CHAIRE ÉPIGÉNÉTIQUE ET MÉMOIRE CELLULAIRE

Année 2023-2024 : 11 mars, 2024

L'épigénétique à l'interface organisme-environnement

Cours II

Comment l'environnement influence-t-il les phenotypes ?

E. Heard

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L'épigénétique à l'interface organisme-environnement

4 mars
Cours 1: Introduction

11 mars
Cours 2: Comment l'environnement influence-t-il les phénotypes ?

18 mars
Cours 3: Exemples d'impacts environnementaux sur le règne animal

25 mars
Cours 4: Exemples d'impacts environnementaux sur le règne végétal

Summary of last week (Cours I)

. Human activity has created the Anthropocene

Ecosystems are being destroyed and some life forms are unable to adapt and are lost.

Major impact for human health and human economies.

E. Heard

Defining the Anthropocene

Simon L. Lewis[1,2] & Mark A. Maslin[1]

Time is divided by geologists according to marked shifts in Earth's state. Recent global environmental changes suggest that Earth may have entered a new human-dominated geological epoch, the Anthropocene. Here we review the historical genesis of the idea and assess anthropogenic signatures in the geological record against the formal requirements for the recognition of a new epoch. The evidence suggests that of the various proposed dates two do appear to conform to the criteria to mark the beginning of the Anthropocene: 1610 and 1964. The formal establishment of an Anthropocene Epoch would mark a fundamental change in the relationship between humans and the Earth system.

- A panel of experts (reportedly) recently voted down a proposal to officially declare the start of the Anthropocene.
- Current extinction rates of species in various orders are estimated to have risen to 100-1,000 times the average extinction rate over the past tens of millions of years (the 'background rate') of 0.1-1 per million species per year (expressed as E/MSY), and are continuing to rise.
- In absolute terms, 1,000 species are becoming extinct every year if 10 million is taken to be the number of species and 100 E/MSY the current extinction rate.

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. Human activity has created the Anthropocene

. The struggle for life in rapidly changing environments

Many species lack obvious strategies to manmade environmental changes....

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https://www.nytimes.com/interactive/2022/12/09/climate/biodiversity-habitat-loss-climate.html

- The current speed of environmental changes means that some life forms are unable to adapt and are lost, and many species' potential to adapt to future environments is lost.

  Faced with such rapid environmental change, populations could go extinct, migrate to more suitable environments, or stay and adapt to the novel conditions.

  Understanding the processes that underlie adaptation in changed environments is critical.

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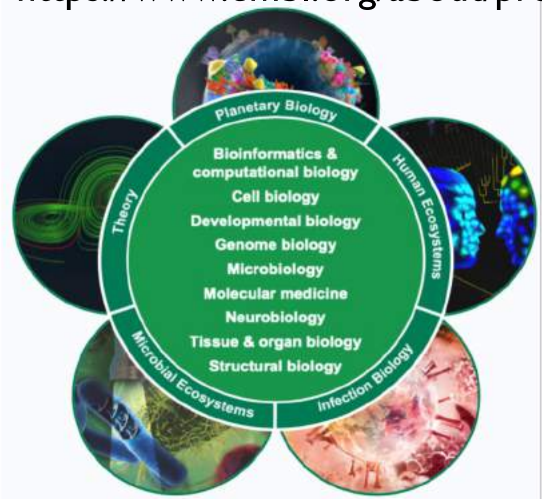
. Exploring life in its rapidly changing natural context
EMBL's Molecules to Ecosystems Programme 2022-2026
https://www.embl.org/about/programme/



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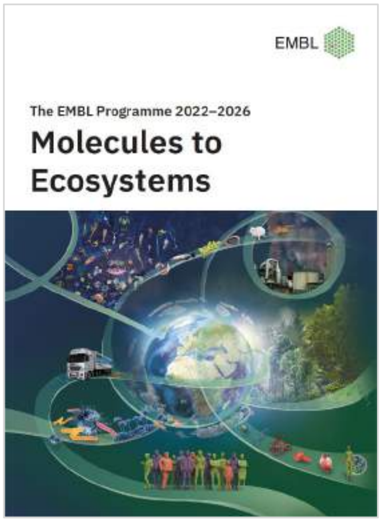

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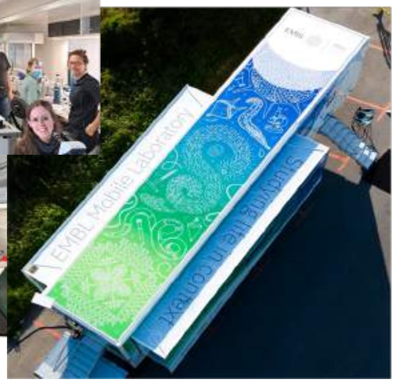
EMBL's Molecules to Ecosystems Programme 2022-2026
Planetary Biology Transversal Theme
TREC Flagship Project in partnership with TARA and EMBRC:

