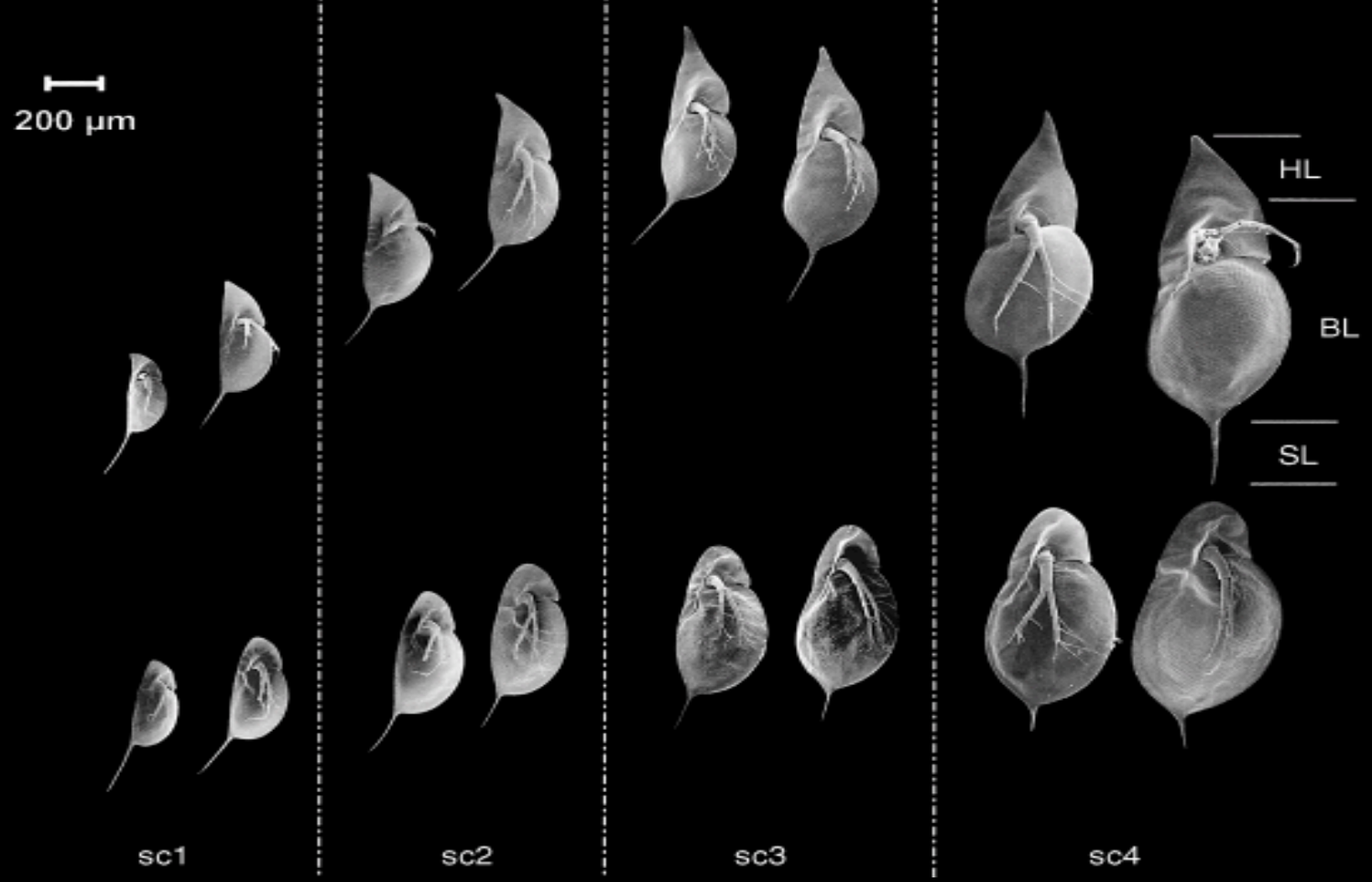


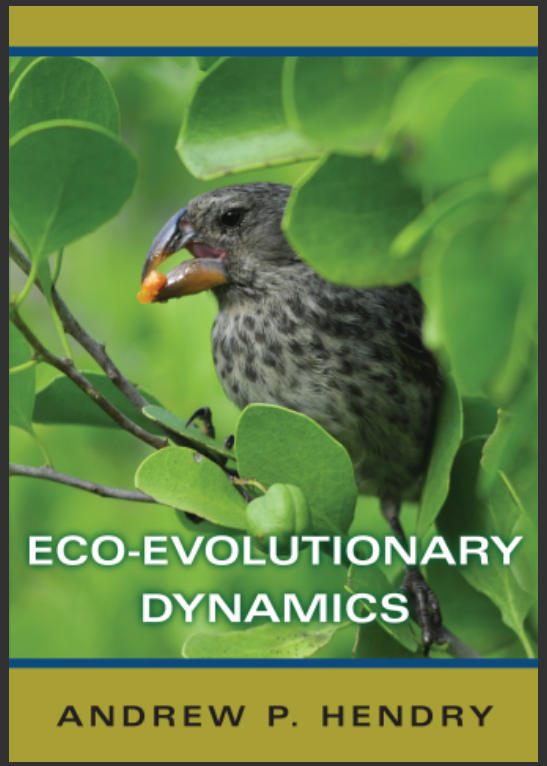
Adaptive Phenotypic Plasticity and Epigenetics

Kevin Wong

BIO 594 | Feb. 28 2019

Outline

Phenotypic Plasticity



Q1: What is phenotypic plasticity?

Q2: Is plasticity **adaptive**?

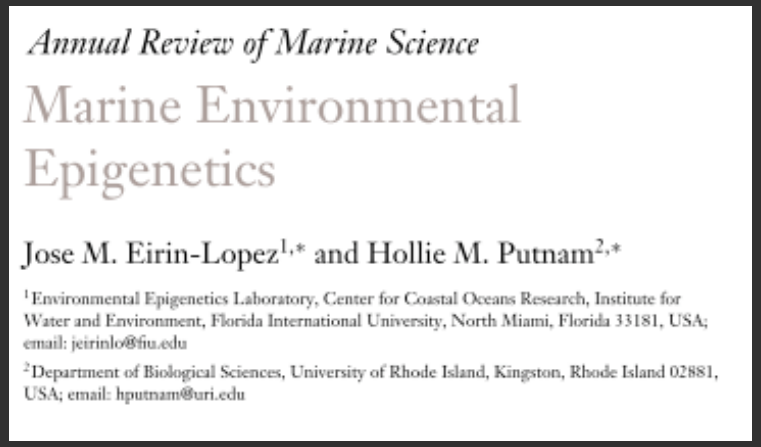
Q3: What are the **cost-benefits** of plasticity?

Q4: Does plasticity **promote** or **constrain** genetic evolution?

Q5: How can we **quantify** phenotypic plasticity?

Outline

Epigenetics



Annual Review of Marine Science

Marine Environmental Epigenetics

Jose M. Eirin-Lopez[1,*] and Hollie M. Putnam[2,*]

[1]Environmental Epigenetics Laboratory, Center for Coastal Oceans Research, Institute for Water and Environment, Florida International University, North Miami, Florida 33181, USA; email: jeirinlo@fiu.edu

[2]Department of Biological Sciences, University of Rhode Island, Kingston, Rhode Island 02881, USA; email: hputnam@uri.edu

Q1: What is epigenetics?

Q2: Epigenetic **effect** vs **inheritance**

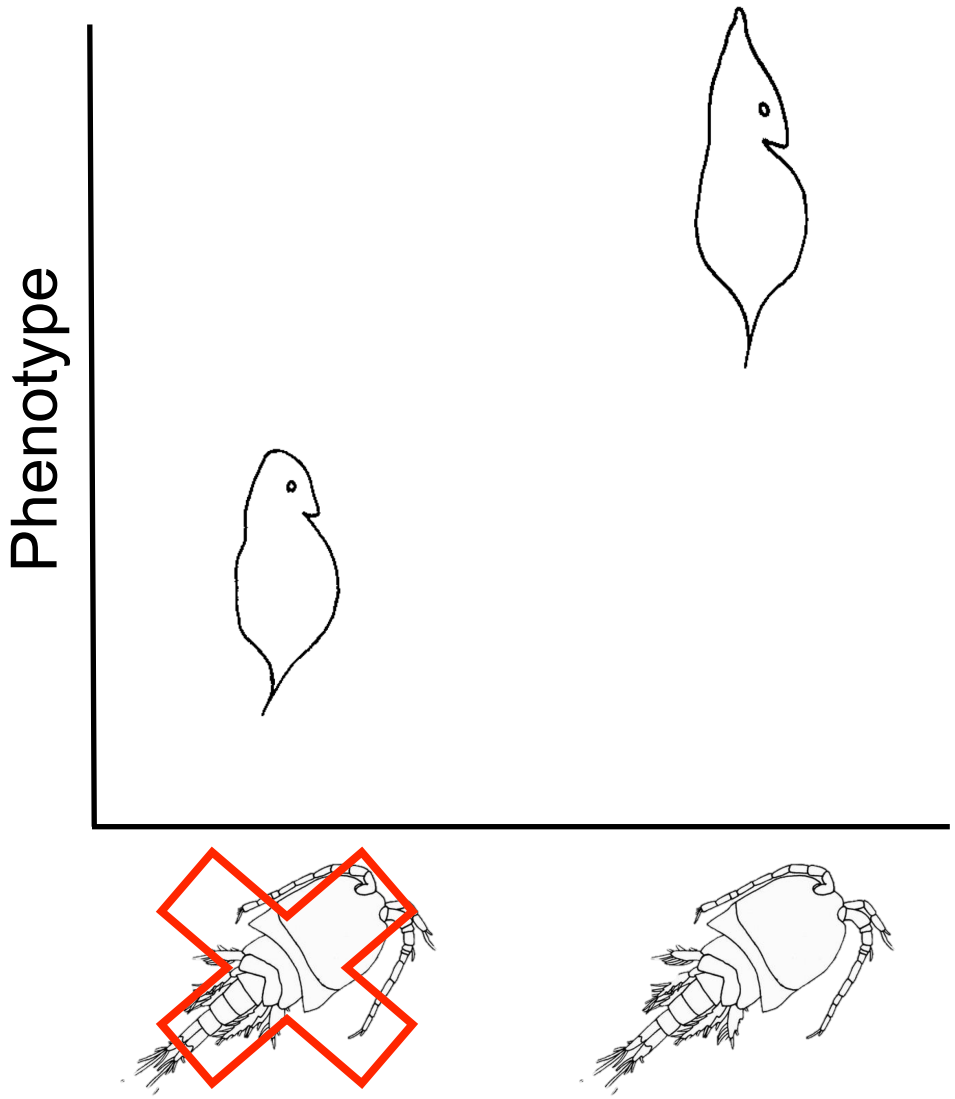
Q3: What are epigenetic **mechanisms**?

Q4: How can we **quantify** epigenetics?

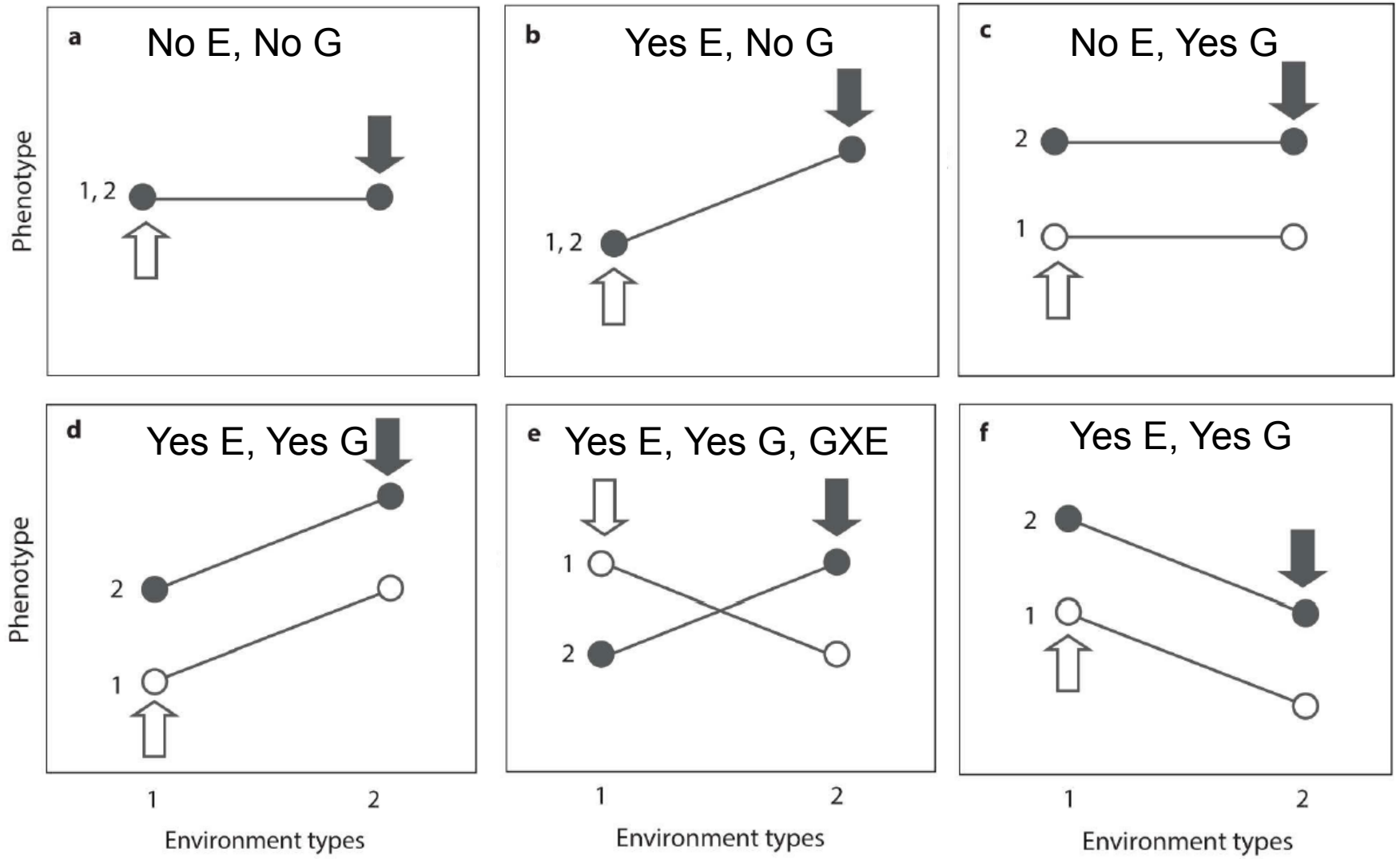
Q5: What is the epigenetic role in **environmental acclimatization**?

Q1: What is phenotypic plasticity?

