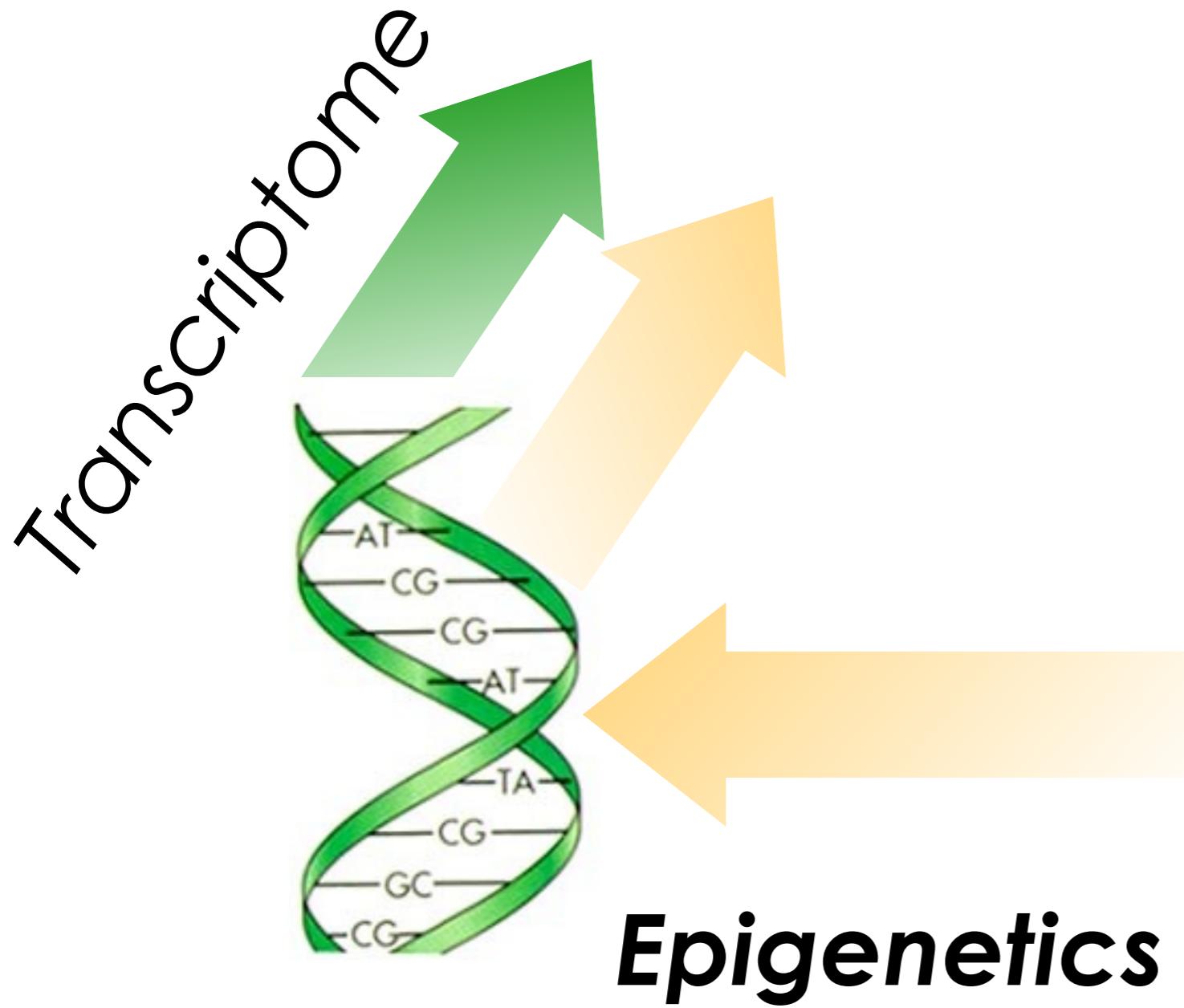
High temp.

### Genes inactivated by DNA methylation



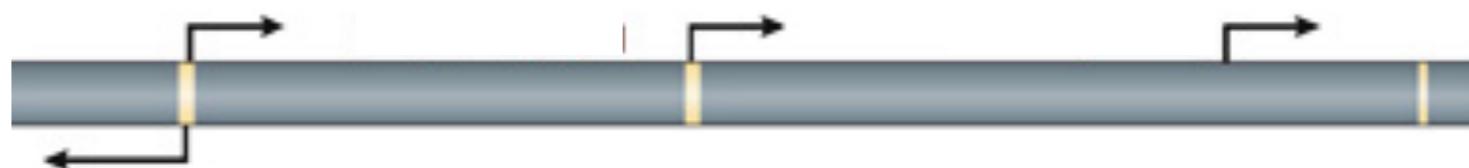
Methylated

Unmethylated



# traditional - vertebrate model

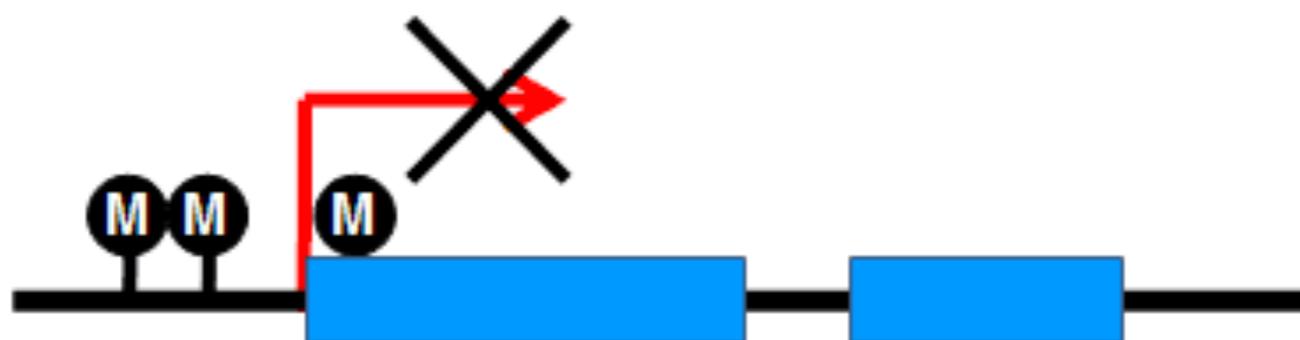
**Global DNA methylation**  
(animals, for example, *Homo sapiens*)



methylation

Nature Reviews Genetics 9, 465-476 (June 2008)

## Genes inactivated by DNA methylation



Methylated

Unmethylated



# Epigenetics: Marine Invertebrates

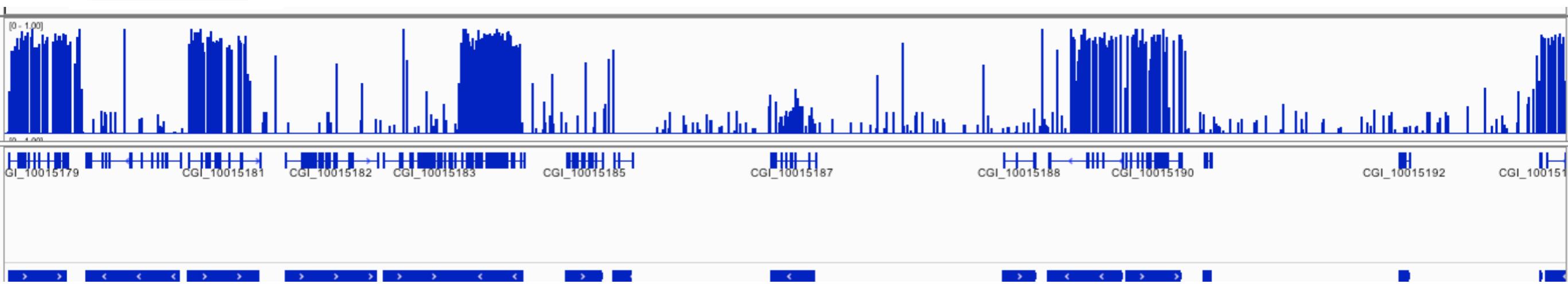
Non-  
Vertebrates?

*Absent in  
several  
model  
organisms*



Shellfish?