A scientific discovery voyage to explore land-water interfaces



https://www.embl.org/about/info/trec/

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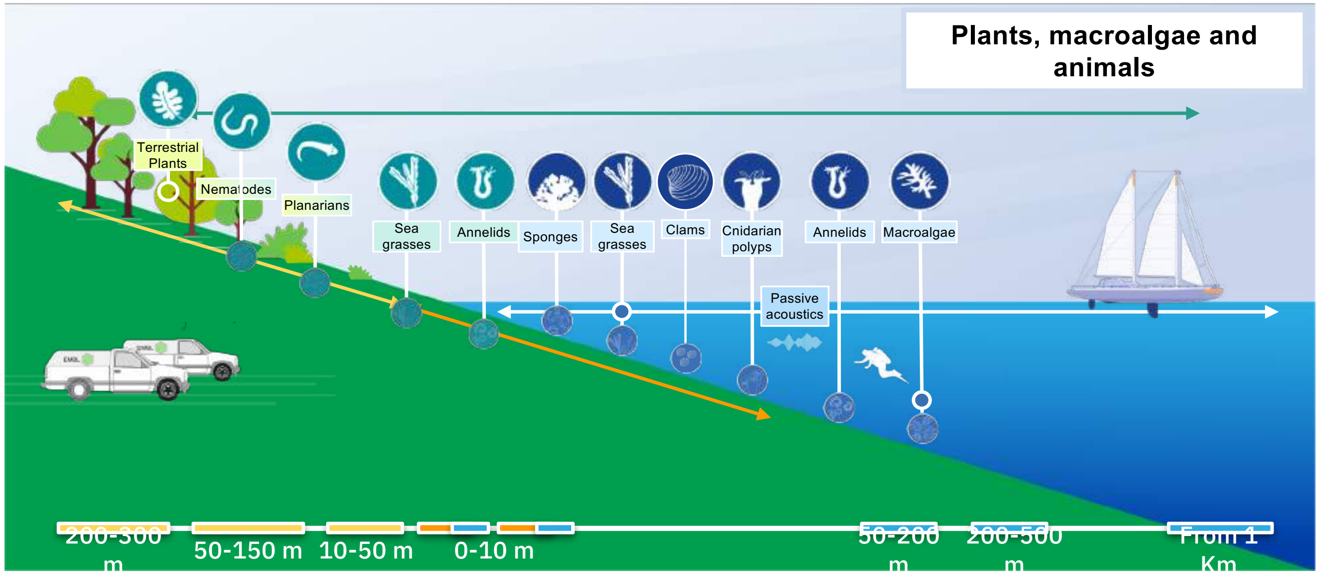

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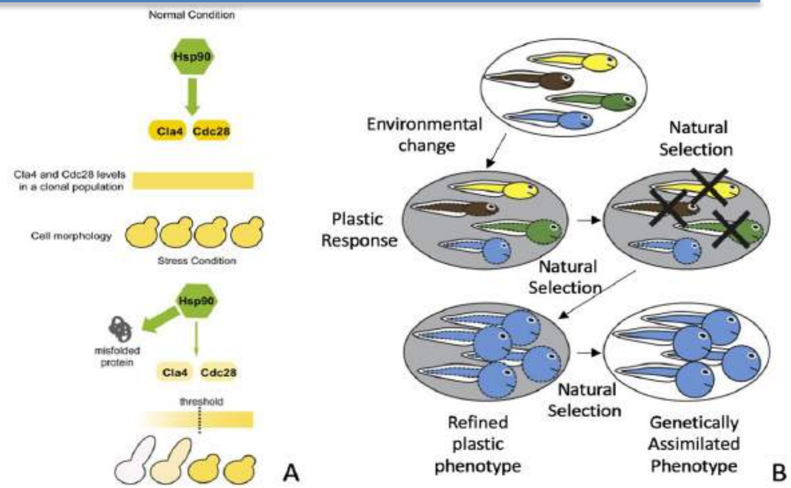
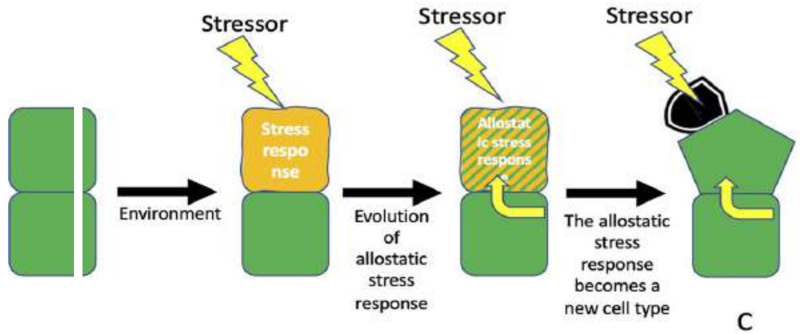
. What processes underlie successful responses to cope with acute stress





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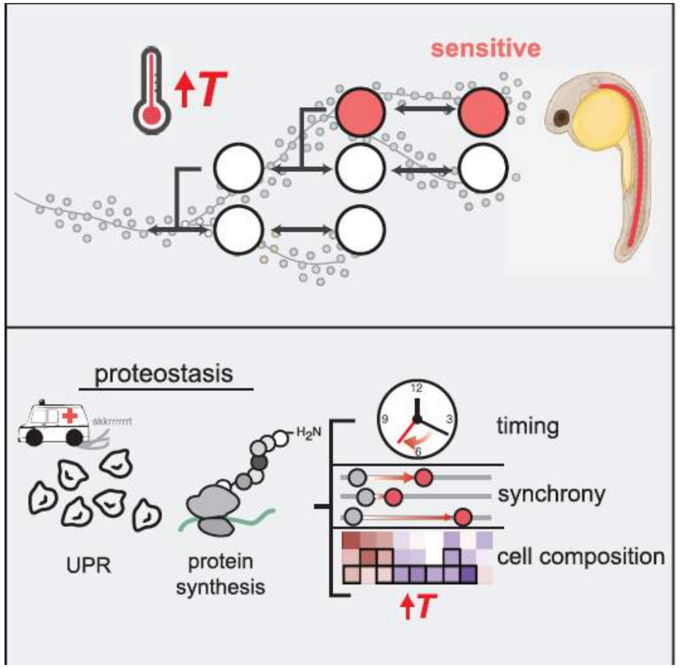
. Maladaptive response to increased temperature can lead to reduced fitness