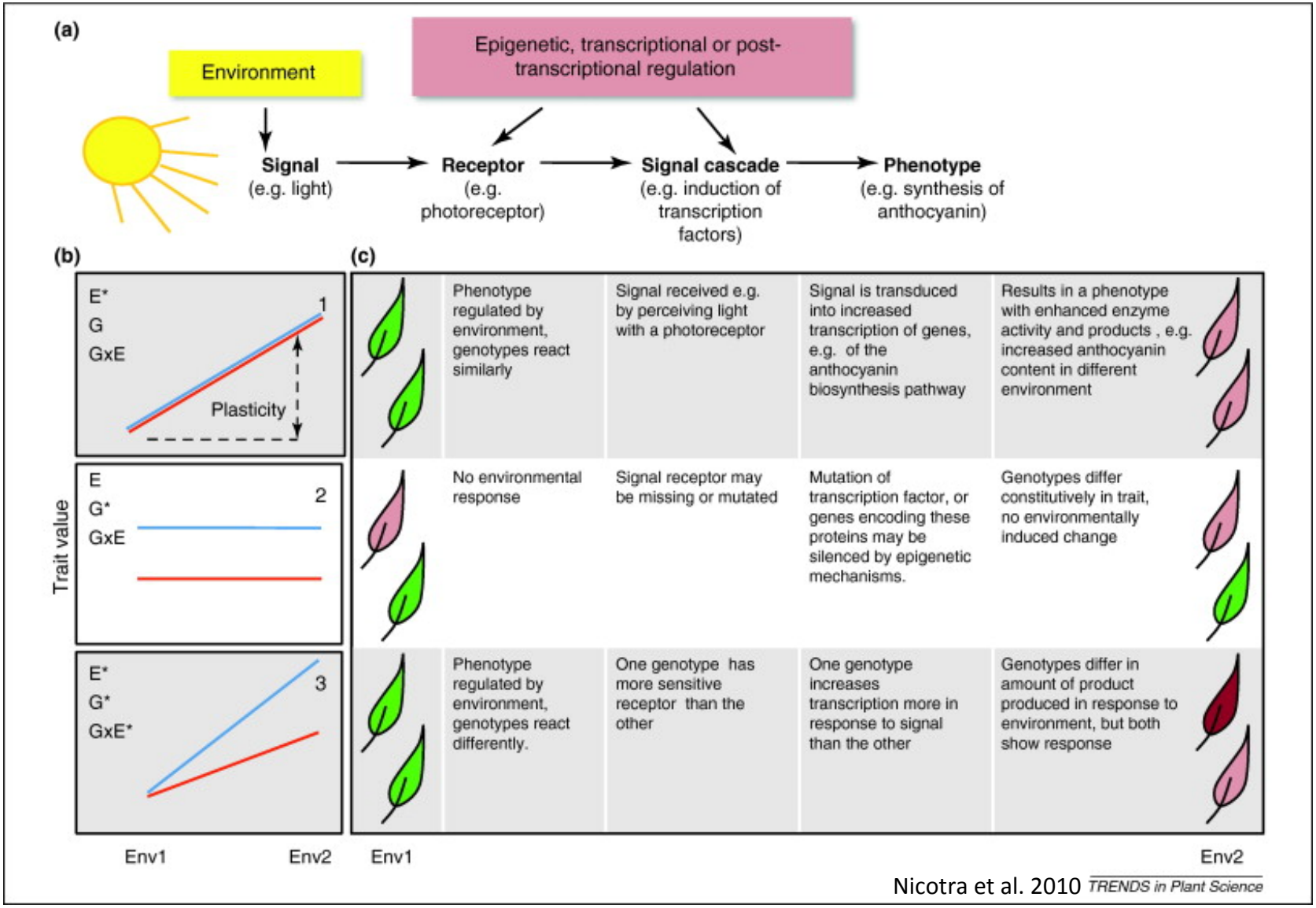
"The ability of one genotype to express different phenotypes in different environments"



Environment (E), Genotype (G), or both (GXE)?



Plasticity and Reaction Norms



Nicotra et al. 2010 *TRENDS in Plant Science*

Q1: What is phenotypic plasticity?

Within-generation (WGP)

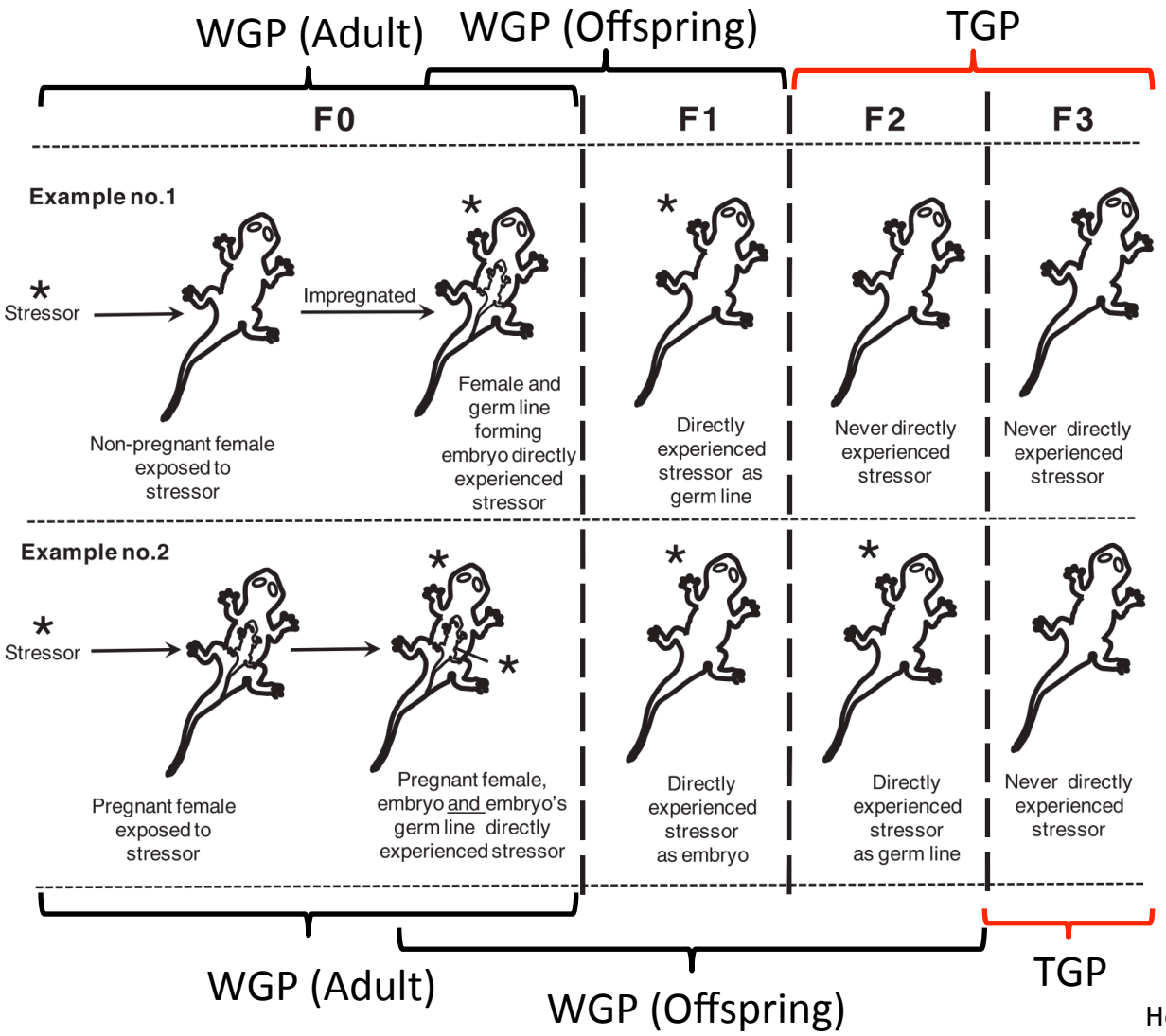
- A change in phenotype within the same individual under altered environmental conditions

Trans-generational (TGP)

- Differences in offspring phenotype that occur due to the interaction between the current generation and previous generation's environmental conditions

But what defines different generations?

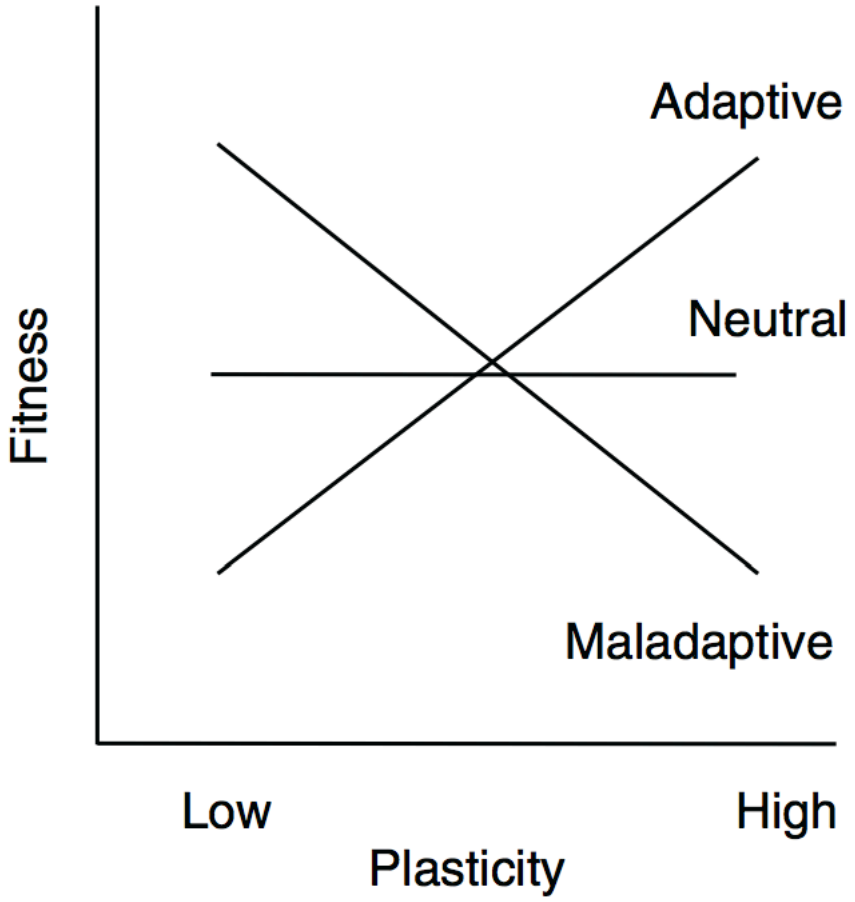
Types of plasticity: WGP and TGP



Ho and Burggren, 2010

Q2: Is plasticity adaptive?

"Plasticity is sometimes adaptive, sometimes maladaptive, and sometimes neutral"
– Andrew Hendry

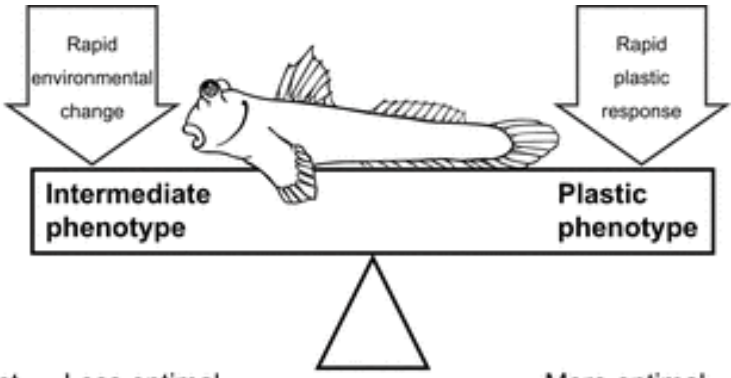


Nicotra et al. 2010

Q3: What are the cost-benefits of plasticity?

Energetic costs:

- Building new structures (and reversing)
- Maintenance costs for detecting environmental change
- Lag time effects – when is it worth it?



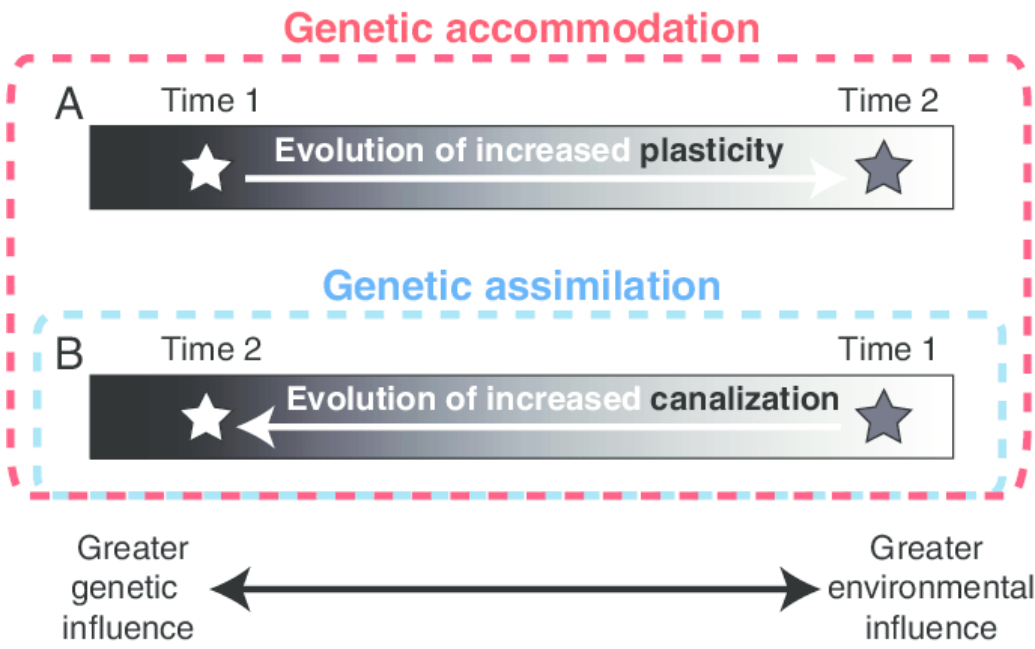
1. Phenotype–environment match	Less optimal	More optimal
2. Energetic costs • production • maintenance	Inexpensive	Expensive

Wright and Turko, 2016

Q5: Does plasticity promote or constrain evolution?