Epigenetic variation **1**

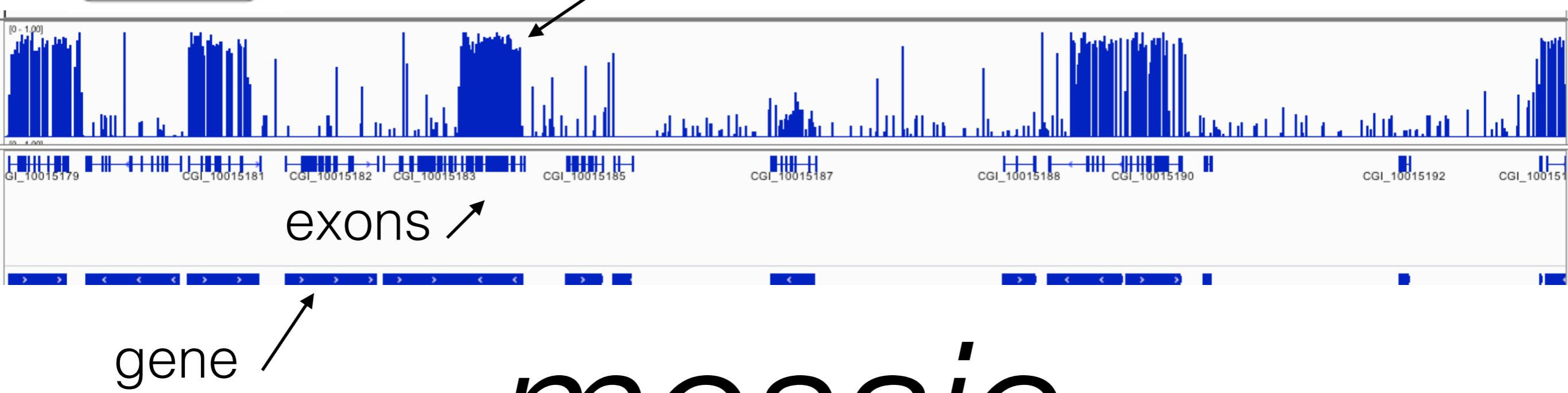


# *mosaic*

associated with gene bodies

Epigenetic variation **1**

DNA methylation level (0-100%) @ cytosines

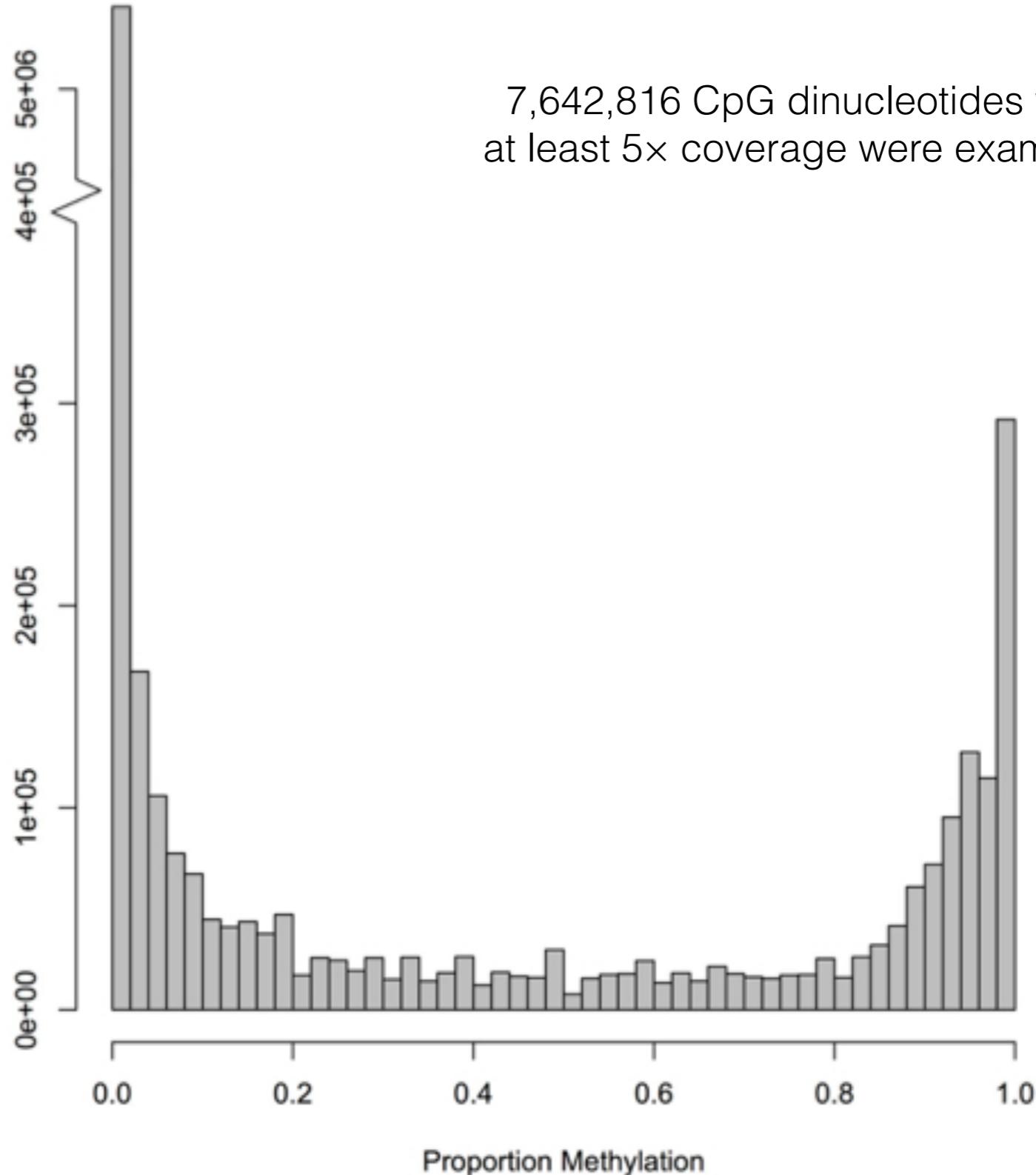
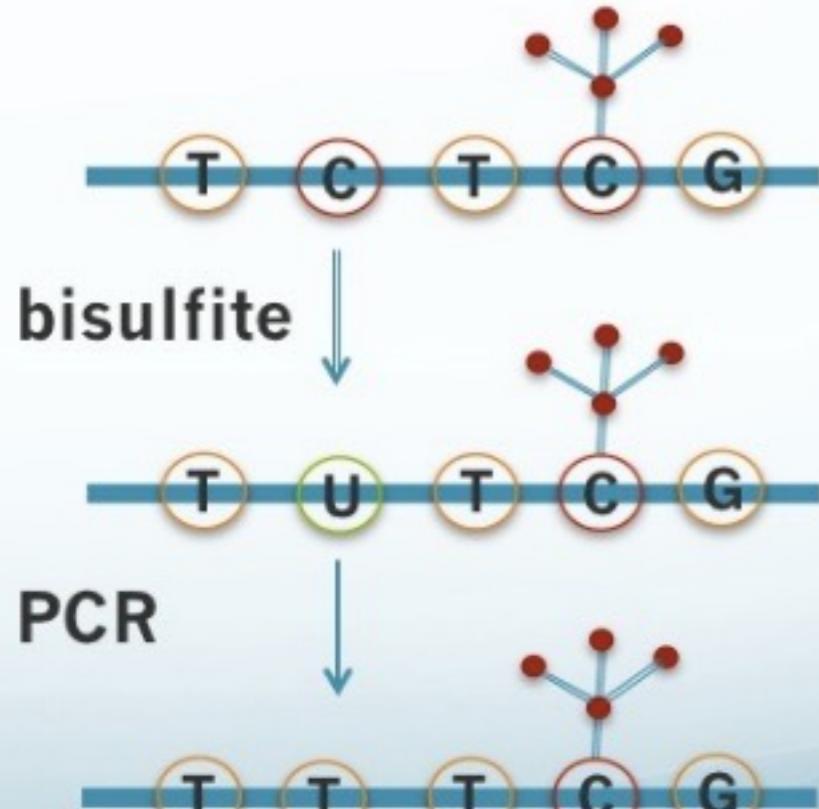