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. Adaptation to novel environmental conditions

. **evolution via selection for particular phenotypes** – which ultimately results in modification of genetic variation at population level
. **the expression of phenotypic plasticity -** the ability of one genotype to express varying phenotypes when exposed to different environmental conditions
- *phenotypic plasticity is an immediate response that can enable individuals to survive under rapid change*
- *a plastic response can pave the way for permanent adaptations (via mutation-selection)*

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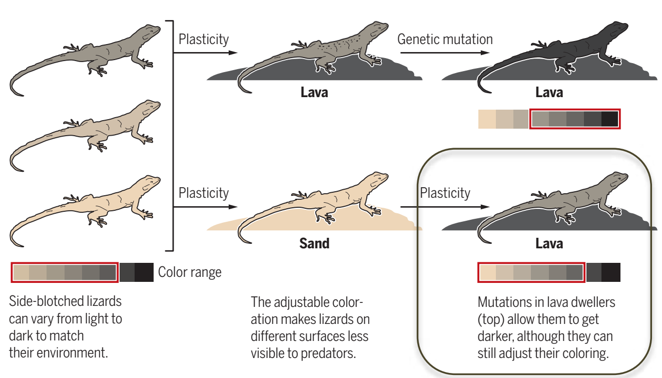
- *PREP* and *PRKA1A* genes regulate coloration and differ between populations on and off the lava
- Mutations in the population adapted to the lava flow make these lizards darker than others.

developed permanent genetic mutations that enabled them to become even darker (photo).



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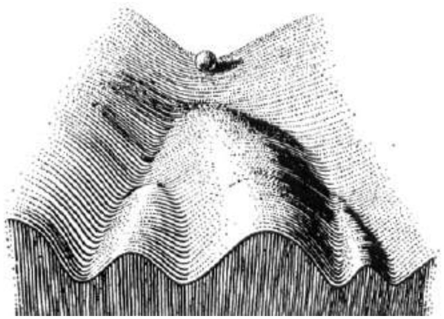
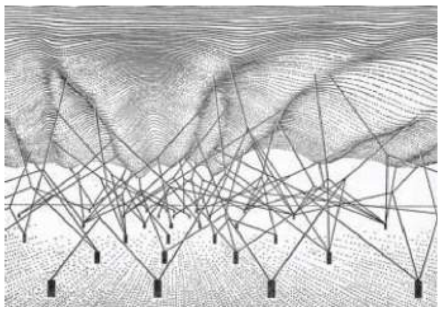
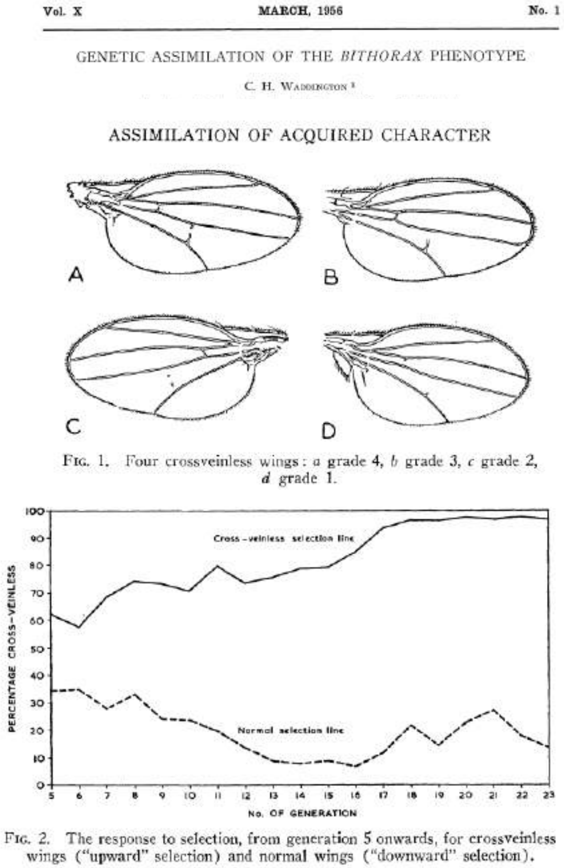
Summary of last week (Cours I)

. Waddington – revisited







Vol. X MARCH, 1956 No. 1

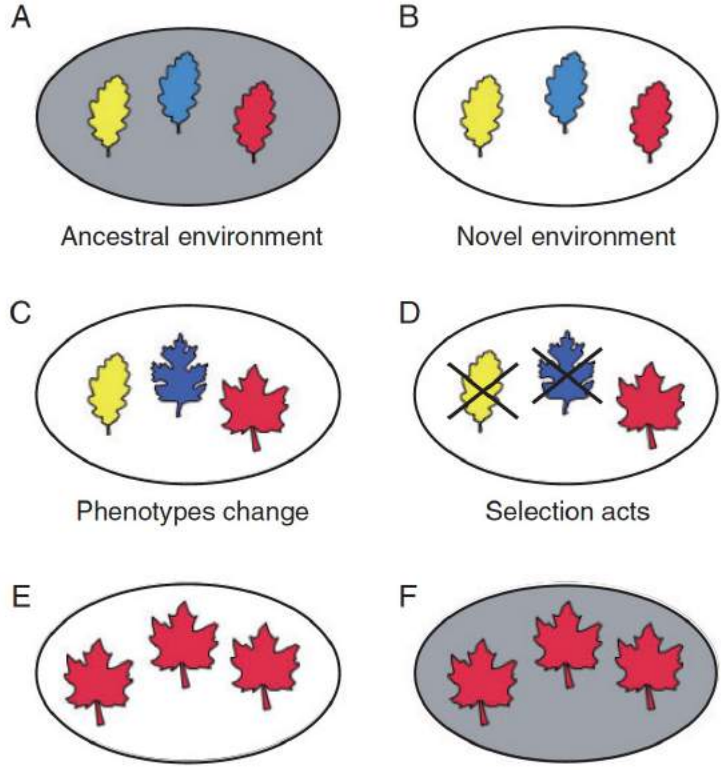
GENETIC ASSIMILATION OF THE *BITHORAX* PHENOTYPE