Genetic canalization

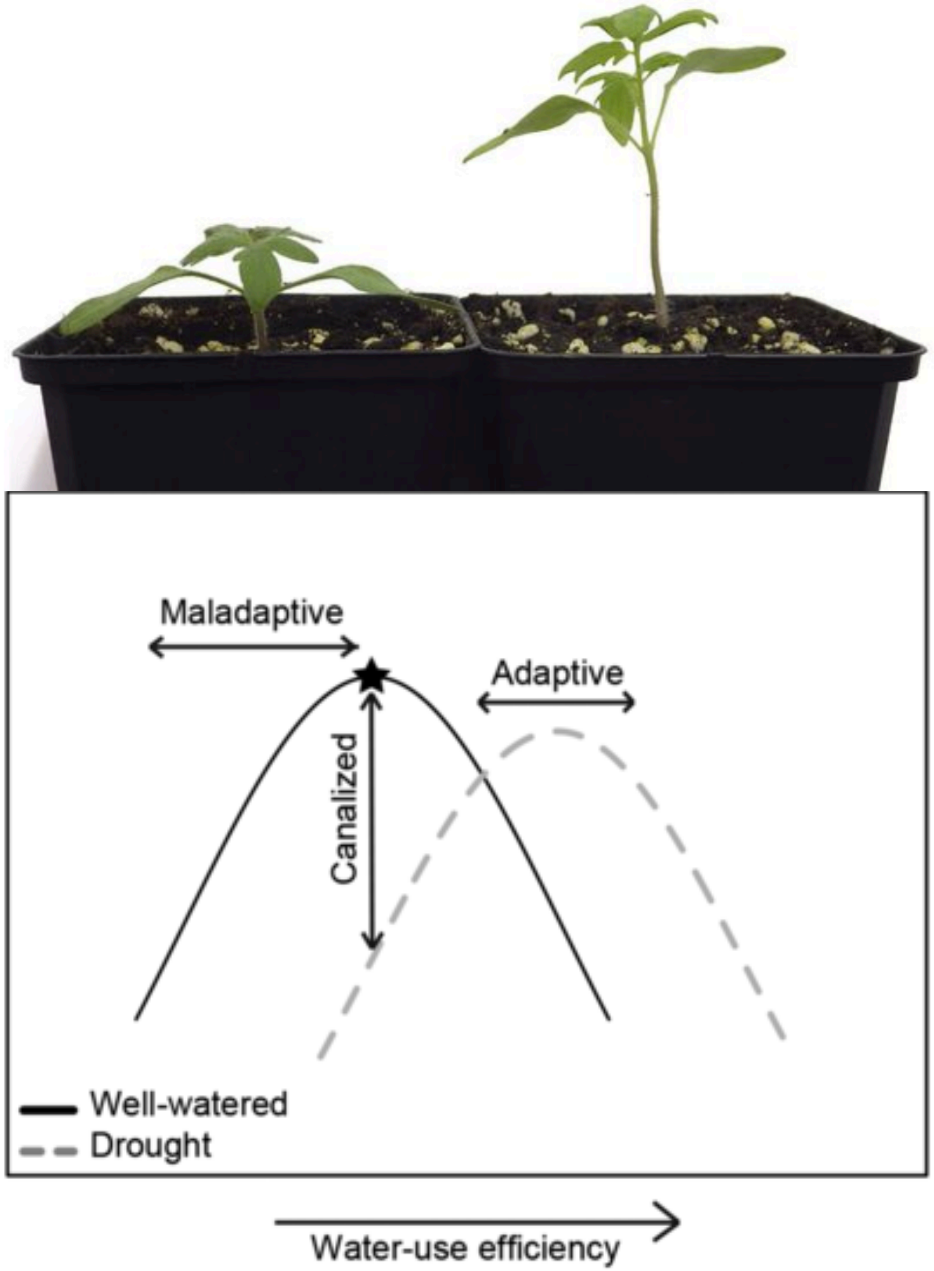
Genetic assimilation



Q4: Does plasticity promote or constrain evolution?

Genetic canalization

- Phenotypic robustness to environmental change

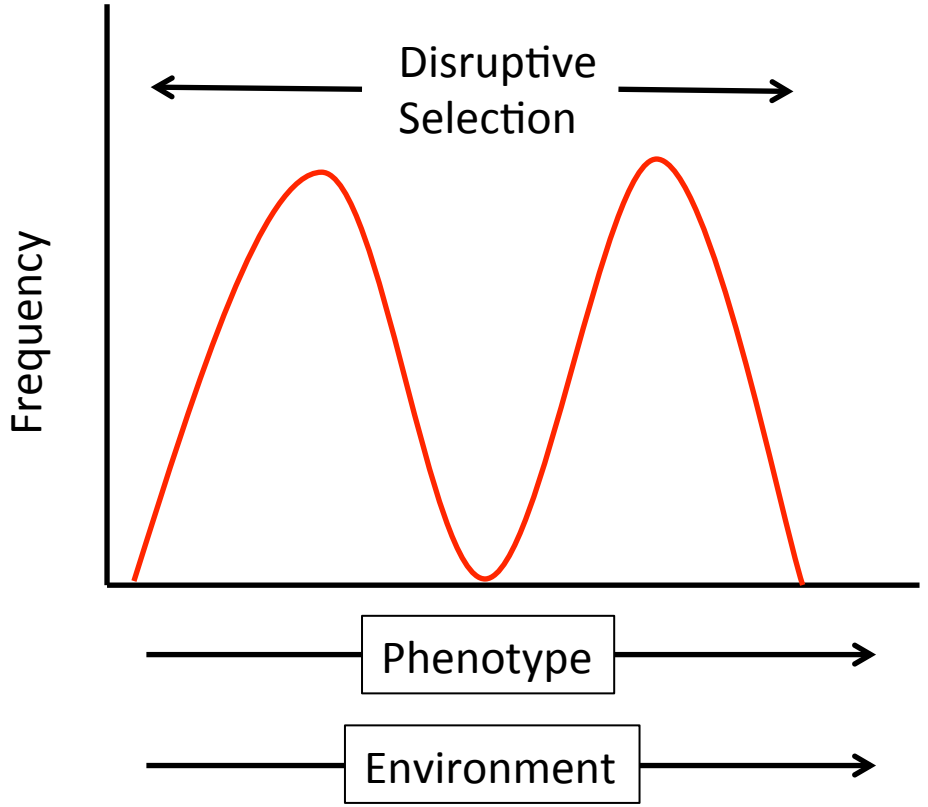


Becklin et al. 2016

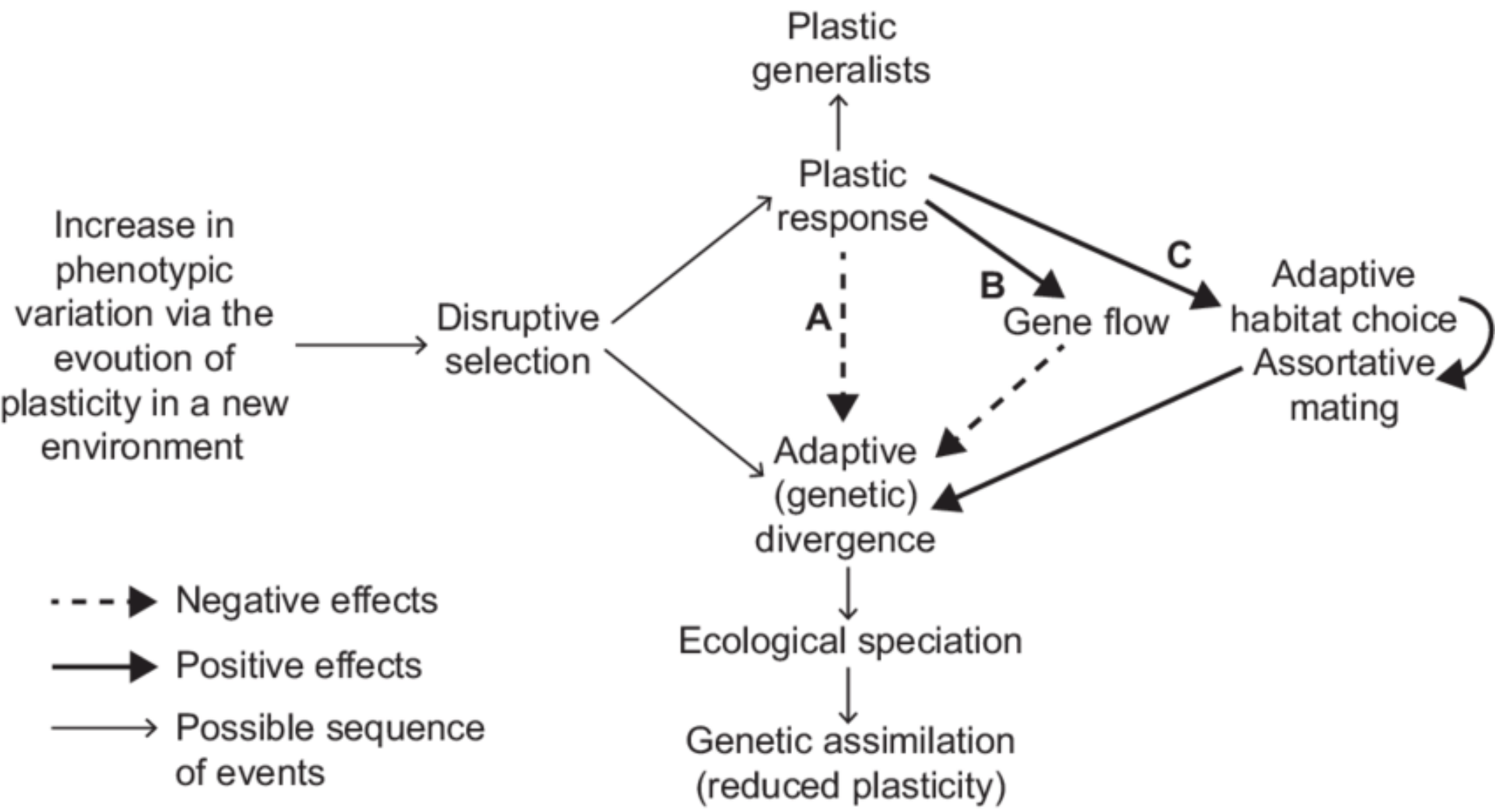
Q4: Does plasticity promote or constrain evolution?

Genetic assimilation

- When a change on phenotype in response to an environmental change is selected for
- Does this increase or decrease long term plasticity?



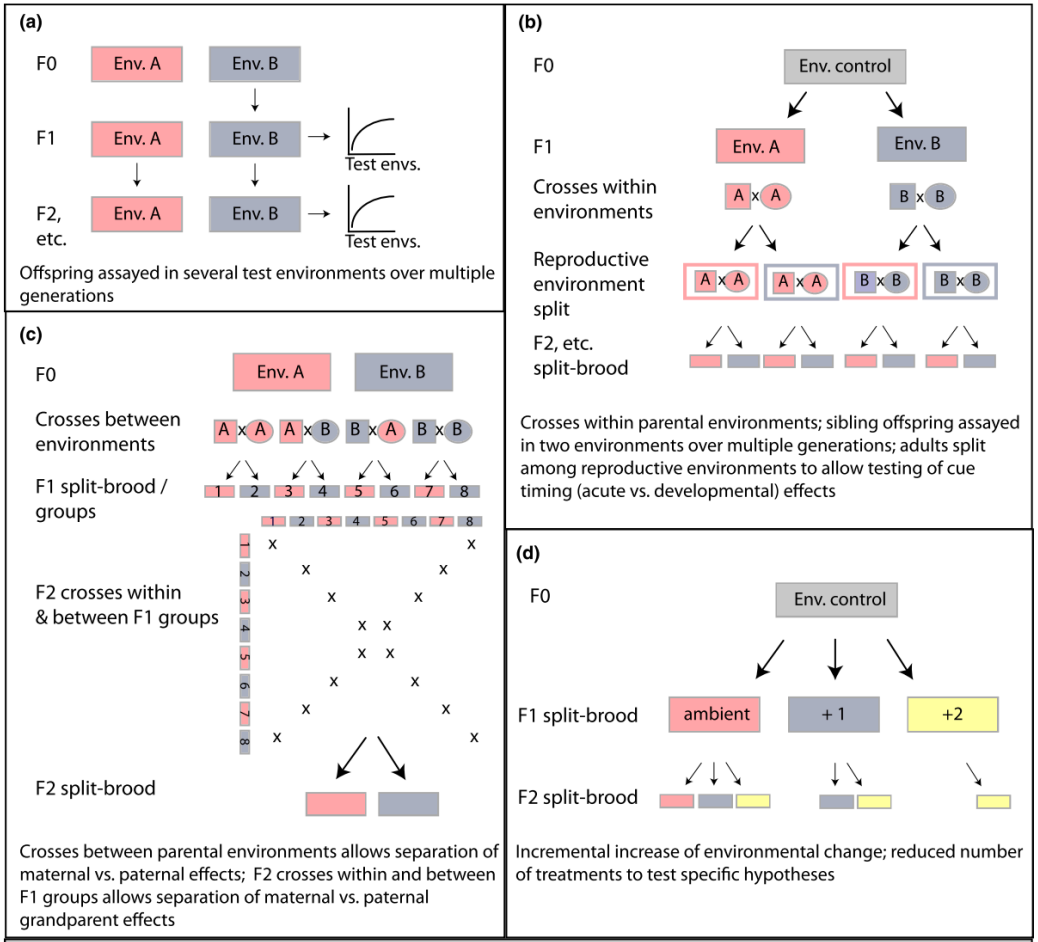
Does this increase or decrease long term plasticity?



Nonaka et al. 2015

Q5: How can we quantify phenotypic plasticity?

- Experimental Design matching the hypothesis
- Known plastic traits and how to measure them
- Are they heritable?



Experiment features:	Design			
	a	*b*	*c*	*d*
Reaction norm in each generation	x	x	x	x
WGP in each generation		x	x	x
Split-brood; test of TGP (PE x OE interaction) possible		x	x	x
Confounded by different genotypes in initial environmental lines	x		x	
Separate maternal vs. Paternal effects			x	
Separate parent vs. Grandparent effects		x	x	x
Separate maternal vs. Paternal grandparent effects			x	
Number of treatments tractable after F2	x			x
Test of cue timing effects possible		x	x*	
Test of WGP x TGP interactions possible		x	x	x
3 or more treatments to test non-linear effects (WGP)				x

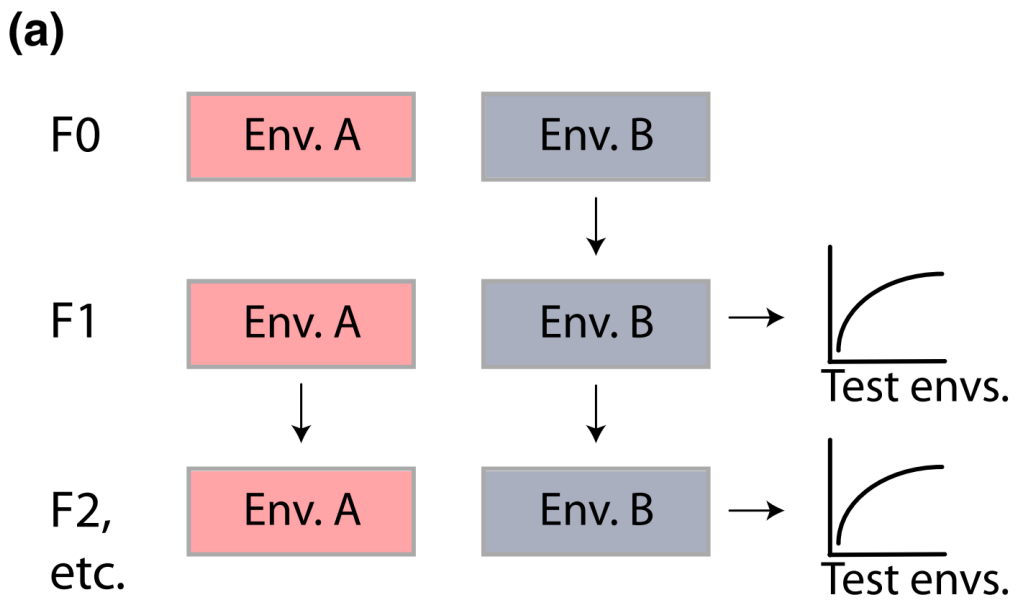
*when acute acclimation of F0

Donelson et al. 2017

Q5: How can we quantify phenotypic plasticity?