*mosaic*

associated with gene bodies

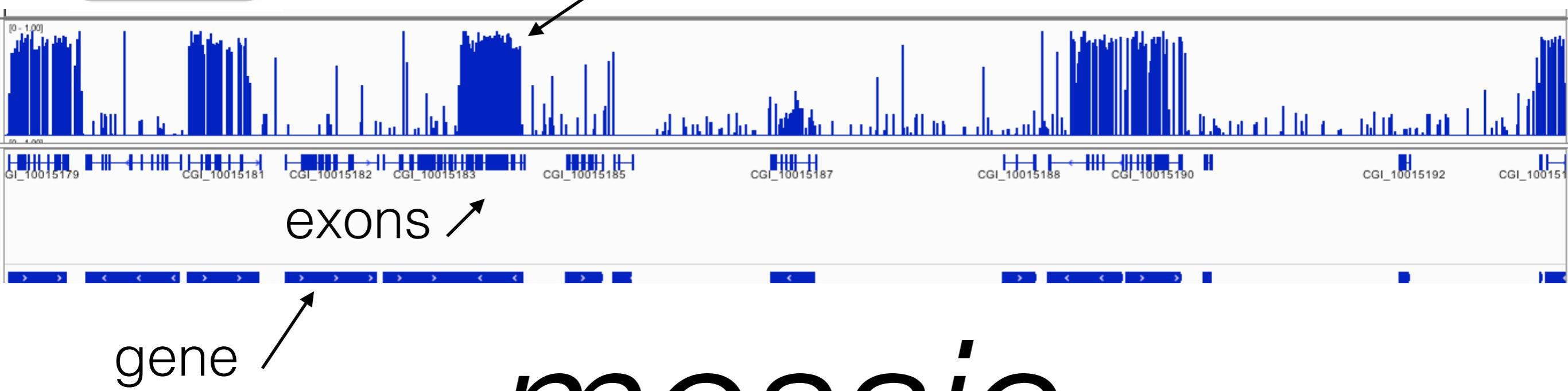
Epigenetic variation **1**

- Bisulfite conversion



Epigenetic variation **1**

DNA methylation level (0-100%) @ cytosines

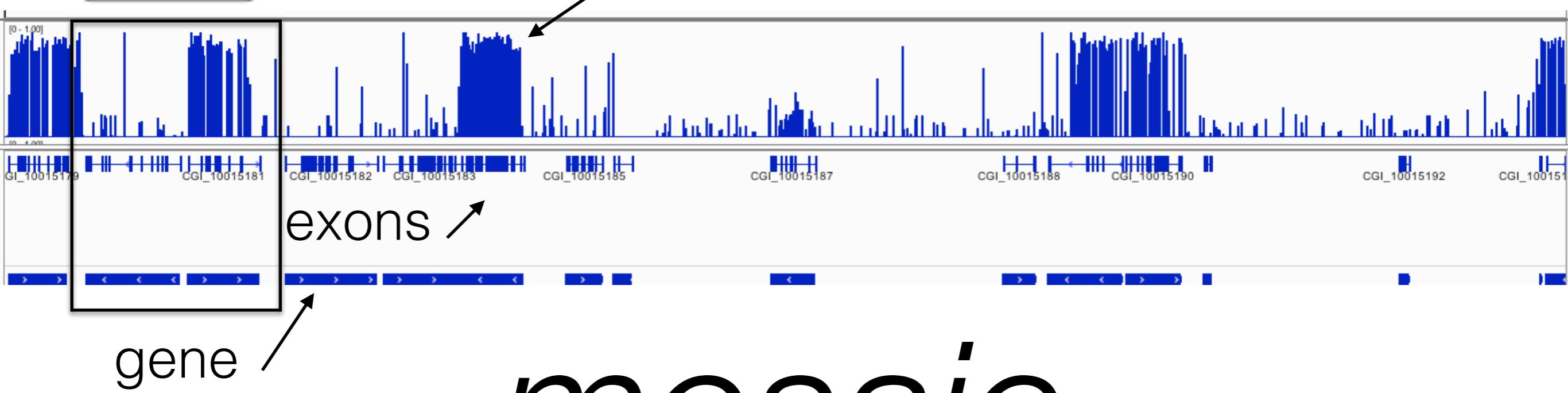


*mosaic*

associated with gene bodies

Epigenetic variation **1**

DNA methylation level (0-100%) @ cytosines

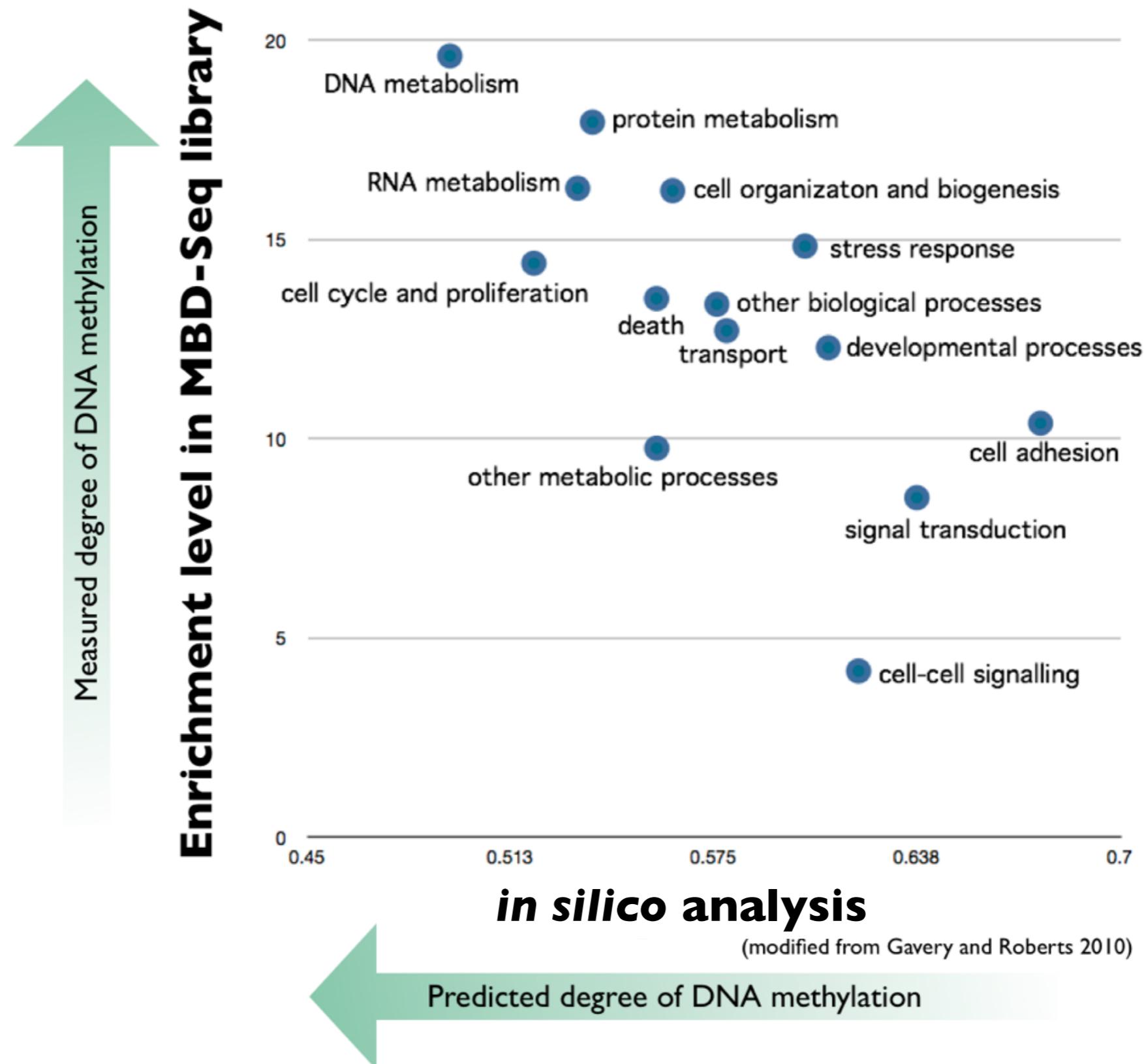


*mosaic*

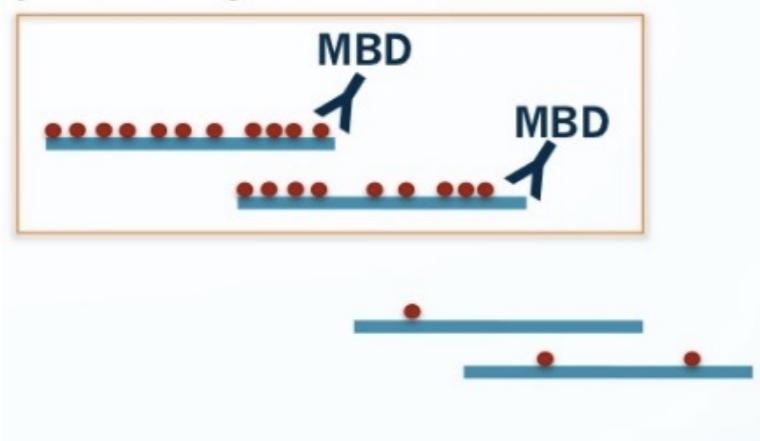
**Why are only a subset of genes methylated?**