C. H. WADDINGTON

ASSIMILATION OF ACQUIRED CHARACTER

FIG. 1. Four crossveinless wings: *a* grade 4, *b* grade 3, *c* grade 2, *d* grade 1.

FIG. 2. The response to selection, from generation 5 onwards, for crossveinless wings ("upward" selection) and normal wings ("downward" selection).



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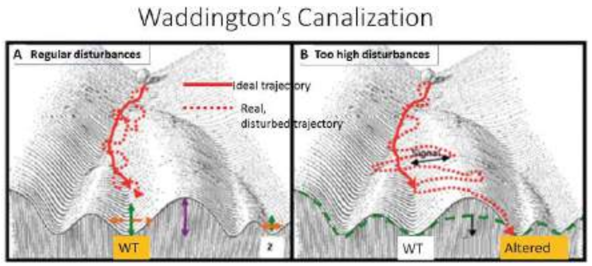
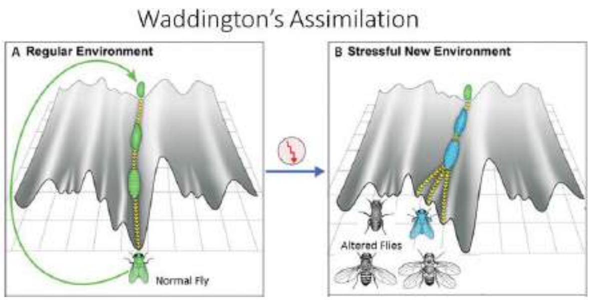
Summary of last week (Cours I)

.Waddington – revisited



(A–B) Waddington's canalization and epigenetic landscape: Diverse and inevitable environmental disturbances and internal developmental noise systematically disturb developmental trajectory on the epigenetic landscape. However, the developmental process usually returns to the basin of normal development (creod), that is, the development is canalized and the canal walls keep the process in the basin prescribed by the genetic program (after http://www.gen.cam.ac.uk/research-groups/martinez-arias).



(A–B) Waddington's genetic assimilation: The environmental stress causes a series of the Drosophila's divergent phenotypes. The untypical, high environmental disturbances deform, change the epigenetic landscape. By doing so, it causes the appearance of new phenotypes in the population under stress. If some of the phenotypes are beneficial, it can be stabilized in the genotype by further selection (after [4]).

Systems Evolutionary Biology of Waddington's Canalization and Genetic Assimilation
Alexander V. Spirov, Marat A. Sabirov and David M. Holloway

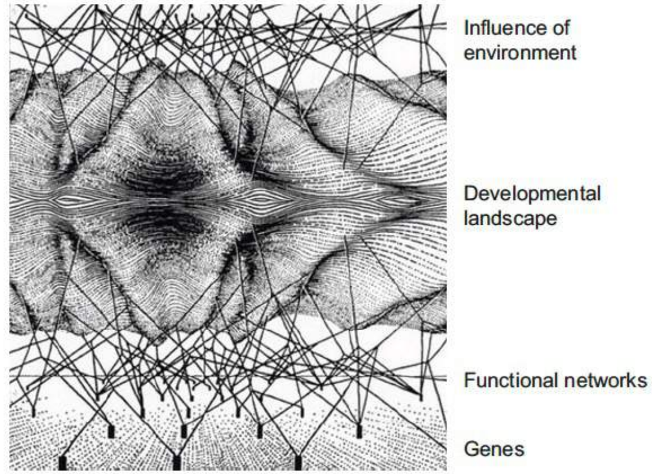


Fig. 2. Waddington's diagram to show how the developmental landscape relates to individual genes (bottom pegs) through networks of interactions in the organism. Since he also showed the influence of the external environment on canalisation of development, I have extended the diagram by adding the top part to represent the environmental influences. It is the combination of these influences that can lead to an evolutionary change without mutations (modified from Waddington, 1957).

From D. Noble, J. Exp. Biol, 2015

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Returning to Waddington

Genetic Assimilation

Genetic assimilation is a process by which a phenotype originally produced in response to an environmental condition, such as exposure to thermal shock or ether, later becomes genetically "fixed" either via artificial selection or natural selection.

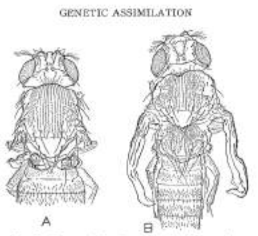
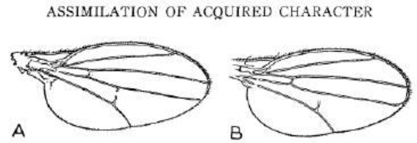
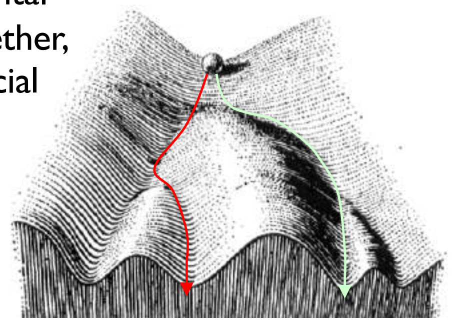


Fig. 2. Two typical phenocopies (medium and extreme in grade). Mesothoracic wings removed in 2a, metathoracic wings partly concealed by the abdomen in 2b.