Experimental Design (a):

- Population Level
- Rxn norm for each generation
- Confounded by different genotypes in each environmental line

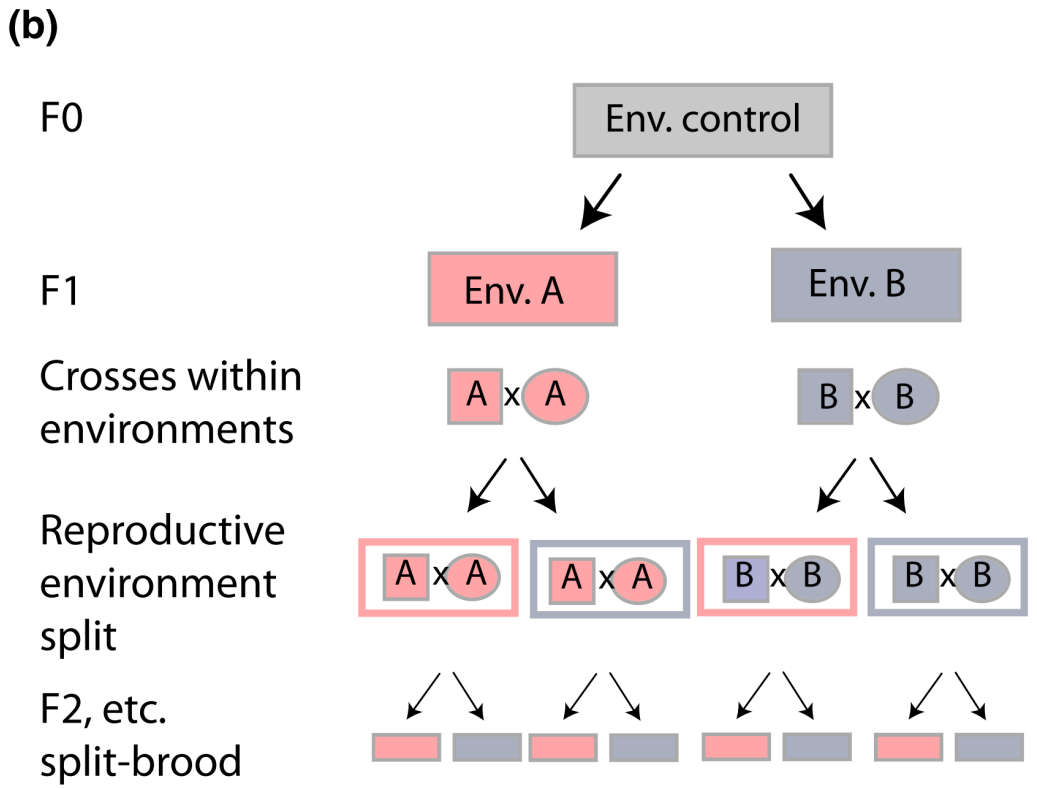


Donelson et al. 2017

Q5: How can we quantify phenotypic plasticity?

Experimental Design (b):

- Rxn norm for each generation
- WGP in each generation
- Split –brood, testing TGP (PE X OE)
- Separate parent/grandparent effects
- Can test for cue timing effects
- Can test WGP X TGP interactions

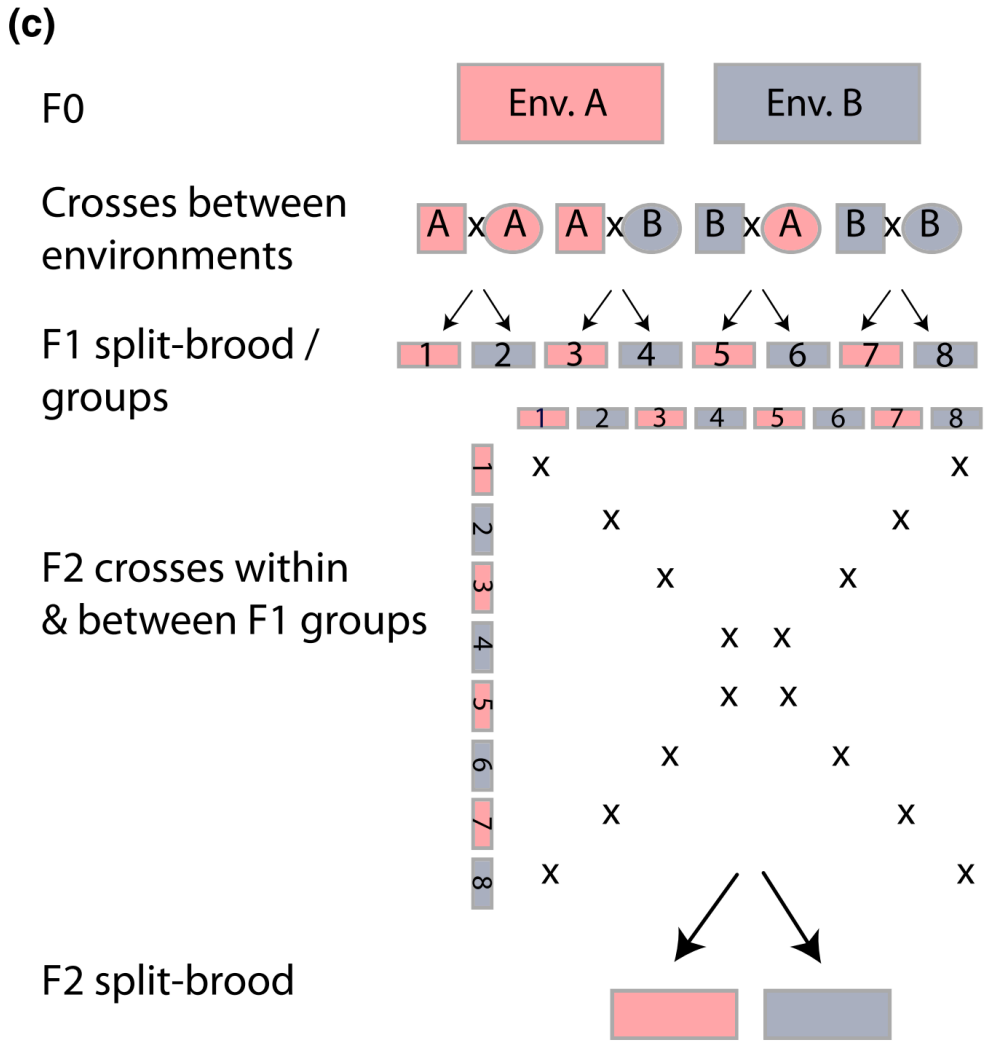


Donelson et al. 2017

Q5: How can we quantify phenotypic plasticity?

Experimental Design (c):

- Rxn norm for each generation
- WGP in each generation
- Split –brood, testing TGP (PE X OE)
- Confounded by different genotypes in each environmental line
- Separate maternal/paternal effects
- Separate parent/grandparent effects
- Can test WGP X TGP interactions

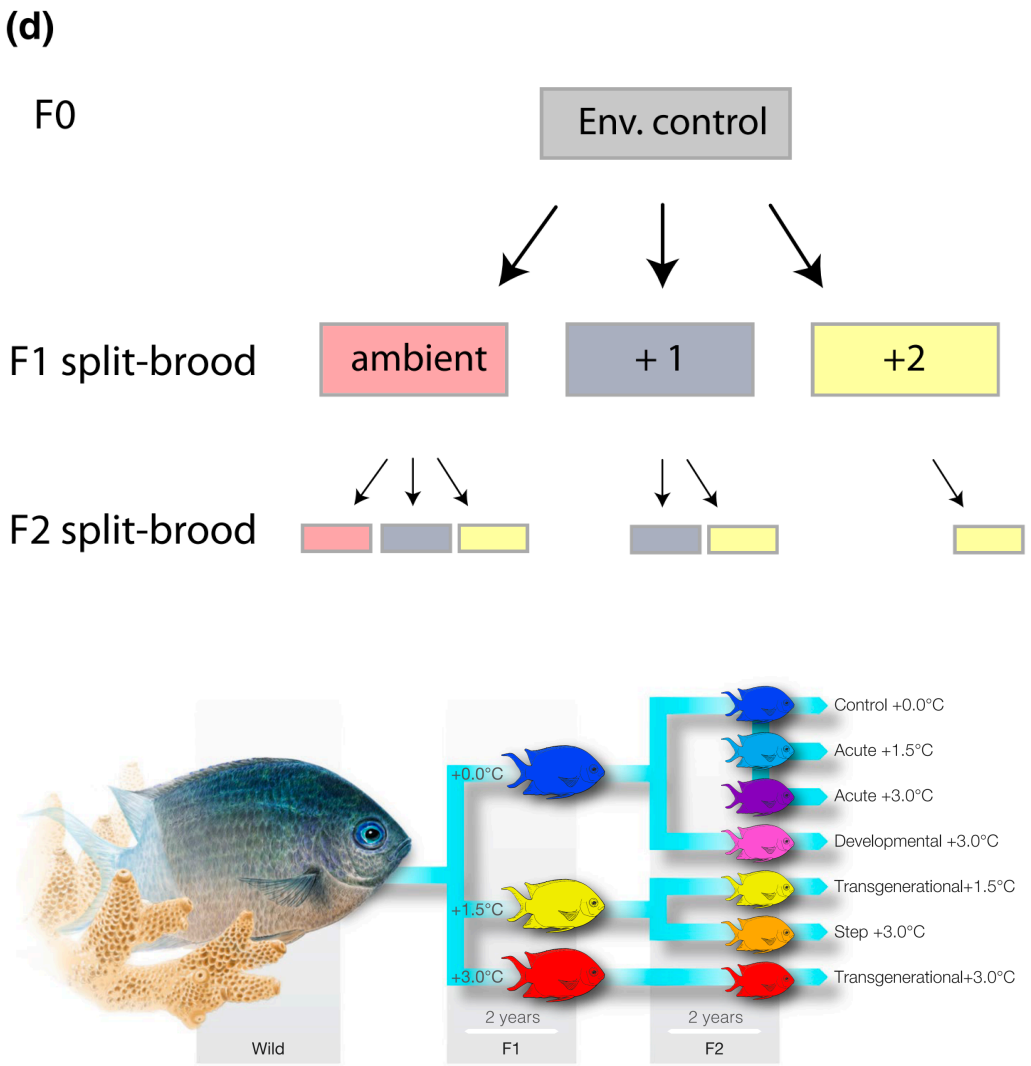


Donelson et al. 2017

Q5: How can we quantify phenotypic plasticity?

Experimental Design (d):

- Rxn norm for each generation
- WGP in each generation
- Split –brood, testing TGP (PE X OE)
- Separate parent/grandparent effects
- Can test WGP X TGP interactions
- Can test for cue timing effects
- 3 or more treatments to test non-linear effects



Donelson et al. 2017, Bernal et al. 2018

Outline

Epigenetics

Q1: What is epigenetics?

Q2: Epigenetic **effect** vs **inheritance**

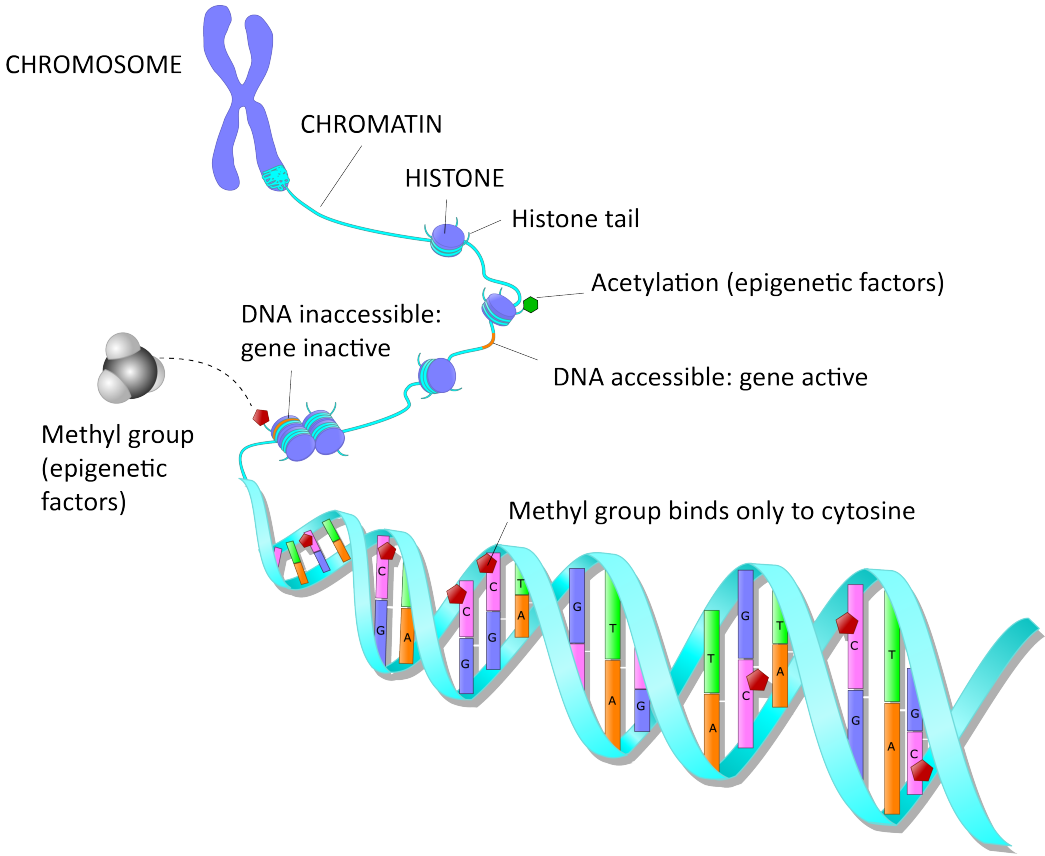
Q3: What are epigenetic **mechanisms**?

Q4: How can we **quantify** epigenetics?

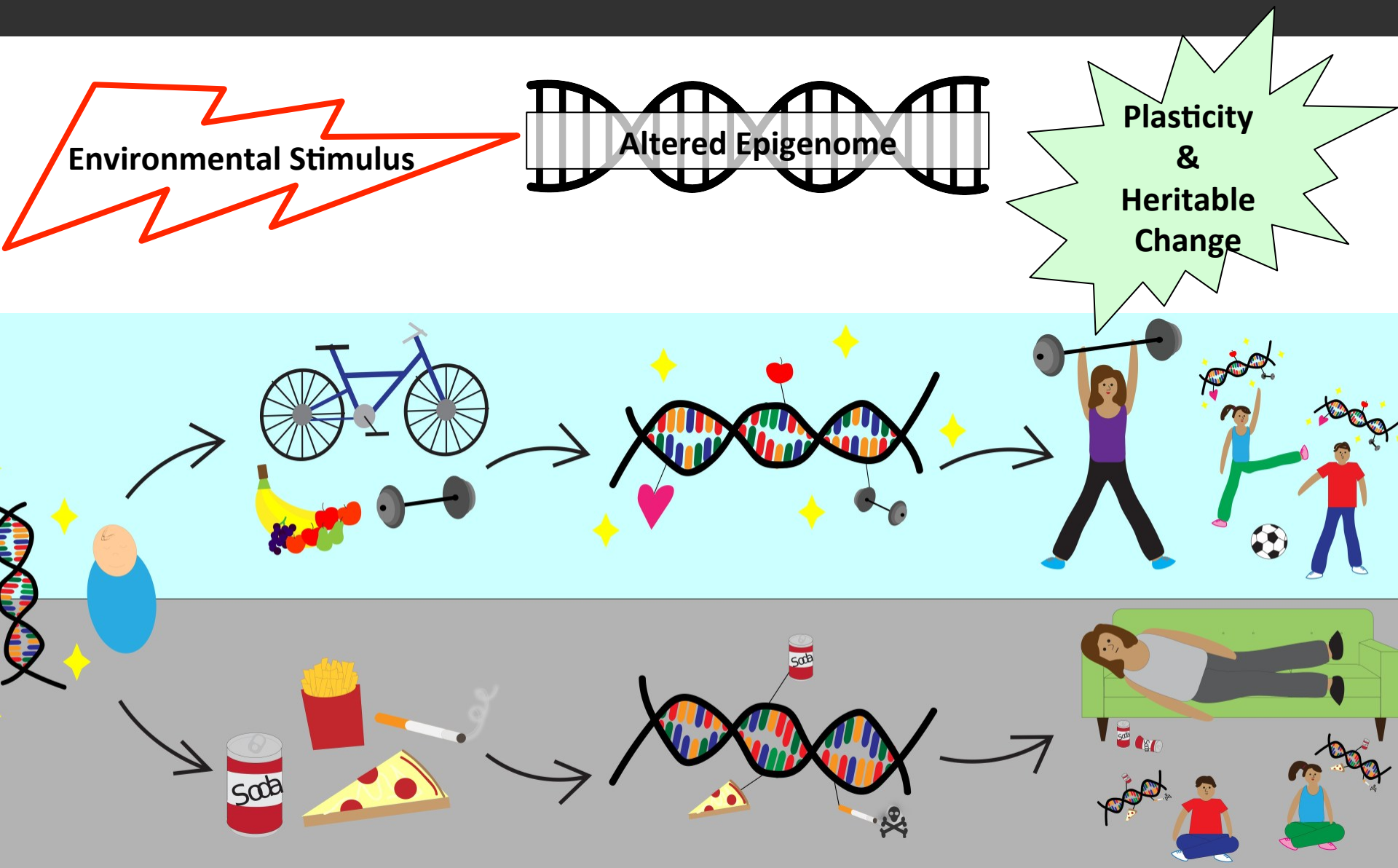
Q5: What is the epigenetic role in **environmental acclimatization**?