associated with gene bodies

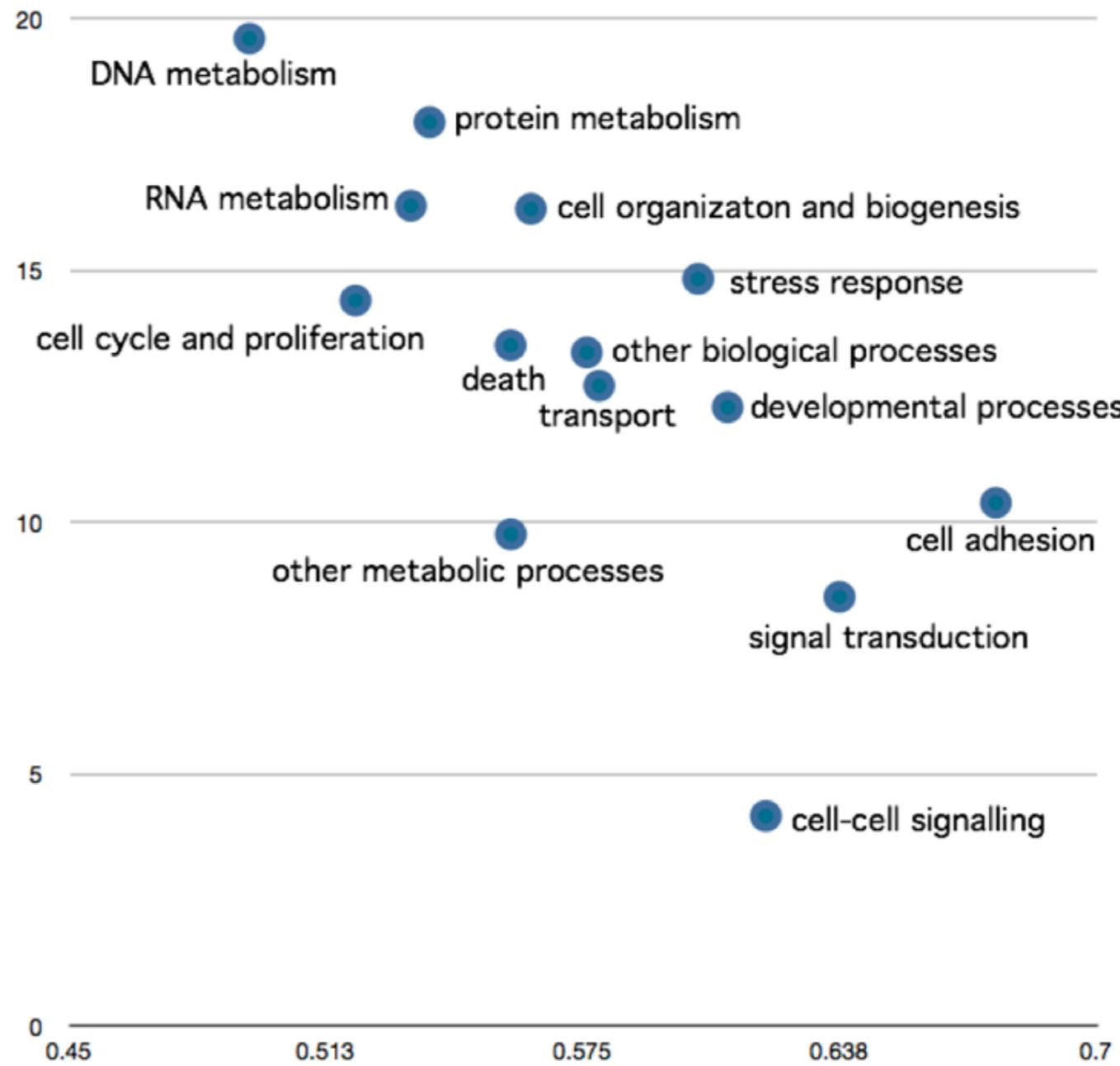
Epigenetic variation **1**



## Epigenetic variation 1



### Enrichment level in MBD-Seq library

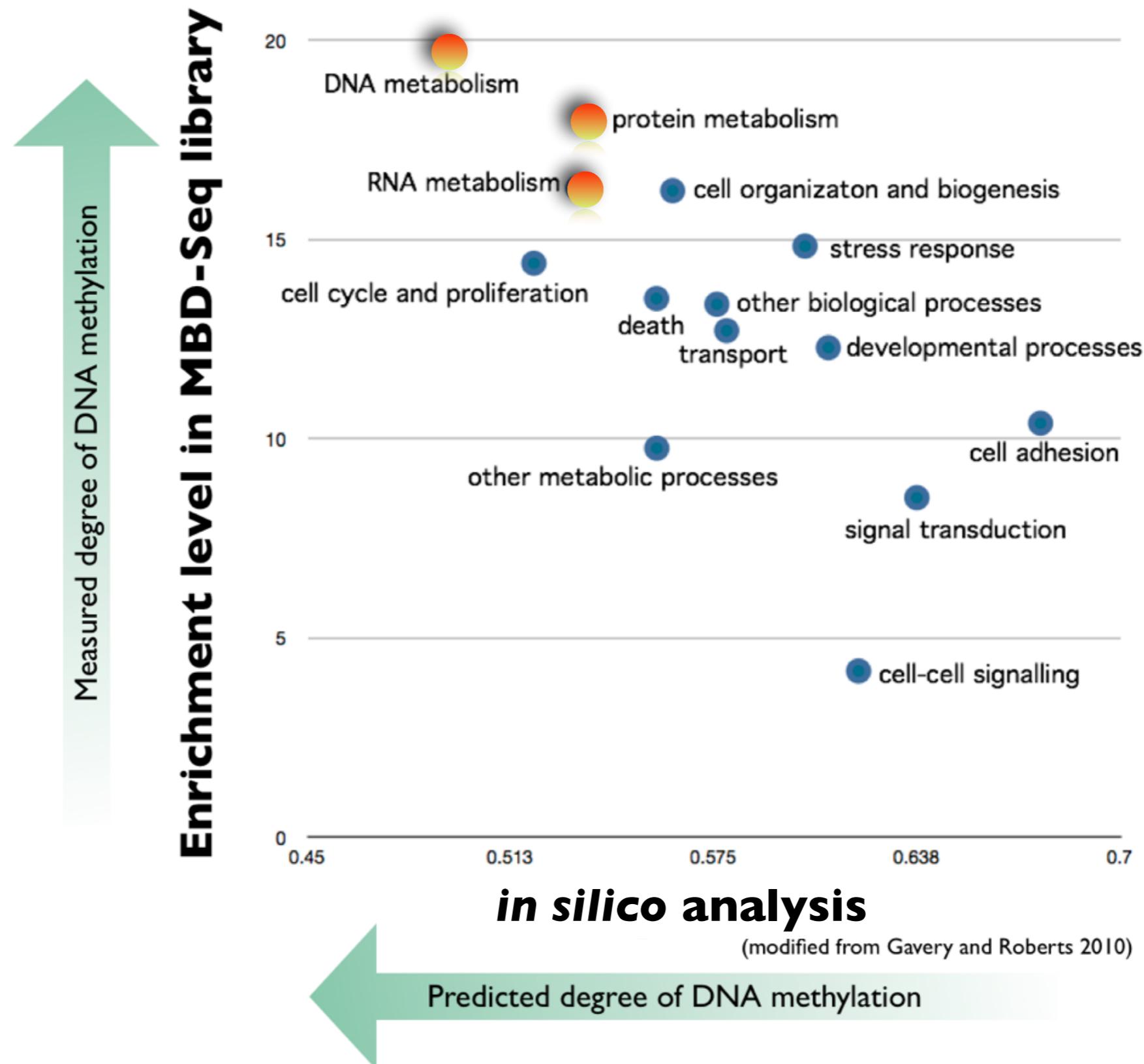


### *in silico* analysis

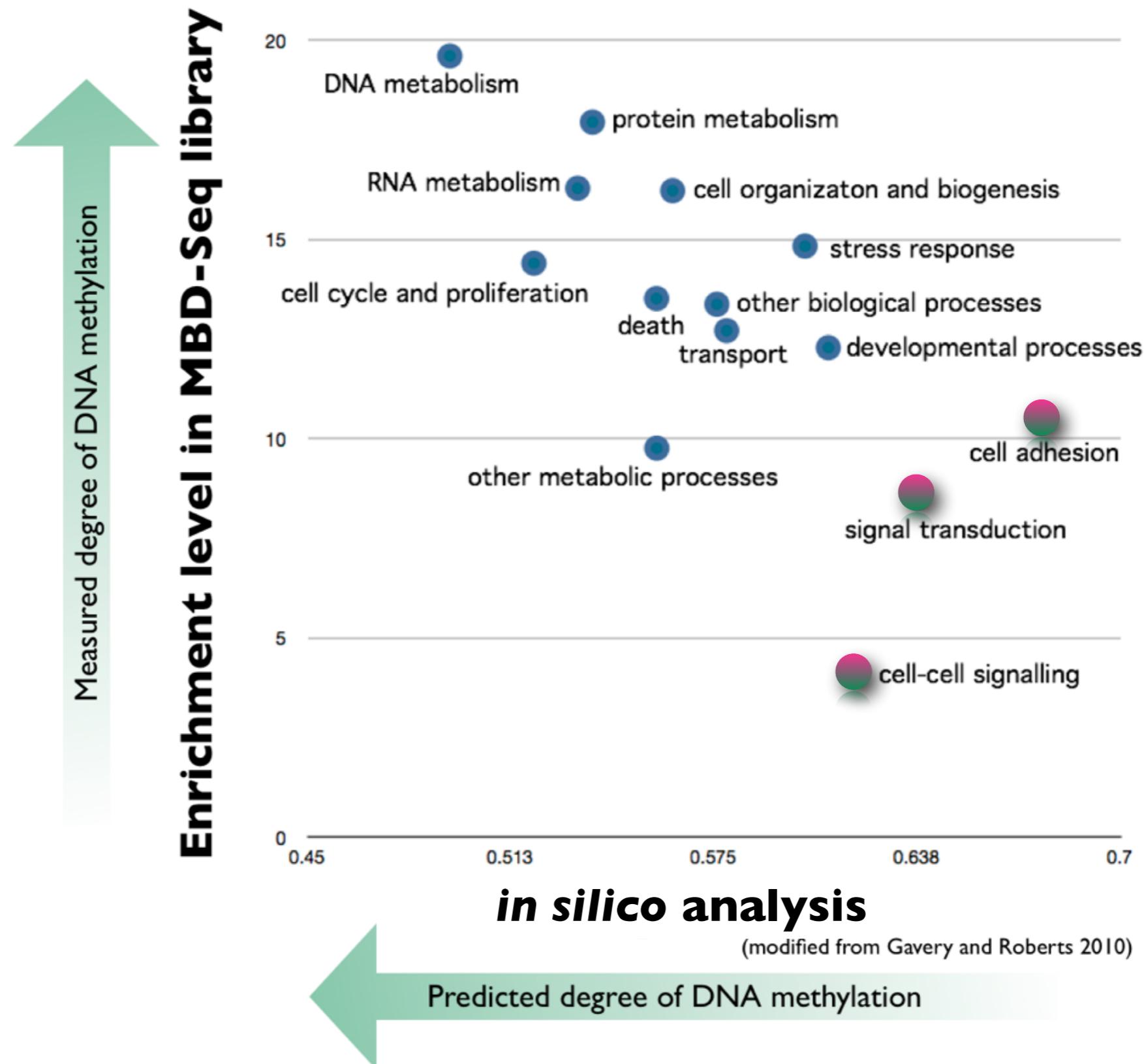
(modified from Gavery and Roberts 2010)

Predicted degree of DNA methylation

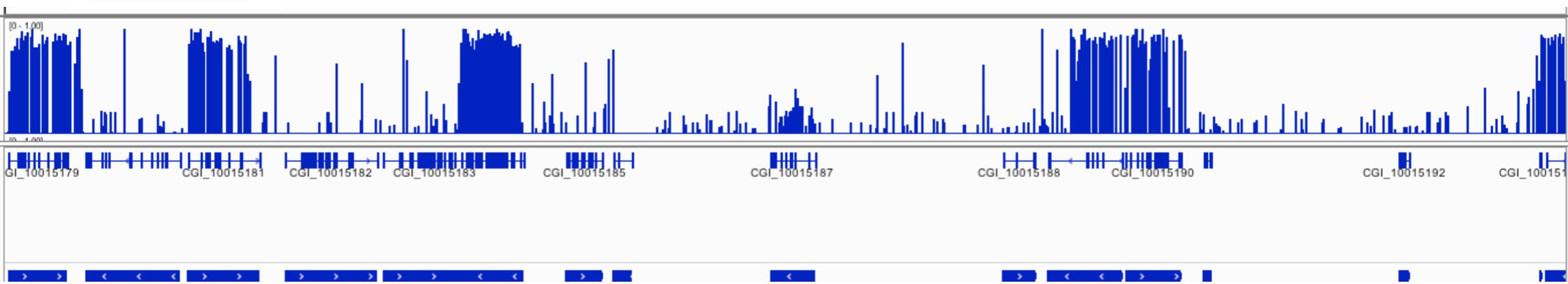
Epigenetic variation **1**



Epigenetic variation **1**



Epigenetic variation **1**



# *mosaic*

associated with gene bodies  
based on gene function

*explanation?*

- Sparsely (~16 %), mosaic methylated genome
- Gene body methylation correlated with function
- DNA methylation patterns are inherited
- DMRs are predominant in transposable elements

# DNA Methylation Function in Marine Invertebrates

Gene  
expression



Epigenetic  
variation

# Function?



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



## *in silico analysis*

(modified from Gavery and Roberts 2010)