Different fates

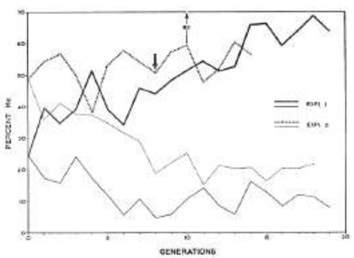


Fig. 1. Percentage of He (= bithorax-like) phenocopies in successive generations of upward and downward selection, following ether treatment of the eggs. The figures relate to flies which emerged from the puparia. At generation 10 in Experiment II, a count was made of all flies in a sample, including those failing to emerge and a percentage of 82 He found. The arrow at gen. 8 in Experiment II indicates the point at which the first assimilated stocks appeared.

E. Heard,

articles

Hsp90 as a capacitor for morphological evolution

Suzanne L. Rutherford*† & Susan Lindquist*

*Howard Hughes Medical Institute, University of Chicago, 5841 South Maryland Avenue MC1028, Chicago, Illinois 60637, USA

The heat-shock protein Hsp90 supports diverse but specific signal transducers and lies at the interface of several developmental pathways. We report here that when *Drosophila* Hsp90 is mutant or pharmacologically impaired, phenotypic variation affecting nearly any adult structure is produced, with specific variants depending on the genetic background and occurring both in laboratory strains and in wild populations. Multiple, previously silent, genetic determinants produced these variants and, when enriched by selection, they rapidly became independent of the Hsp90 mutation. Therefore, widespread variation affecting morphogenic pathways exists in nature, but is usually silent; Hsp90 buffers this variation, allowing it to accumulate under neutral conditions. When Hsp90 buffering is compromised, for example by temperature, cryptic variants are expressed and selection can lead to the continued expression of these traits, even when Hsp90 function is restored. This provides a plausible mechanism for promoting evolutionary change in otherwise entrenched developmental processes.

Buffering (canalization):

Up to a certain threshold, genetic or environmental variation will not affect the pathway

'Canalization' means that, up to a certain threshold, any genetic variation or environmental noise will be 'buffered' and not affect the pathway, but above this threshold, the cell would flip over into an adjacent pathway.

Canalization, or phenotypic robustness is the resistance of developing organisms to change when perturbed genetically or environmentally.
The molecular underpinnings have now started to be uncovered: for ex the molecular chaperone Hsp90, is a protein that facilitates the folding of many key regulators of growth and development
It ensures canalization of phenotypes but can lead to de-canalization in times of stress.

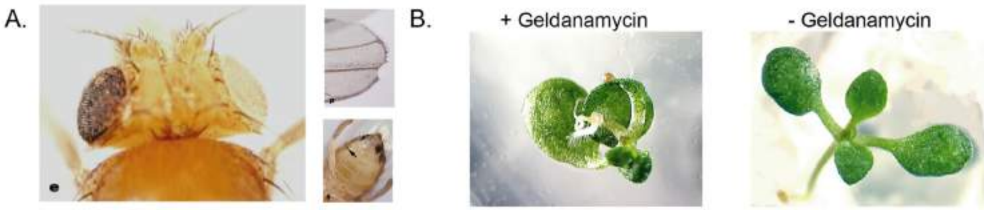
Some genes can change the **topology** of the landscape
- Leading to alternate paths if activated
- Changing cell pathways if mutated

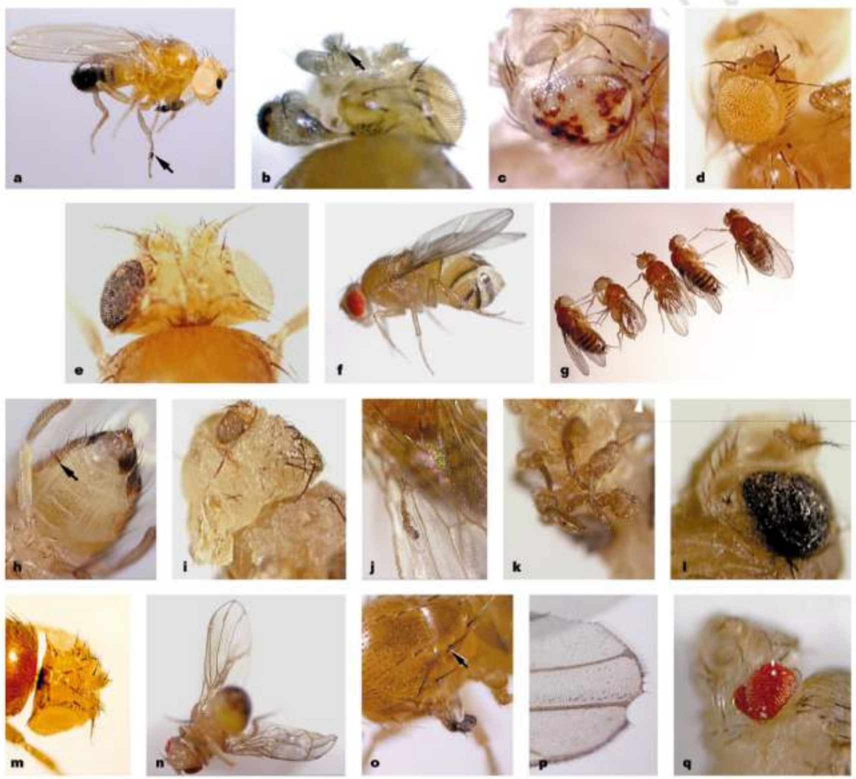
The environment can also alter the landscape….