Q1: What is epigenetics?

"Change in **heritable** (mitotic/ meiotic) gene function that **cannot** be explained by changes in the DNA sequence"

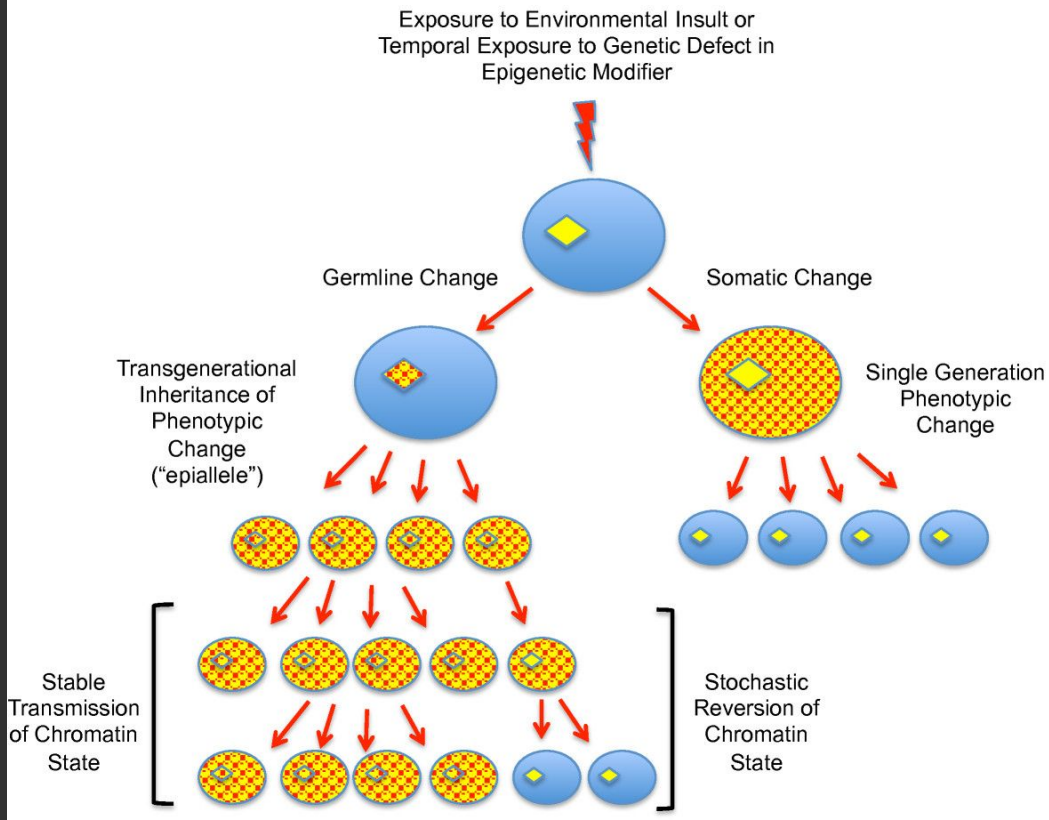


Plasticity and Epigenetics

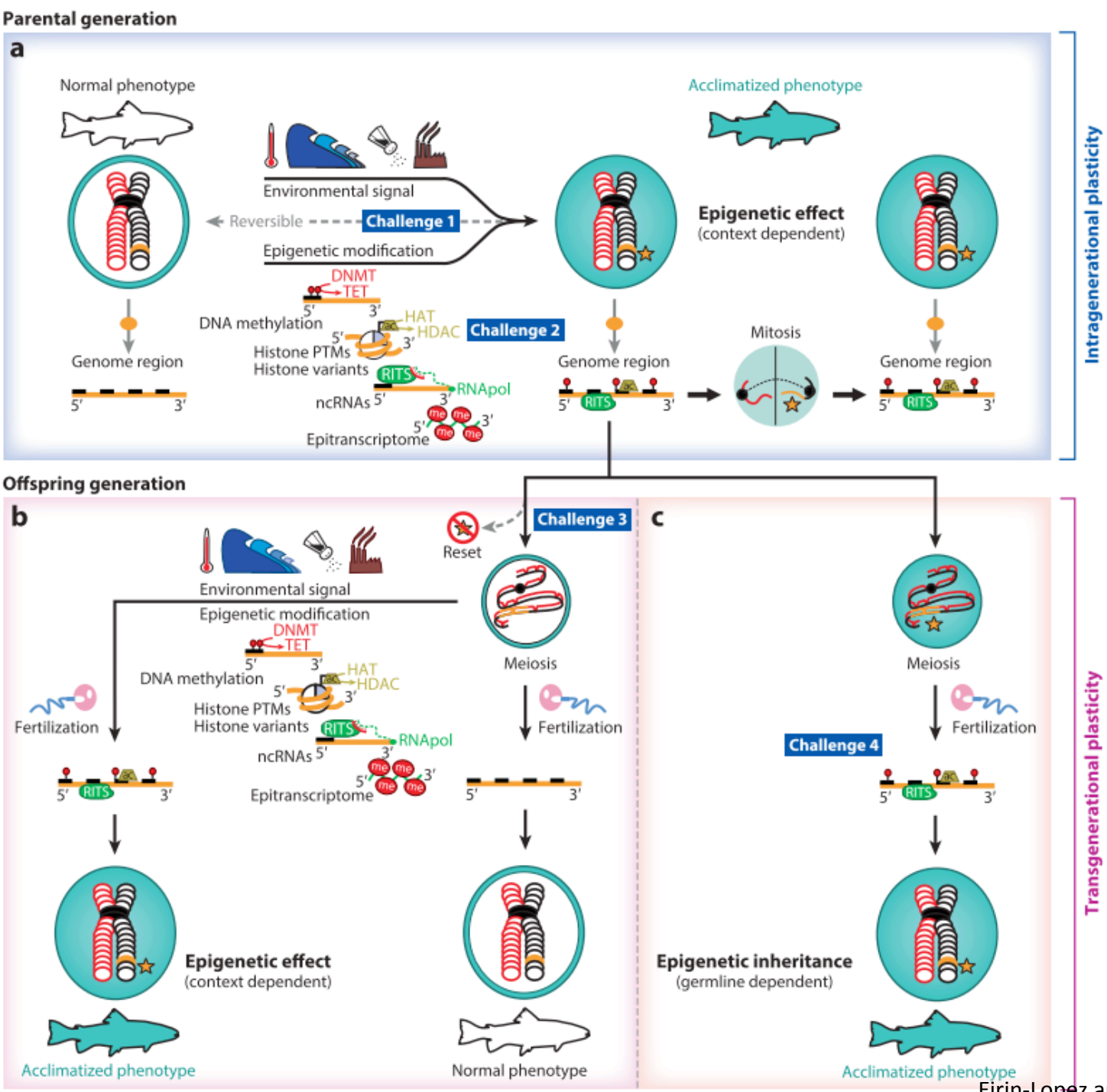


Q2: Epigenetic effect vs inheritance

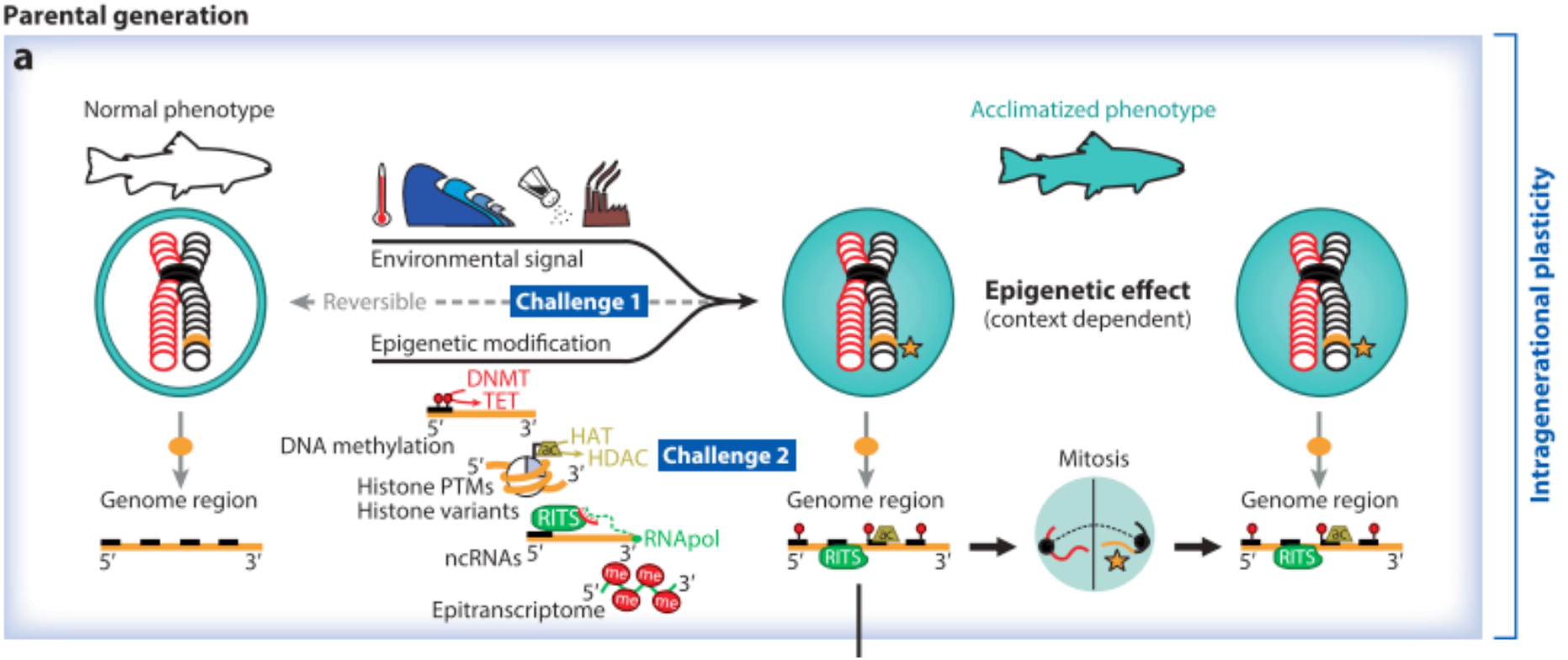
- Transmission of epigenetic states in the soma and germline
- Epigenetic effects on soma
- Epigenetic inheritance through germline cells