Predicted degree of DNA methylation

Roberts and Gavery 2012

Gene expression



Epigenetic variation

cell adhesion

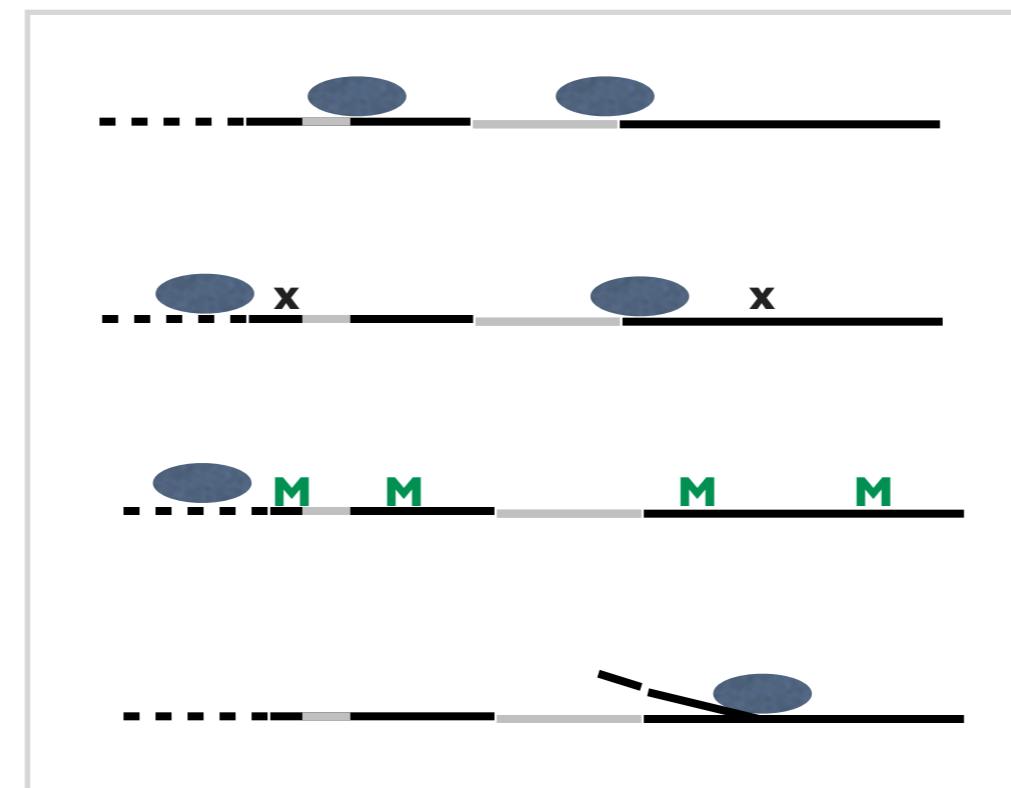
signal transduction

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

promoter exon intron exon



Gene  
expression



Epigenetic  
variation

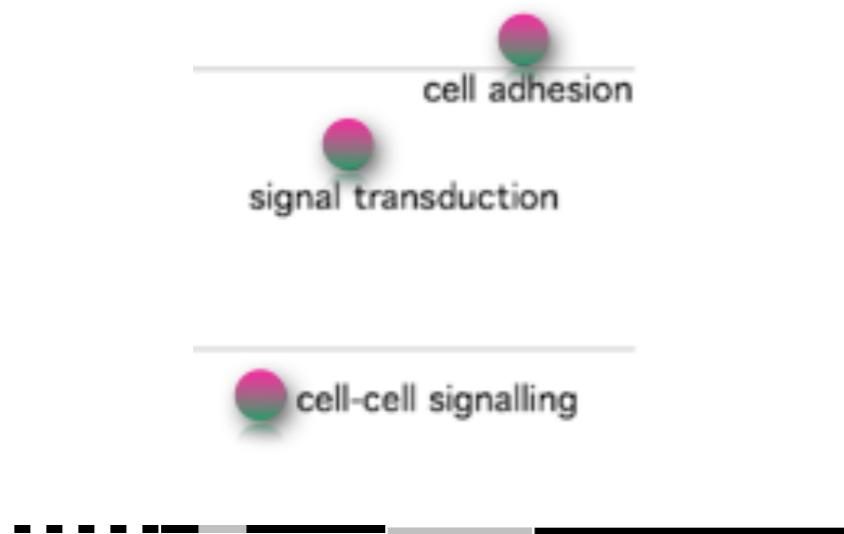
transcript



Gene expression

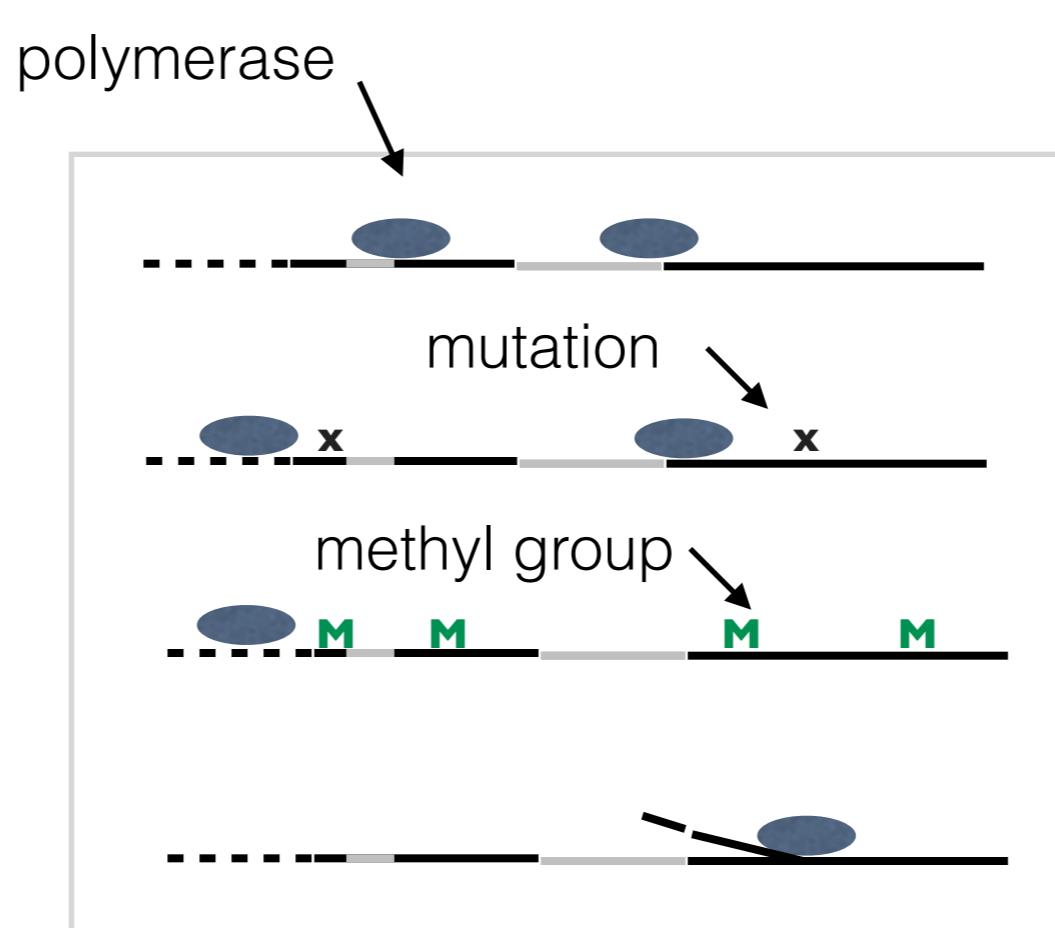
2

Epigenetic variation



## sparse methylation

*tissue / temporal specific and inducible genes*



Gene expression



Epigenetic variation

## Transcriptional opportunities



**germline methylation**

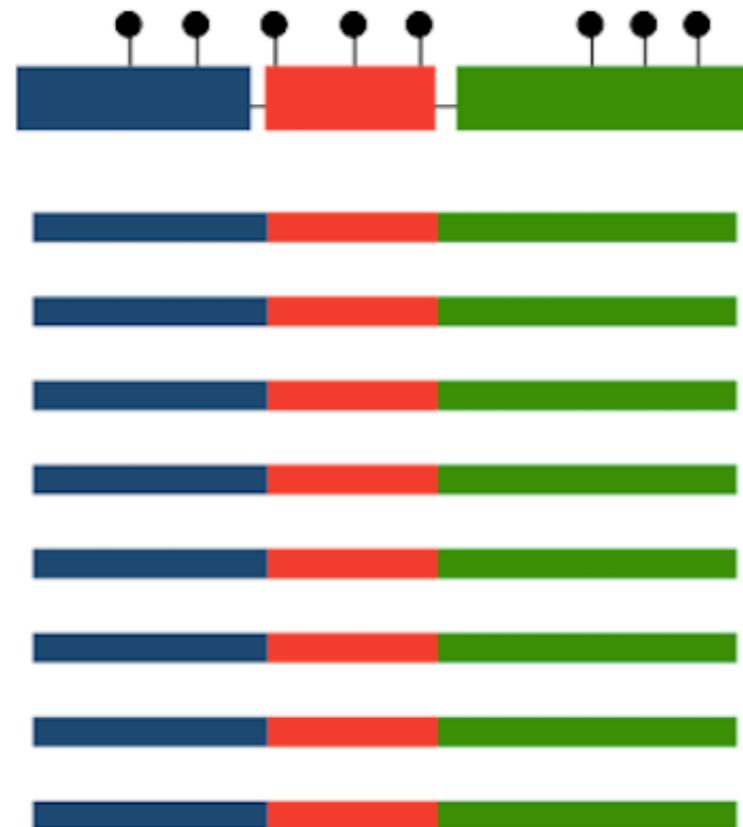
*ubiquitously expressed,  
critical genes*

methyl group

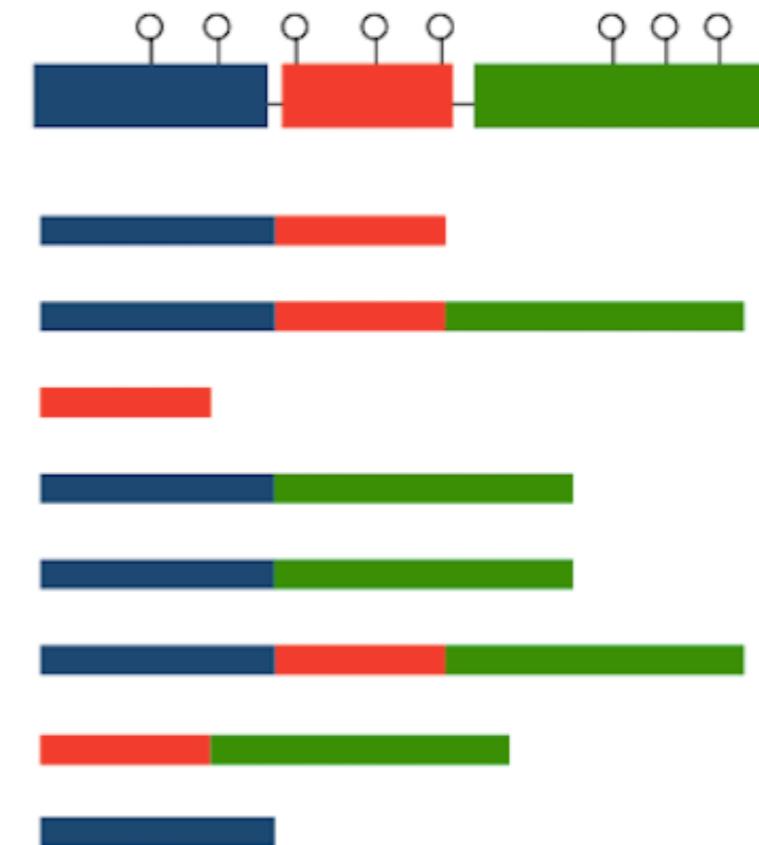


conventional transcription  
5' UTR promotor

transcript



housekeeping



response to  
change

# A context dependent role for DNA methylation in bivalves

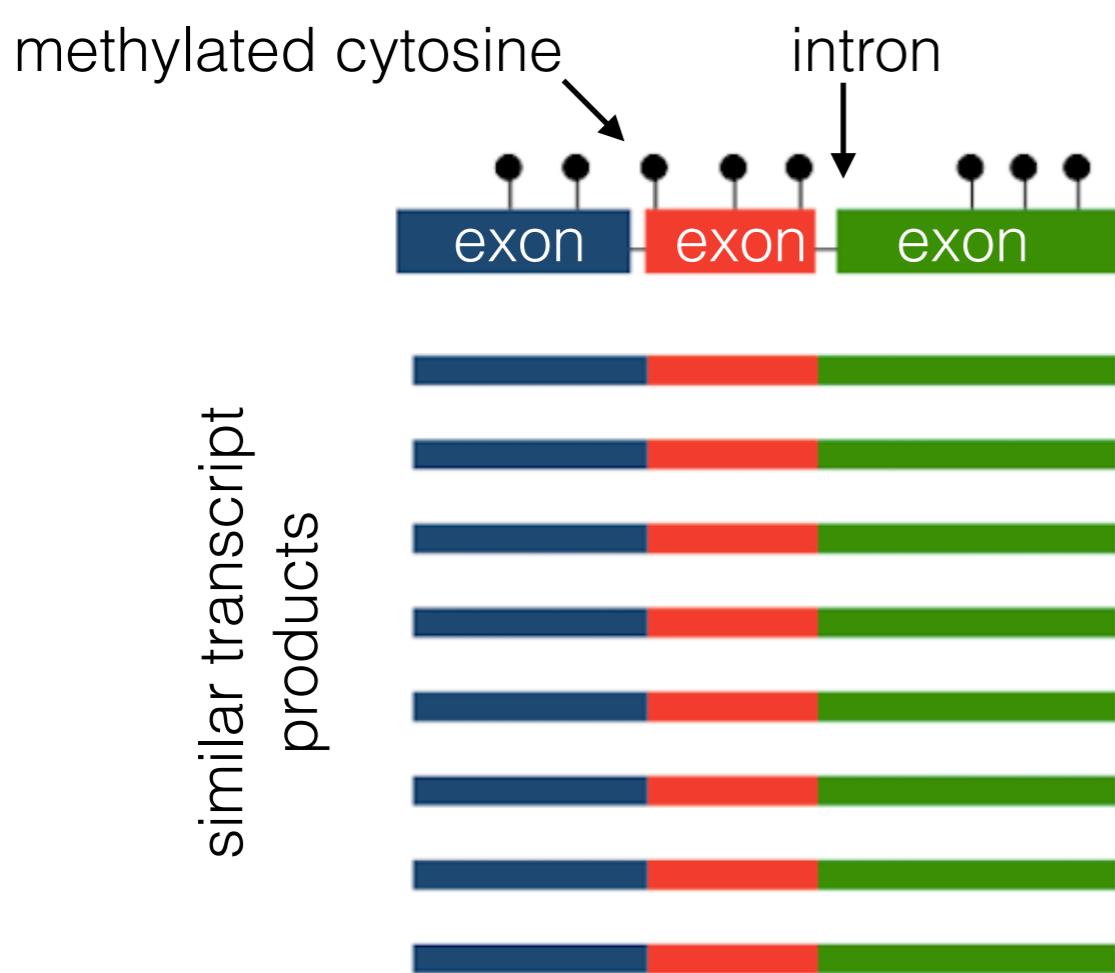
Mackenzie R. Gavery and Steven B. Roberts