The role of Hsp90 in canalization

In Hsp90 mutants, cryptic genetic variation is expressed to a greater extent. Hsp90 is a chaperone for signal-transduction and other factors, normally suppressing the expression of genetic variation affecting many developmental pathways.

R.A. Zabinsky et al. / Seminars in Cell & Developmental Biology 88 (2019) 21–35





Disruption of Hsp90 leads to phenotypic variation in nearly every structure of adult D. melanogaster - with different types of variant depending on the genetic background of the flies (ie combination of specific alleles in each individual).

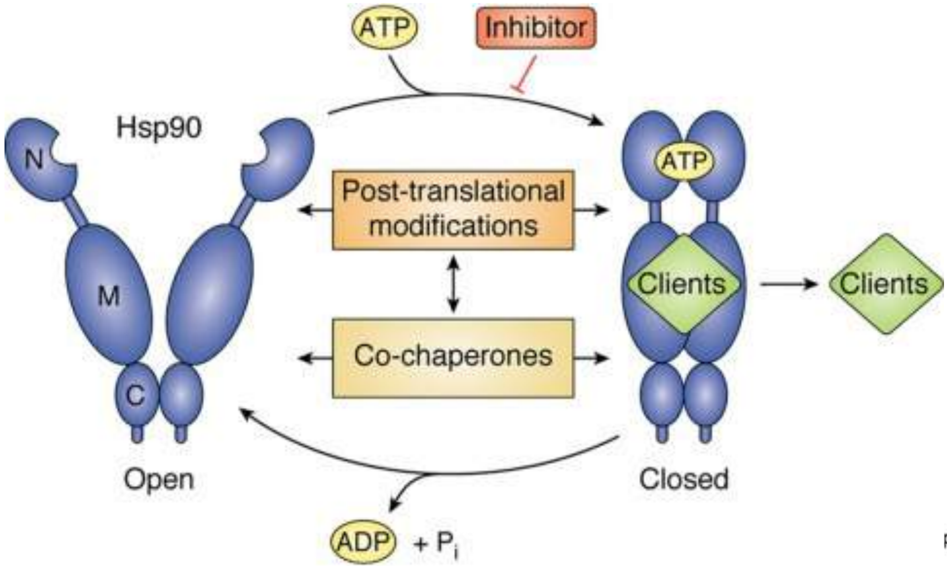
Rutherford and Lindquist concluded that D. melanogaster accumulates hidden genetic variation, which Hsp90 somehow prevents (buffers) from affecting the phenotype. Similar effect in experiments with plants.

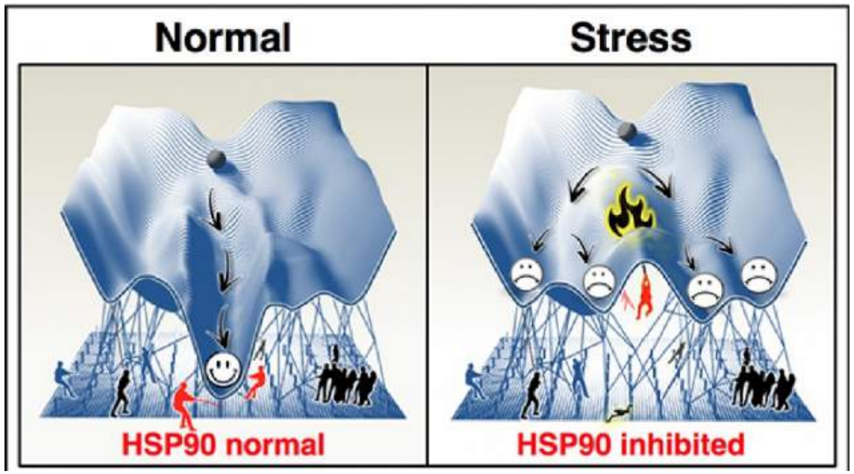
If the function of Hsp90 is partly compromised, the buffer breaks and one can see previously 'unavailable' phenotypic variants. Just like the heat shock or ether shock in Waddington's experiments.

Rutherford and Lindquist also observed rapid genetic assimilation of the Hsp90-dependent traits in D. melanogaster, similarly to Waddington.

Other studies with different organisms/environmental triggers have also shown that the environment can exert a large influence on heritability, <u>presumably by altering the impact of cryptic genetic variation.</u>