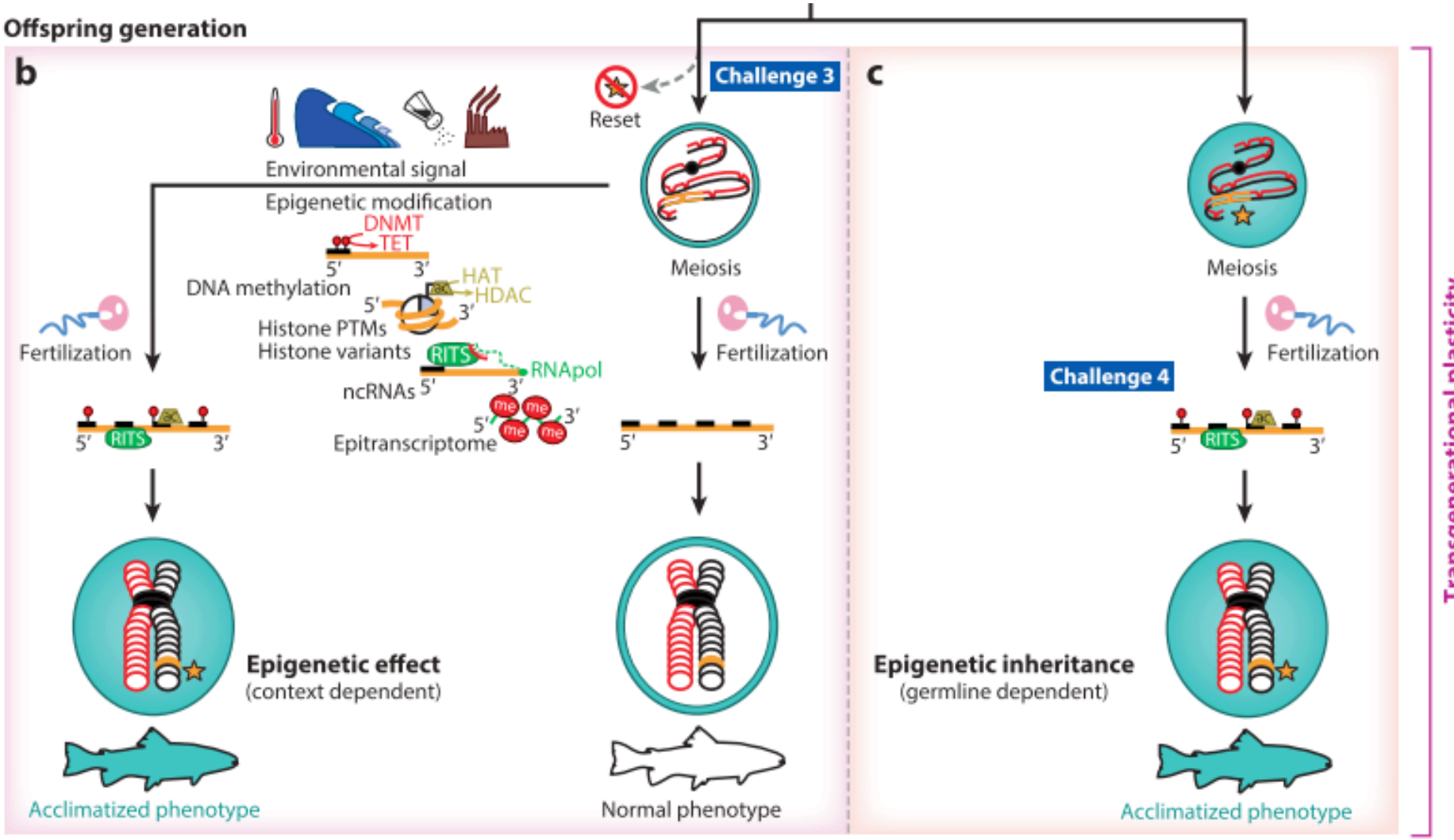
Kelly, 2014



Eirin-Lopez and Putnam, 2019

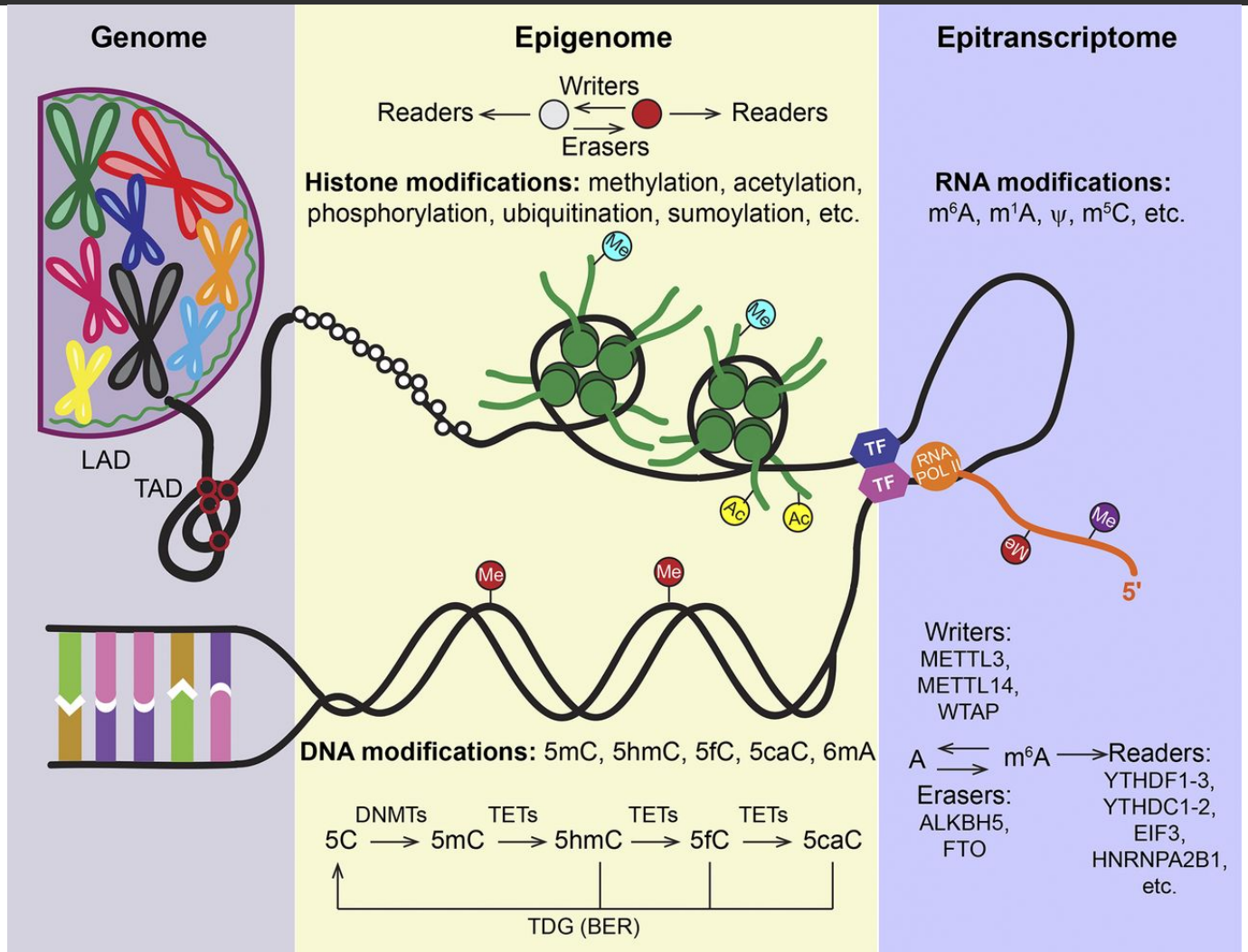


Eirin-Lopez and Putnam, 2019



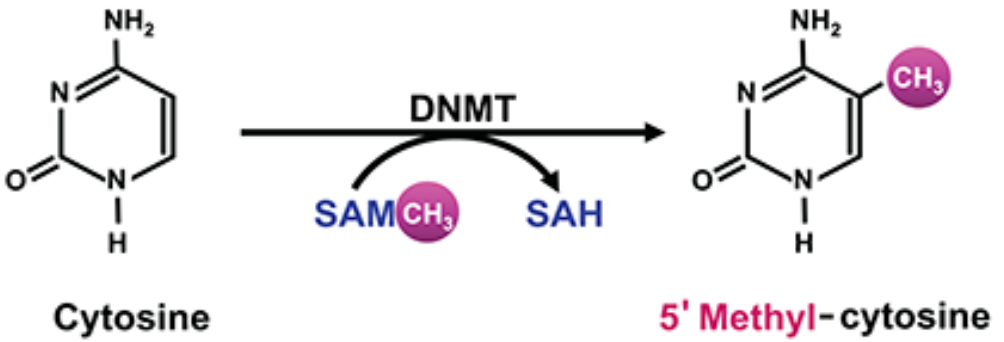
Eirin-Lopez and Putnam, 2019

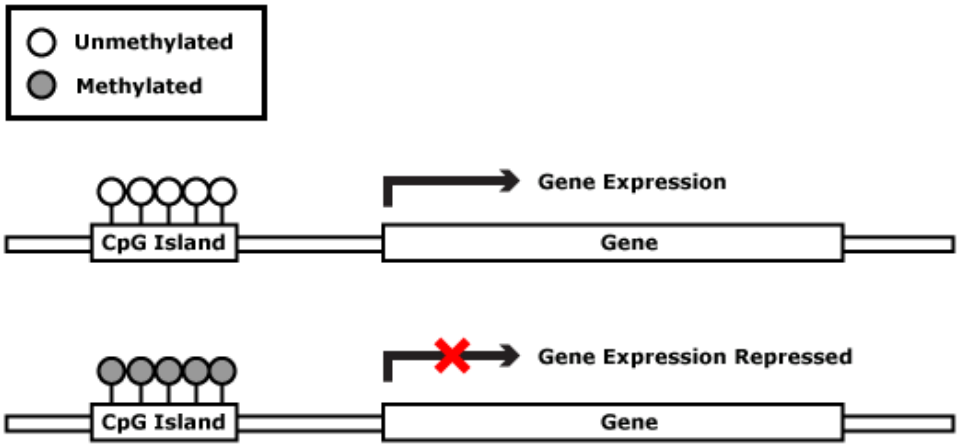
Q3: What are epigenetic mechanisms?



DNA Methylation

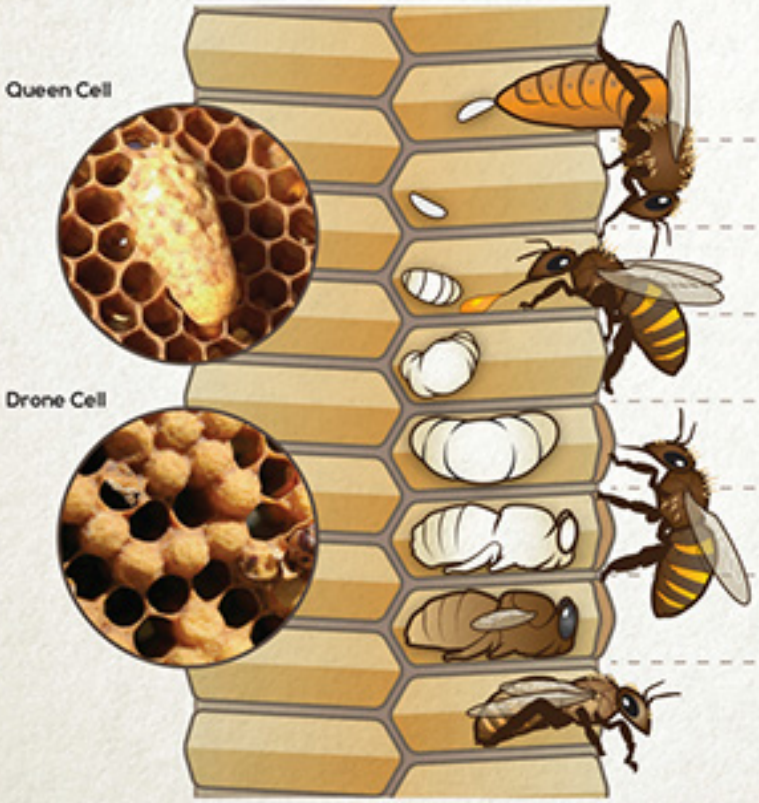
- Methyl group added to cytosine molecules by DNMT enzymes
- Can repress transcription in 2 ways:
  - Binding to DNA directly and impede binding of transcriptional proteins (CpG islands)
  - Methylated DNA may be bound by methyl-CpG-binding domain proteins (MBDs)





Life Cycle of the Honey Bee

Apis Mellifera

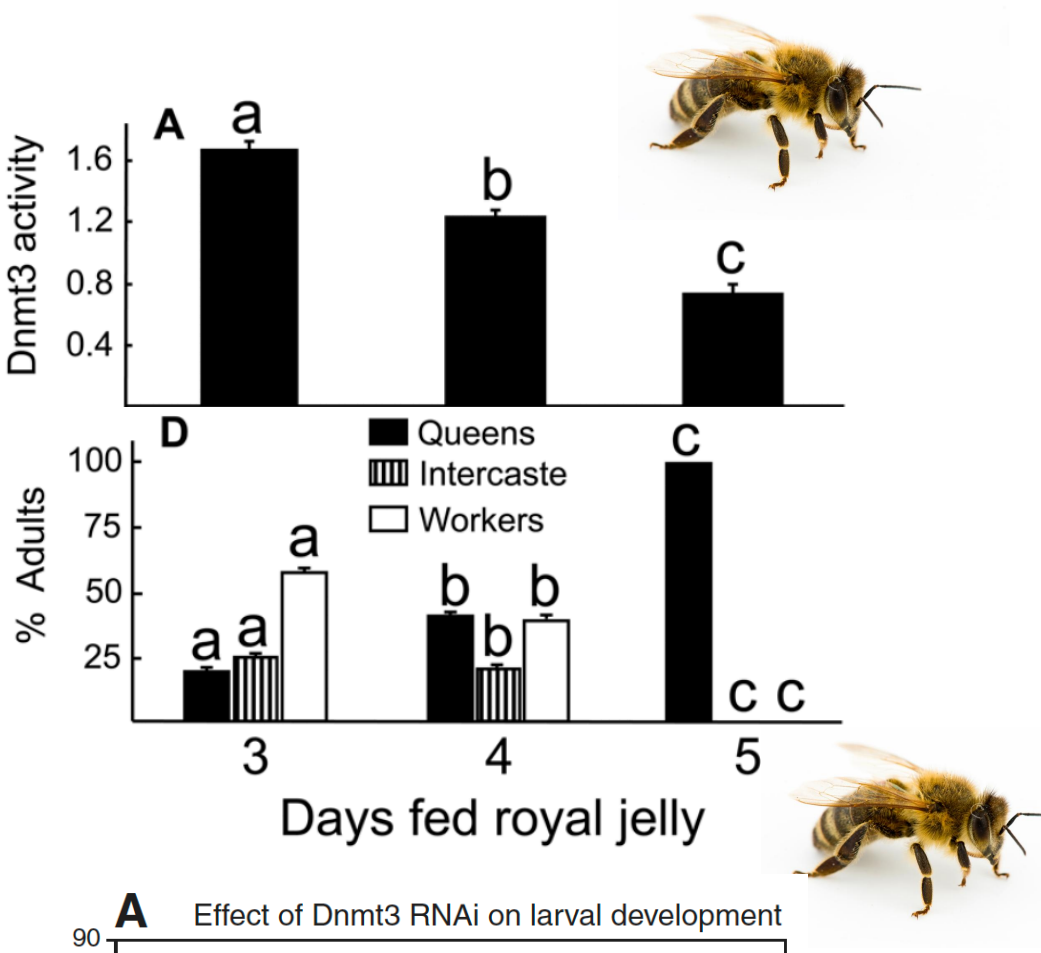


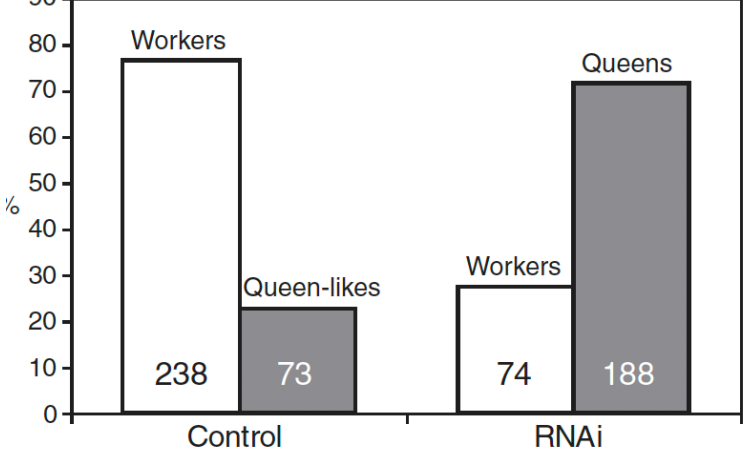
1. Queen lays egg in brood cell.
   Period as an egg.
2. Worker feeds hatched larva.
   Larva continues to grow.
3. Worker bee caps cell.
4. Larva spins cocoon.
   Larva transforms as pupa.
5. Adult bee emerges from brood cell.