Advance Access publication date 7 January 2014

# Stochastic Variation

**A context dependent role for DNA methylation in bivalves**

Mackenzie R. Gavery and Steven B. Roberts  
Advance Access publication date 7 January 2014



housekeeping

similar transcripts  
products

un-methylated cytosine

alternative transcripts  
products

response to  
change

Gene  
expression

2

Epigenetic  
variation

unmethylated



inducible



disease

temperature

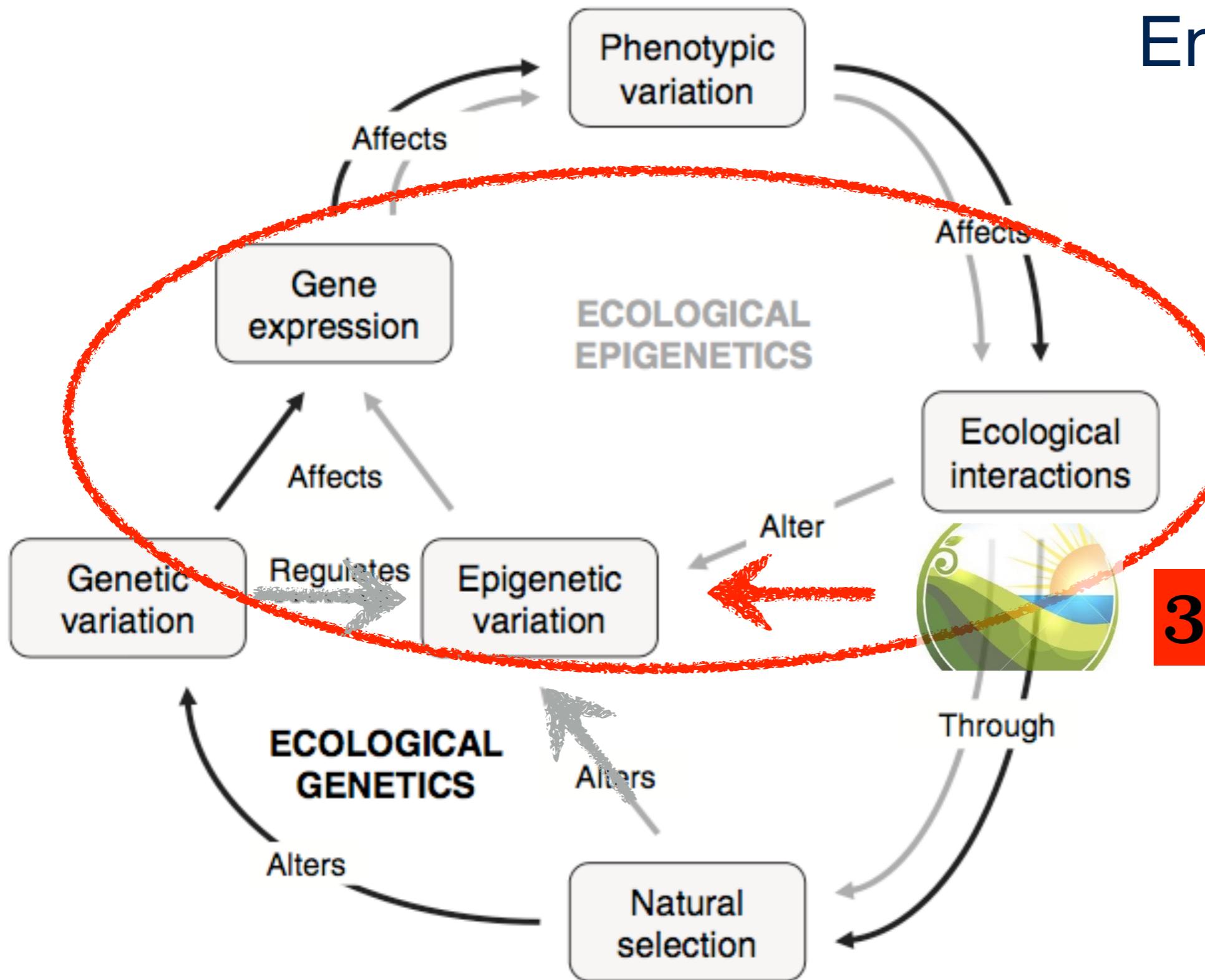
desiccation

salinity

Mackenzie Gavery



# Environmental Influence



3

*Ecology Letters*, (2008) 11: 106–115

doi: 10.1111/j.1461-0248.2007.01130.x

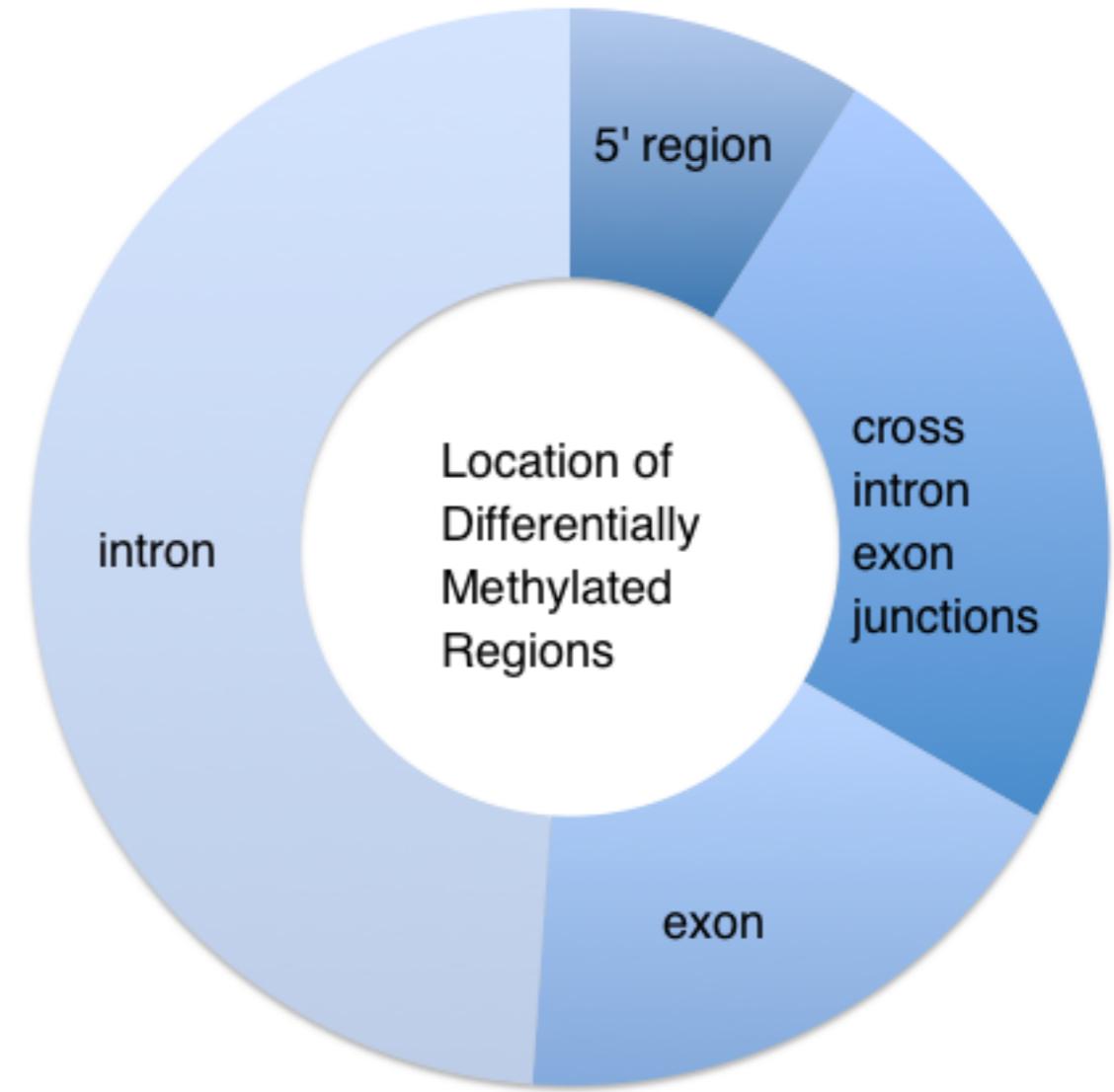
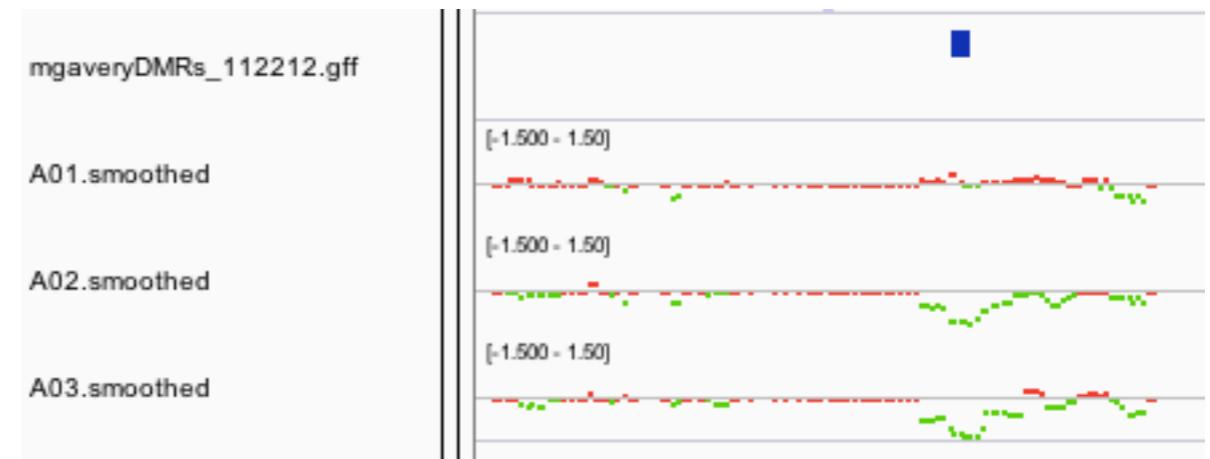
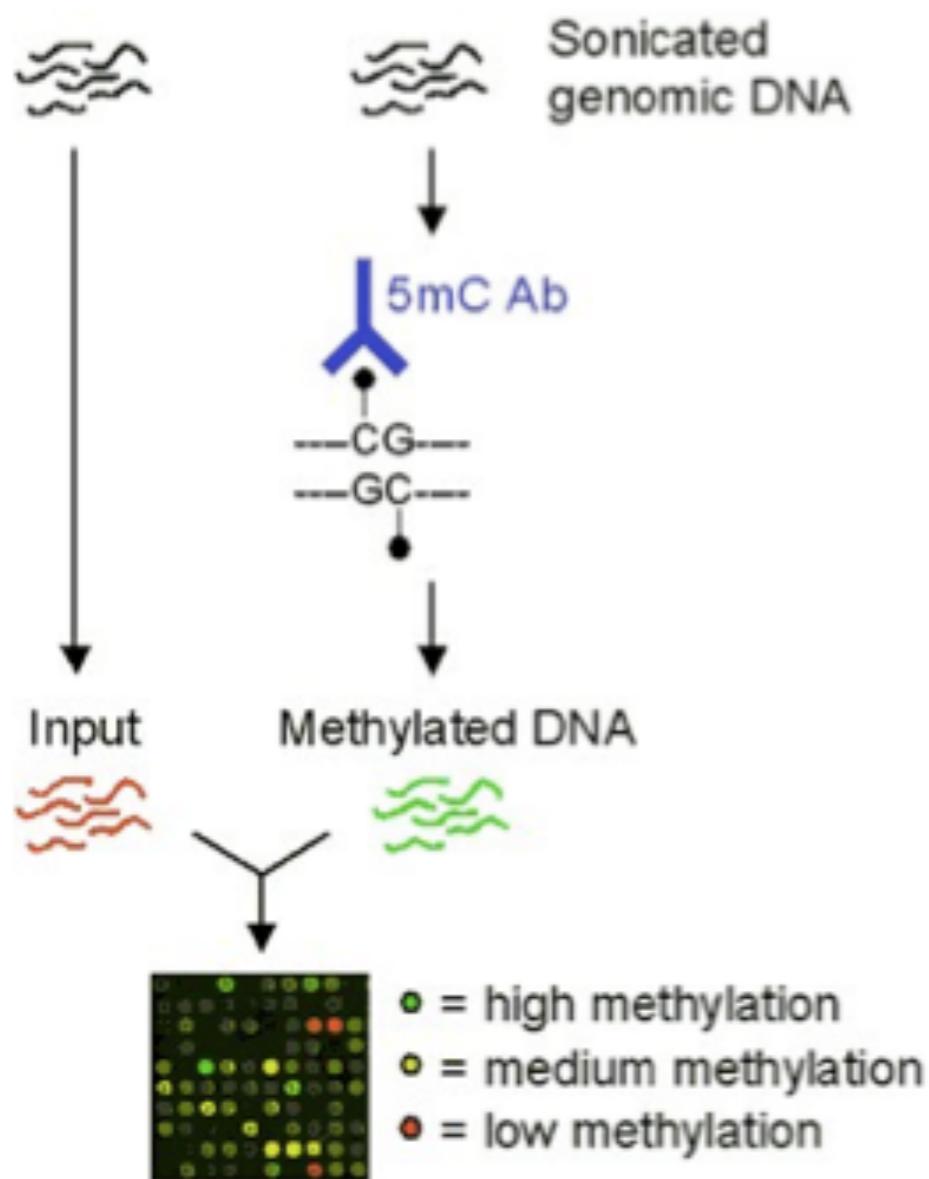
modified from