The role of Hsp90 in canalization





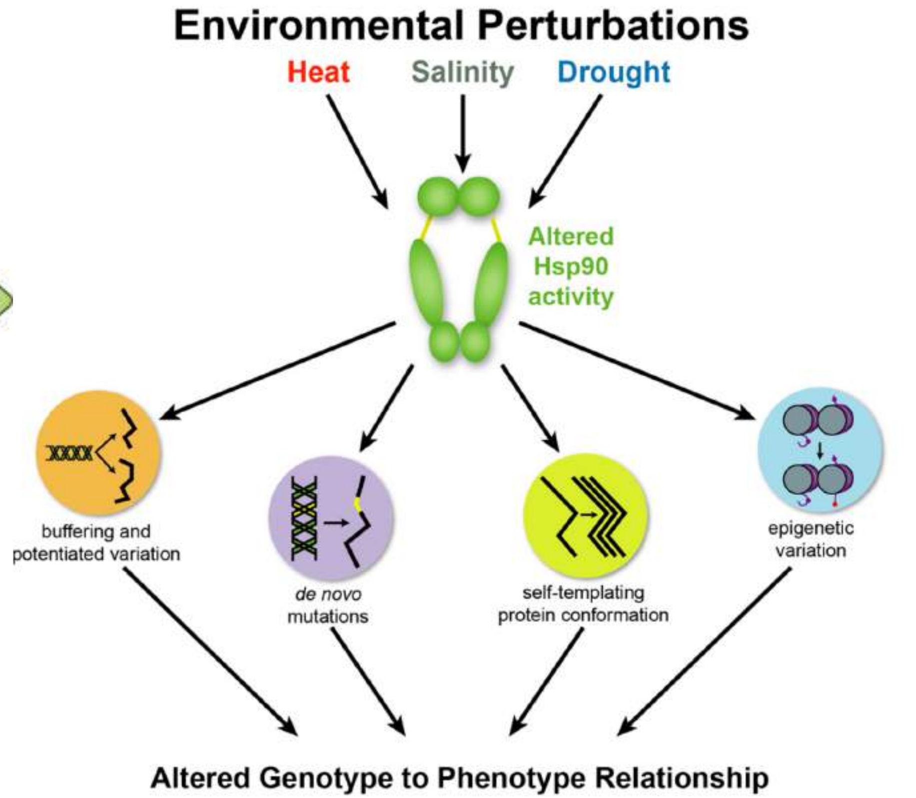
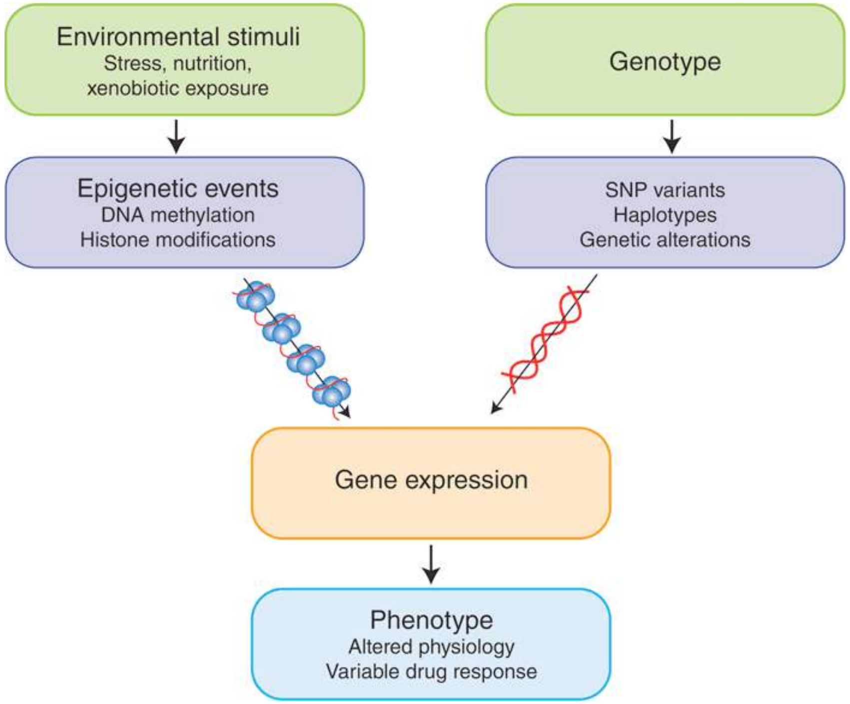
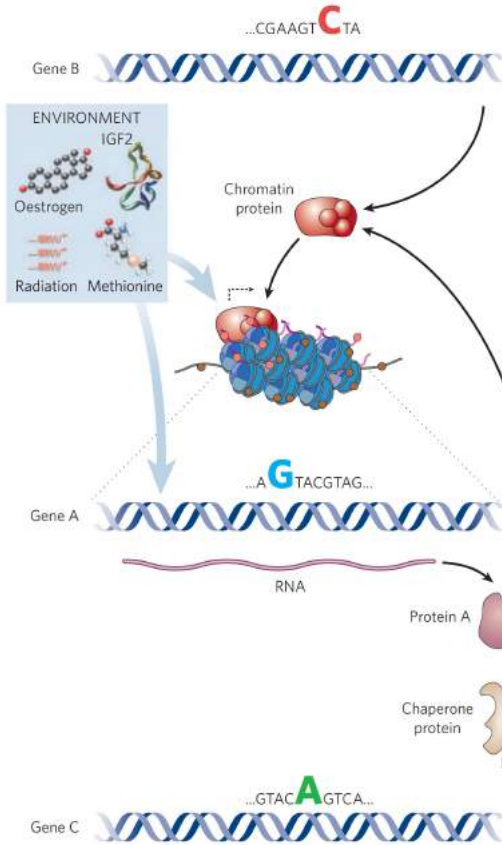


Fig. 5. Environmental perturbations regulate Hsp90, a central node that integrates stress sensing with the manifestation and generation of de novo variants. Many environmental perturbations including heat, salinity, and drought have the potential to alter Hsp90 activity. This altered activity affects cryptic genetic variation, buffered and potentiated variants, *de novo* mutations, self-templating protein conformations, and epigenetic variation. All of these will in turn alter the relationship between genotype and phenotype.

How does the environment influence phenotypes?