	QUEEN	WORKER	DRONE
1	Day 1-3	Day 1-3	Day 1-3
2	Day 4-9	Day 4-9	Day 4-9
3	Day 10-15	Day 10-20	Day 10-23
4	Day 16	Day 21	Day 24

DNA Methylation

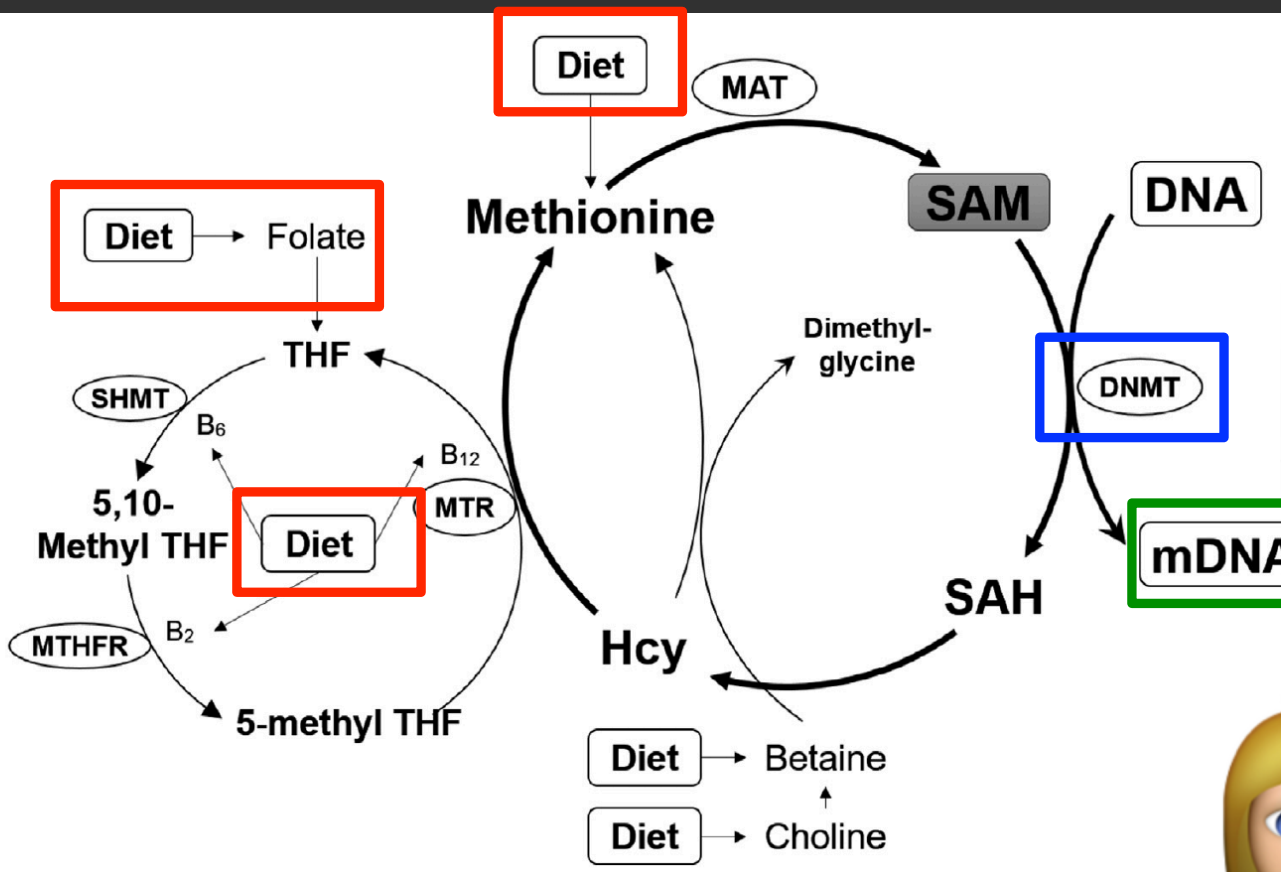
- Larvae of *Apis mellifera* (honey bees) can become either queen or workers
- DNA methylation is known to regulate expression patterns if *dyactin p62* gene resulting in altered phenotypes
- When fed royal jelly, repressed DNMT results in queen phenotype





Shi et al. 2011; Kucharski et al. 2008

DNA Methylation and Nutrition



Nutrition

DNMT abundance

Methylated DNA

dynactin expression

Queen Bee Phenotype

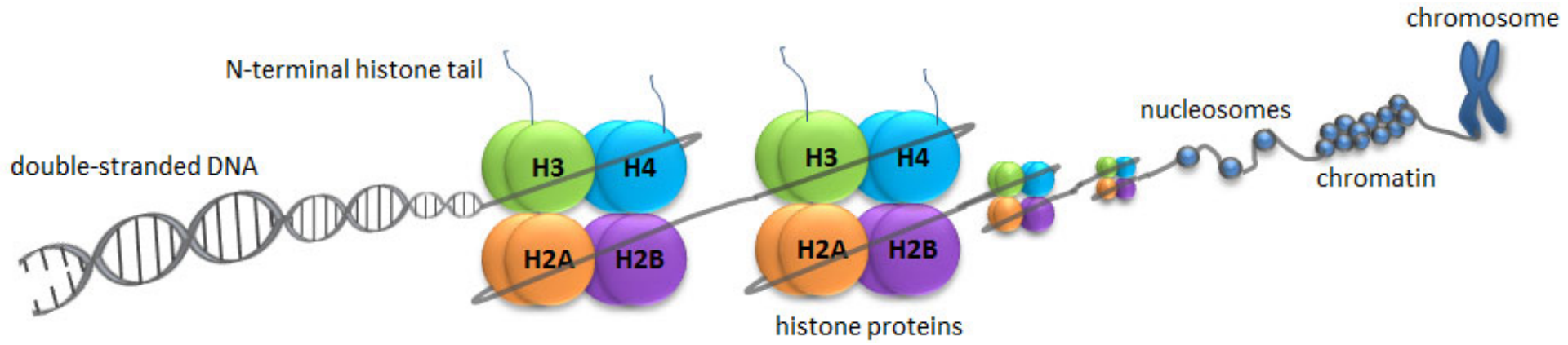
Zhang et al. 2015

Chromatin Structure

Histone modifications are:

- Methylation
- Phosphorylation
- Acetylation
- Ubiquitylation
- Sumoylation

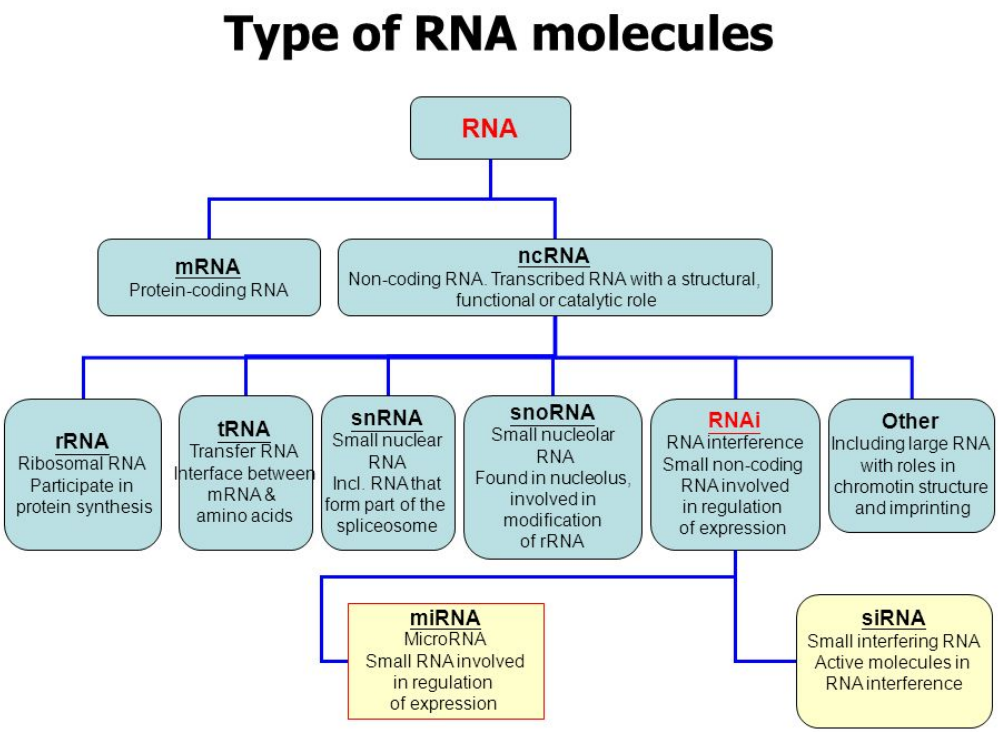
Histone modifications can impact gene expression by altering chromatin structure or recruiting histone modifiers

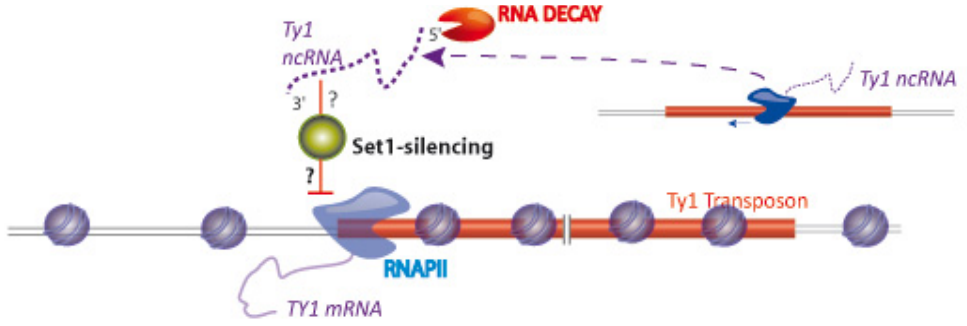


https://www.whatisepigenetics.com/histone-modifications/

Non-coding RNA

- Formation of RNA structures that facilitate the recruitment of chromatin modifiers
- Can be horizontally transferred between cells
- Can be methylated like DNA → refered to as “epitranscriptome”





Q4: How can we quantify epigenetics

- DNA Methylation
  - CpG O/E
  - Global DNA methylation
  - Bisulfite sequencing methods
- Histone Modifications
  - Histone extraction and immuno-detection
  - ChIP sequencing
- Noncoding RNAs
  - sRNA sequencing

Approach	Description[a]	Level of detail	Difficulty[b]	Cost[c]	Advantages	Disadvantages	References[d]
DNA methylation							
CpG O/E	Methylated cytosine has a tendency to undergo deamination to thymine. This can leave a signature of cytosine depletion in the genome that can be quantified by looking at the ratio of observed CpG to expected CpG in silico.	Single-base-pair resolution of historical methylation status	#	$	Can utilize existing data sets	Cannot examine dynamic or inducible methylation changes	Gardiner-Garden & Frommer 1987; Dimond & Roberts 2016, Dixon et al. 2010, Gavery & Roberts 2010
HPLC and LC-MS/MS	An HPLC or LC-MS/MS instrument can detect global DNA methylation following digestion of the DNA.	Methylation relative to cytosines in DNA or total DNA	#	$	Quick and easy	Global signal, low resolution, no ability to assess sequence	Kuo et al. 1980, Song et al. 2005; Mirbahai et al. 2011, Varriale & Bernardi 2006 (HPLC); none found (LC-MS/MS)
ELISA	Enrichment and quantification of global DNA methylation can be done through the addition of a capture antibody for methylated DNA and a detection antibody, followed by colorimetric or fluorescent detection.	Methylation relative to total DNA	#	$	Quick and easy	Global signal, low resolution, no ability to assess sequence	NA; Dabe et al. 2015, García-Fernández et al. 2017, Kuc et al. 2017, Putnam et al. 2016
WGBS	A global picture of DNA methylation with single-base-pair resolution gives the optimal capacity to test hypotheses that go beyond genes or regions to genomic architecture. These data are generated by whole-genome fragmentation, bisulfite conversion, DNA library preparation, and sequencing.	Base pair or whole genome	#####	$$$$$	Provides a complete picture of methylation with single-base-pair resolution, facilitates higher-order analyses	Can potentially damage DNA with bisulfite treatment, has a high cost of sequencing for very-low-percentage methylation	NA; Dabe et al. 2015; Li et al. 2018; Liew et al. 2018a,b; Rondon et al. 2017; Wang et al. 2014

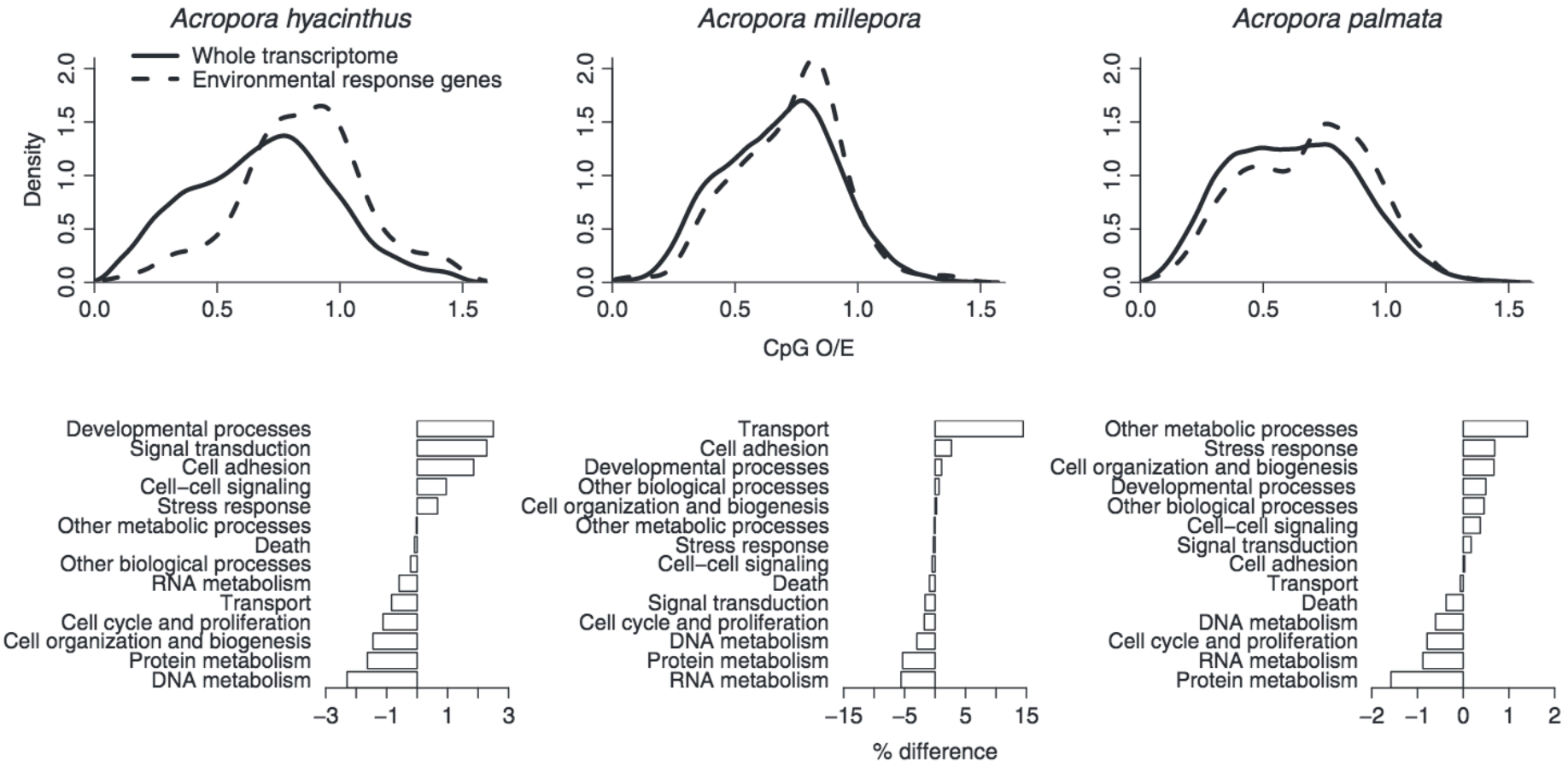
(*Continued*)

DNA Methylation: CpG Observed/Expected

- Methylated cytosines convert to thymines over time

$$\text{CpG O/E} = \frac{\text{number of CpG}}{\text{number of C} \times \text{number of G}} \times \frac{l^2}{l} - 1$$