IDEA AND  
PERSPECTIVE

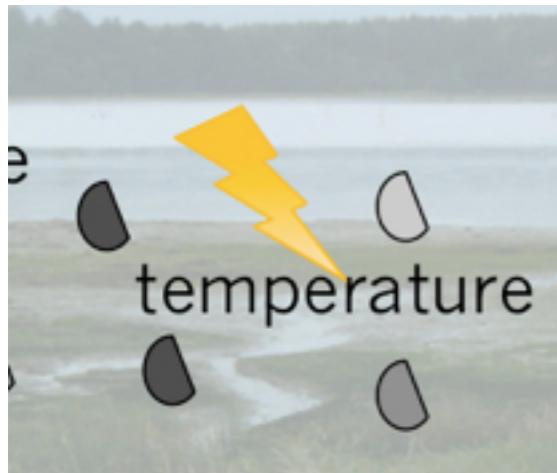
Epigenetics for ecologists

Oliver Bossdorf,<sup>1,\*</sup> Christina L.  
Richards<sup>2</sup> and Massimo Pigliucci<sup>3</sup>

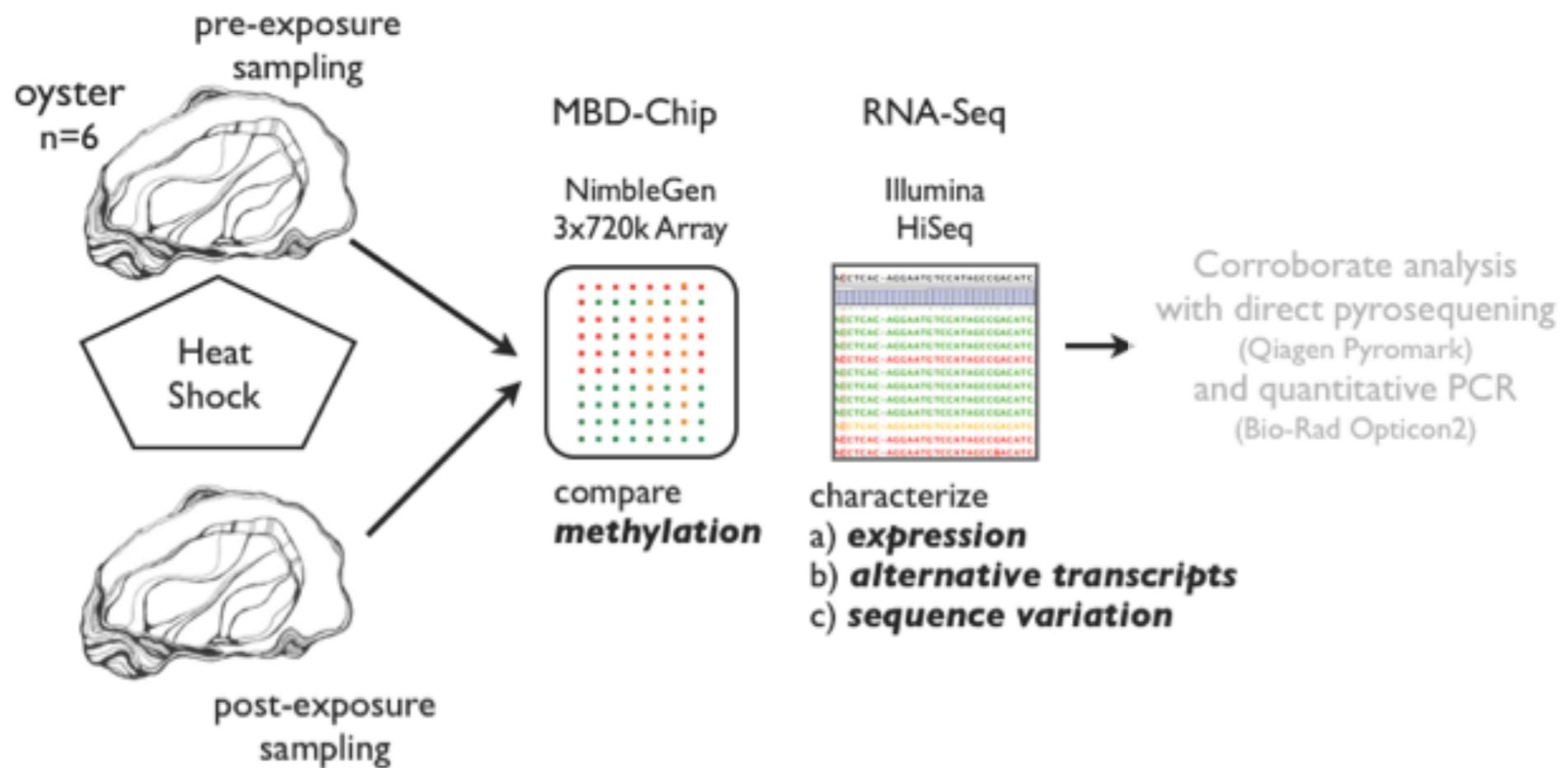
# Environmental impact (Estrogens)



# Environment and gene expression



*stochastic or targeted?*



# Take Home

*Oyster genome has a fantastic degree of diversity contributing to phenotypic plasticity & adaptation potential.*

# Take Home

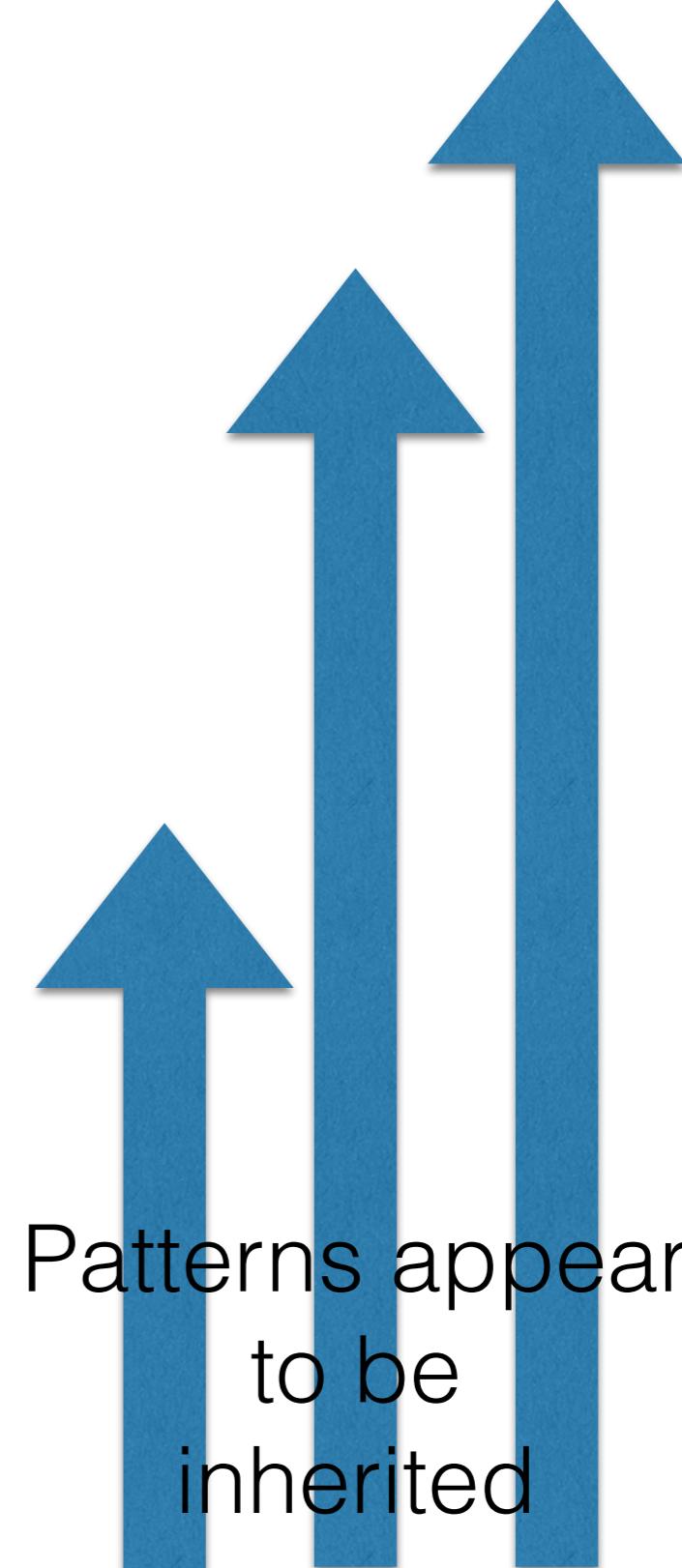
*Oyster genome has a fantastic degree of diversity contributing to phenotypic plasticity & adaptation potential.*

- large gene families
- very high mutation rate (snp/50bp)
- numerous exons per gene (potential for alternatives)
- genome full of repeats region
- high number of transposable elements
- lack of methylation of transposable suggest mobility
- family variation of methylation
- limited methylation environmental response genes  
is associated with spurious transcription
- inheritance of epigenetic marks as mechanism of improved adaptation

# Considerations



Environmental perturbation  
impacts DNA methylation  
(predominantly demethylation)

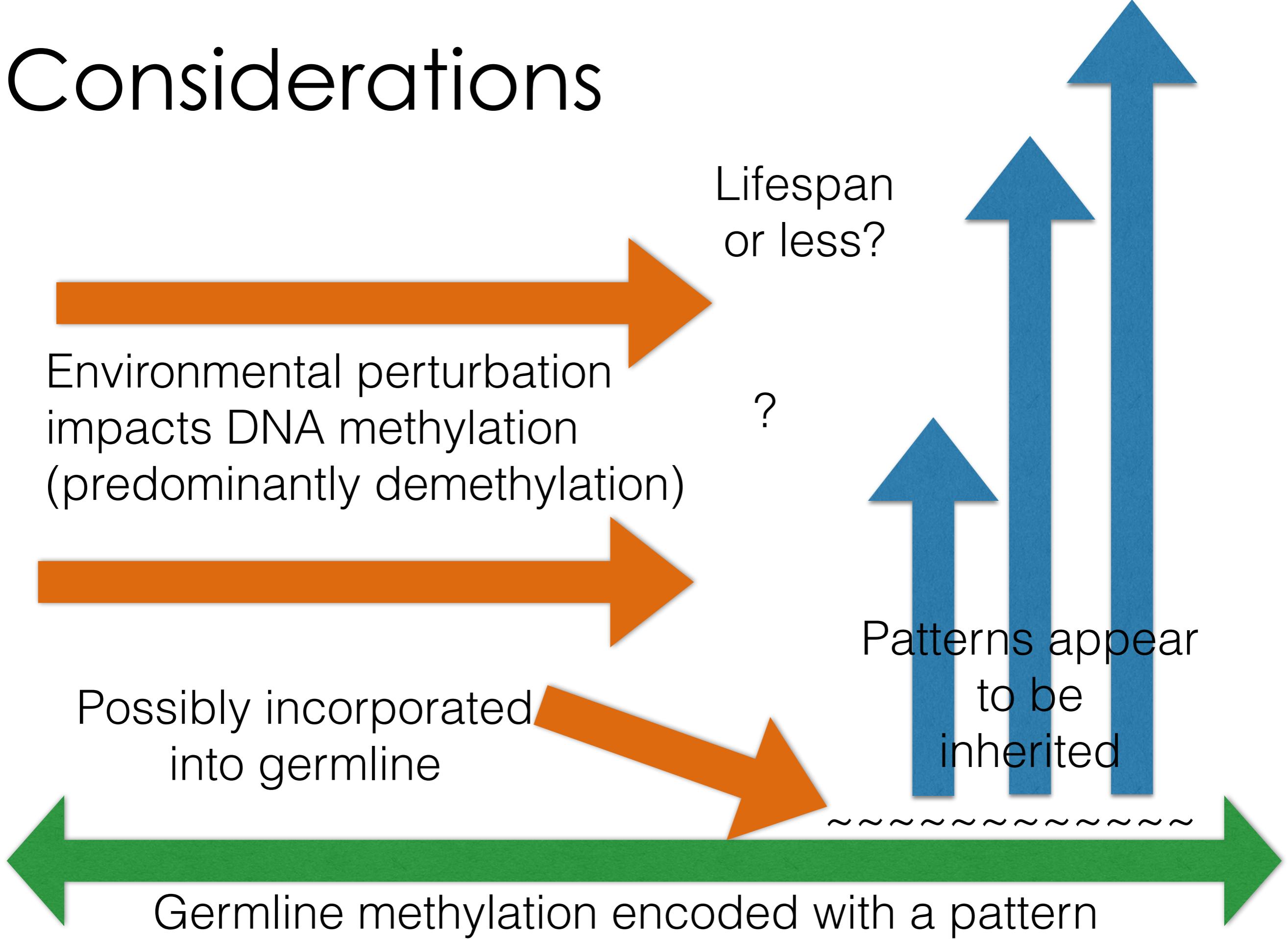


Patterns appear  
to be  
inherited



Germline methylation encoded with a pattern  
product of evolutionary forces

# Considerations



# Considerations:

Could this provide a “memory”  
for subsequent exposure?



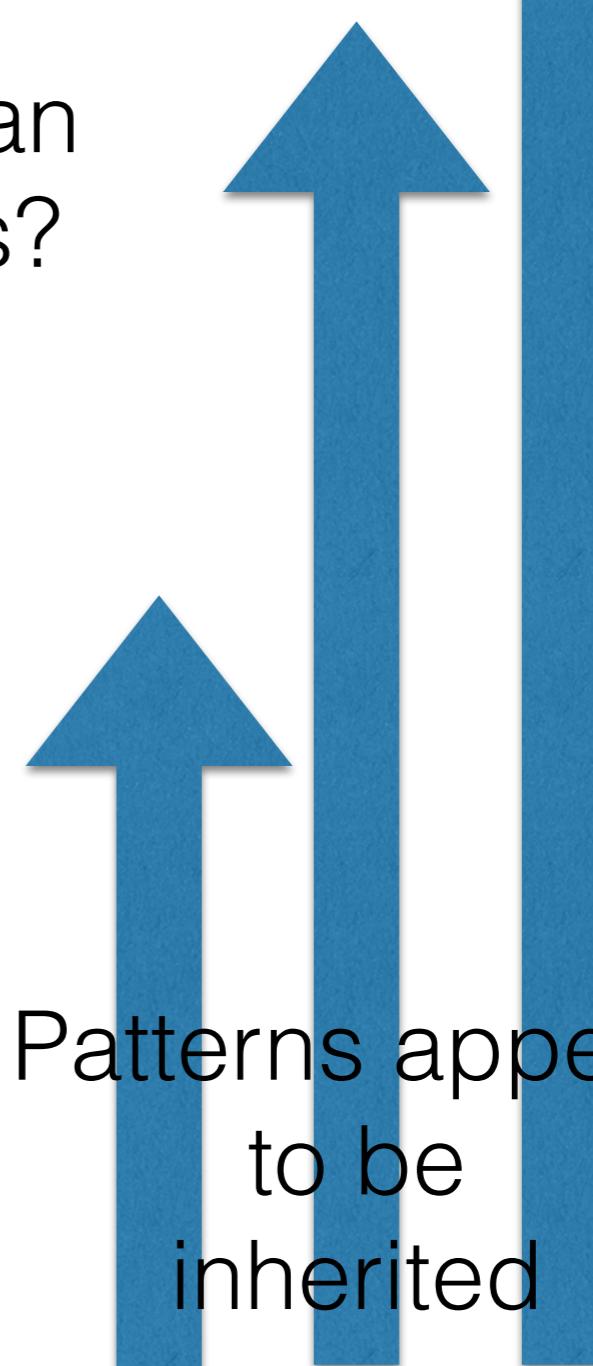
Environmental perturbation  
impacts DNA methylation  
(predominantly demethylation)



**Possibly incorporated  
into germline**



Lifespan  
or less?



Patterns appear  
to be  
inherited

Transgenerational  
Impact

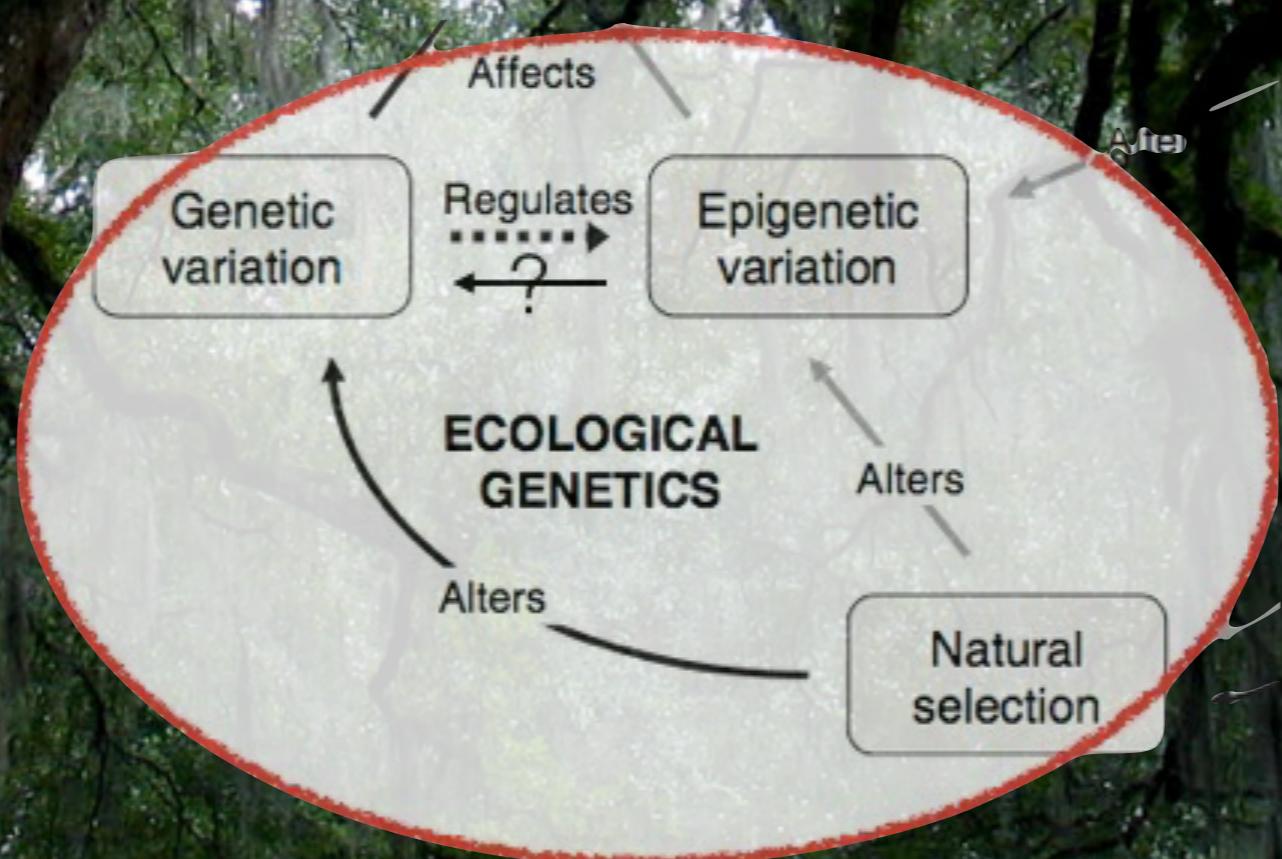


Photo credit: Flickr, Creative Commons, csessums