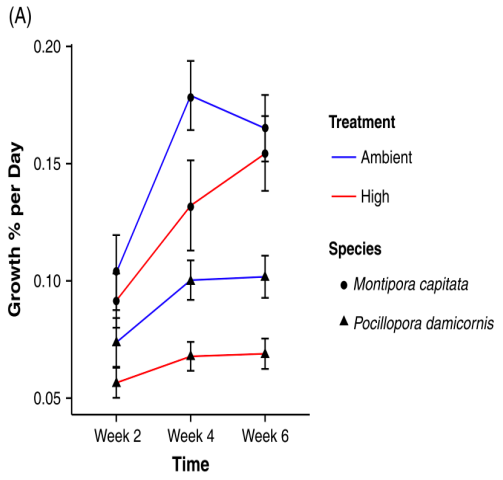
DNA Methylation: CpG Observed/Expected

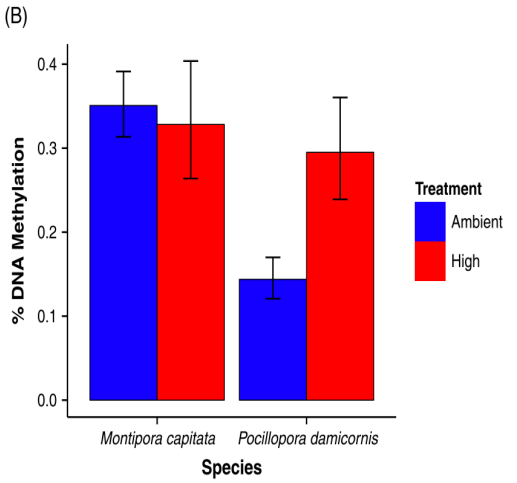


Dimond and Roberts, 2016

DNA Methylation:
Global DNA Methylation

- DNA is bound to strip-wells
- Methylated fraction of DNA is detected using capture and detection anti-bodies
- Quantified colormetrically on a spectrophotometer

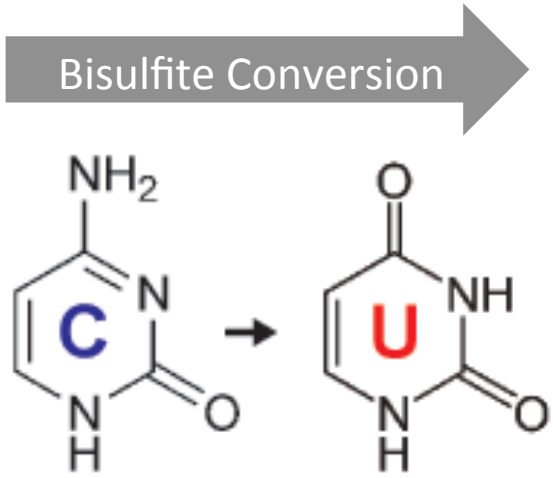


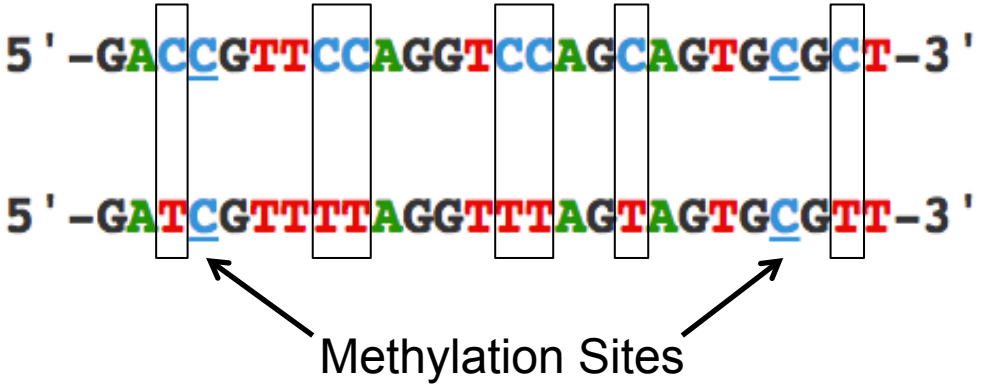


Putnam et al. 2016

DNA Methylation: Bisulfite Sequencing

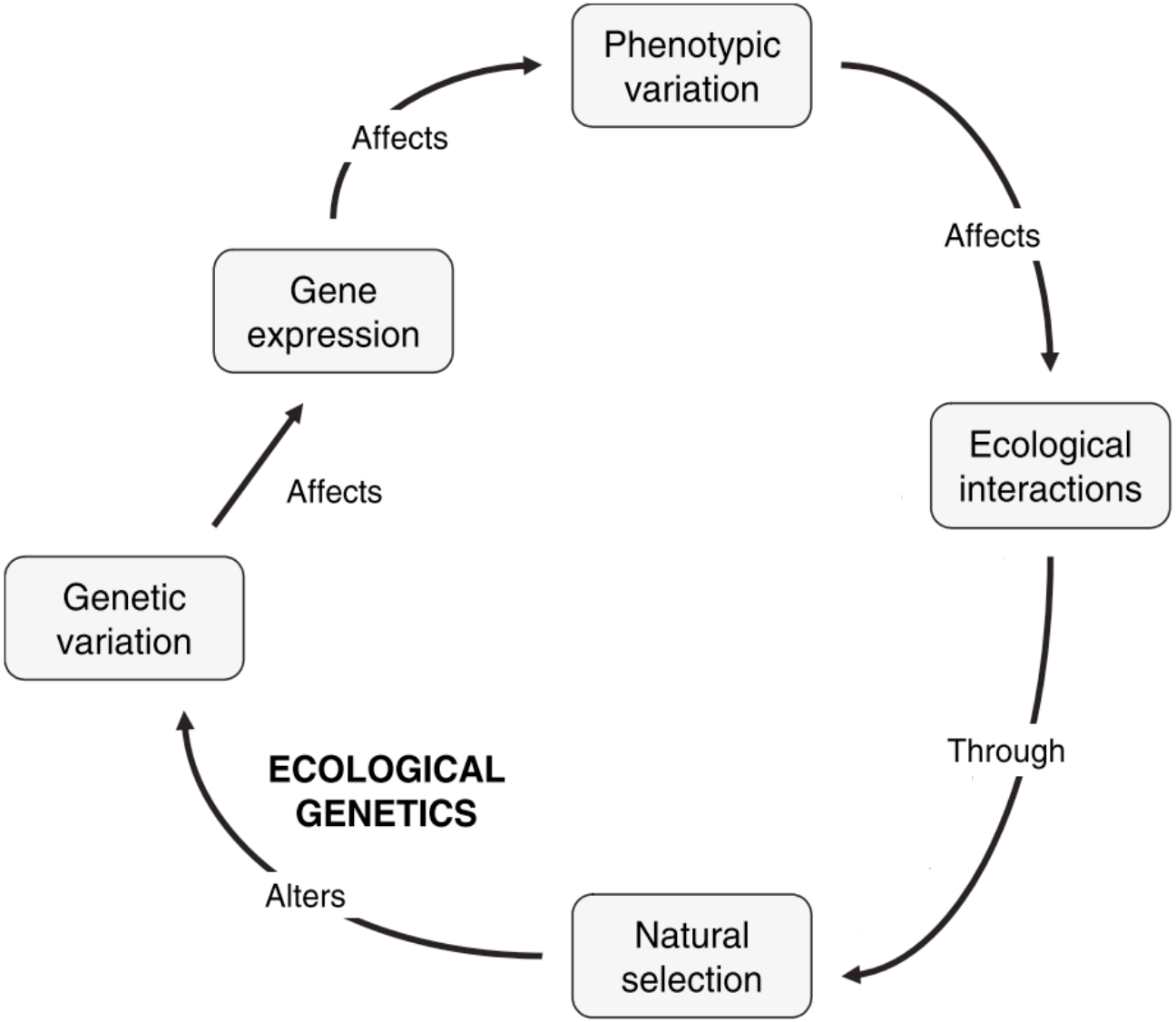
- Gold standard
- Unmethylated cytosines undergo hard bisulfite treatment
- Methylated cytosines are immune to this conversion



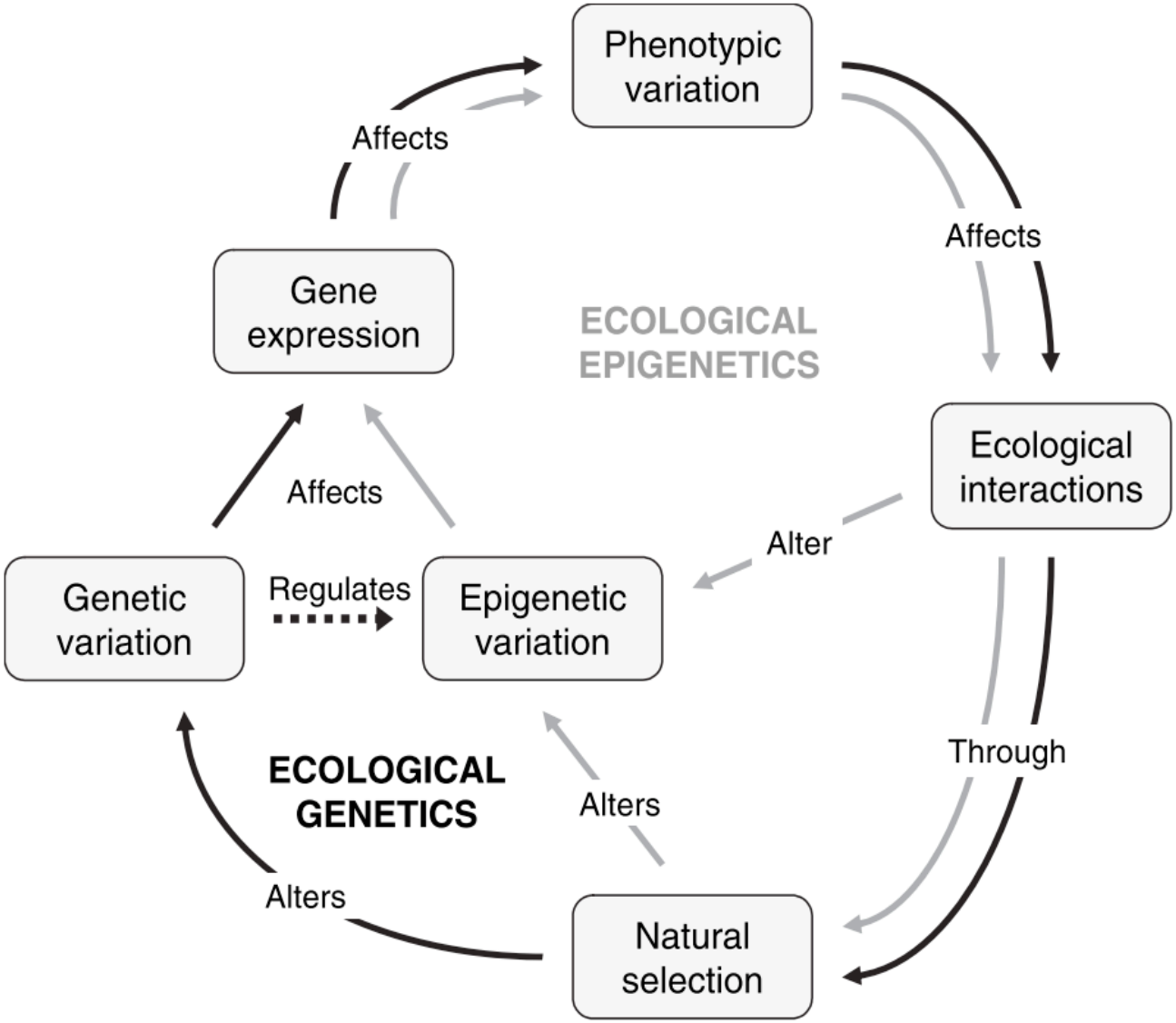


https://www.zymoresearch.com/pages/bisulfite-beginner-guide

Q5: What is the epigenetic role in phenotypic plasticity?

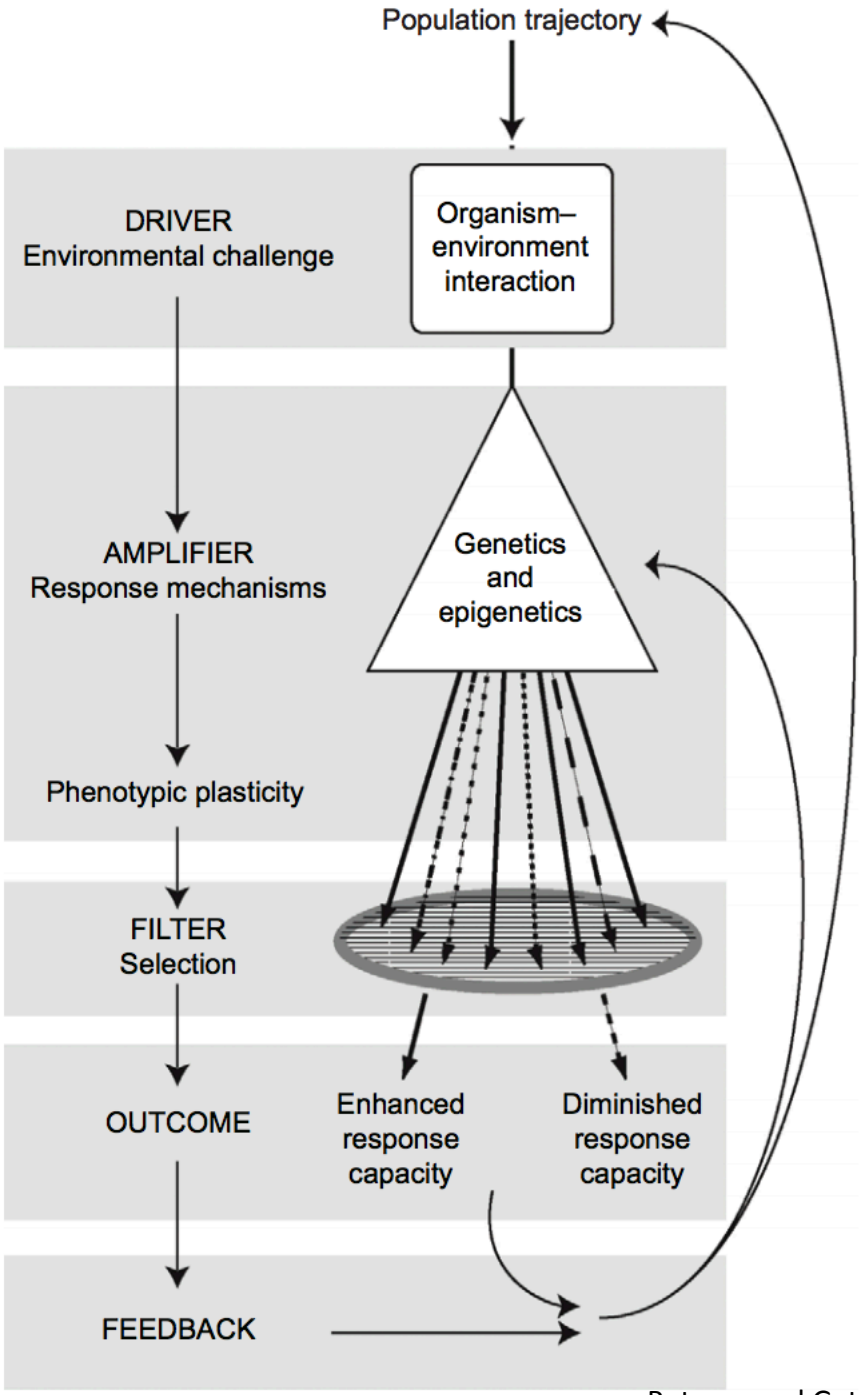


Bossdorf et al. 2008



Bossdorf et al. 2008

Q5: What is the epigenetic role in environmental acclimatization?



Putnam and Gates 2015