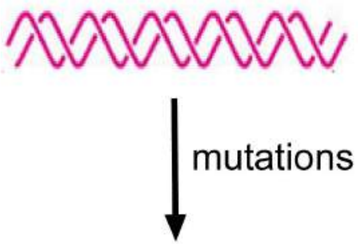




E. Heard

DNA mutations and Epigenetic modifications

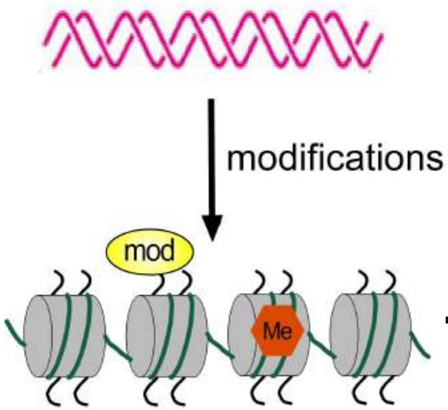
GENETICS



mutations

heritable, stable,
irreversible

EPIGENETICS

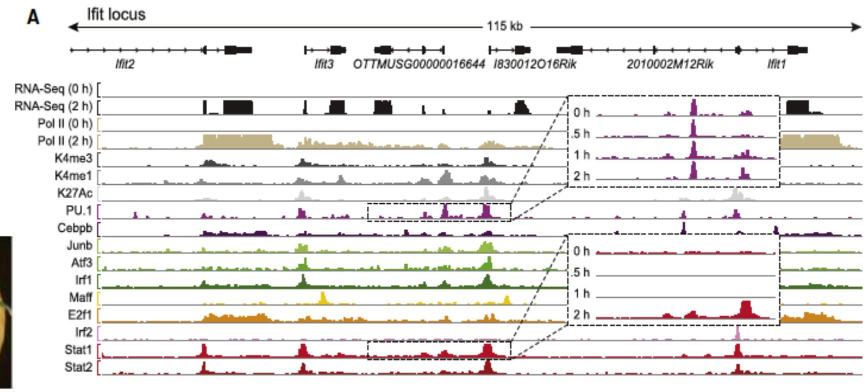


modifications

heritable,
stable (+/-)
reversible

Chromatin states and structures, non-coding RNAs that can be associated with gene expression and genome function

→ EPIGENOMICS

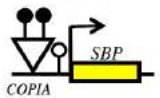


(Manning et al, Nat Genet, 2006)

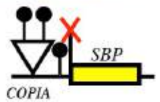
DNA sequence changes :
ATGC -> AGGC

Epigenetic changes :
ATGC -> ATGC*

CNR



cnr



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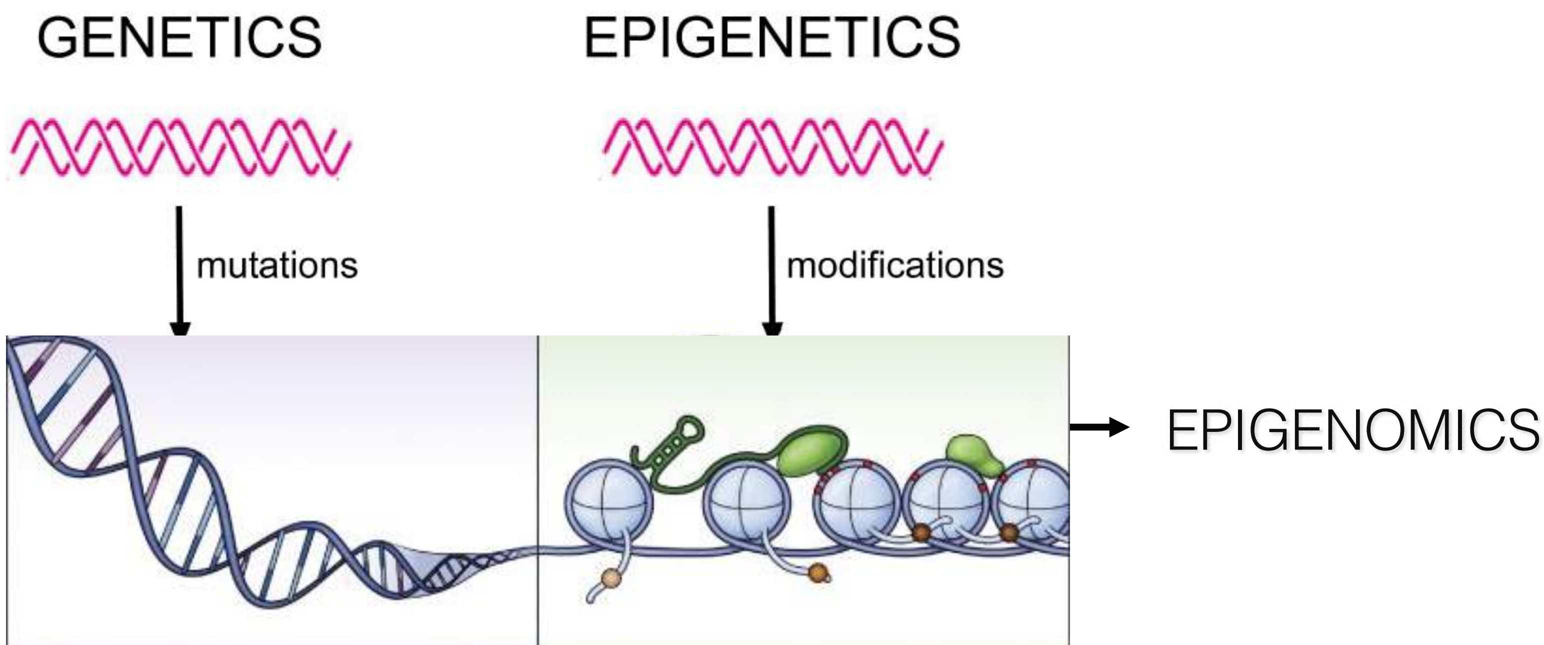
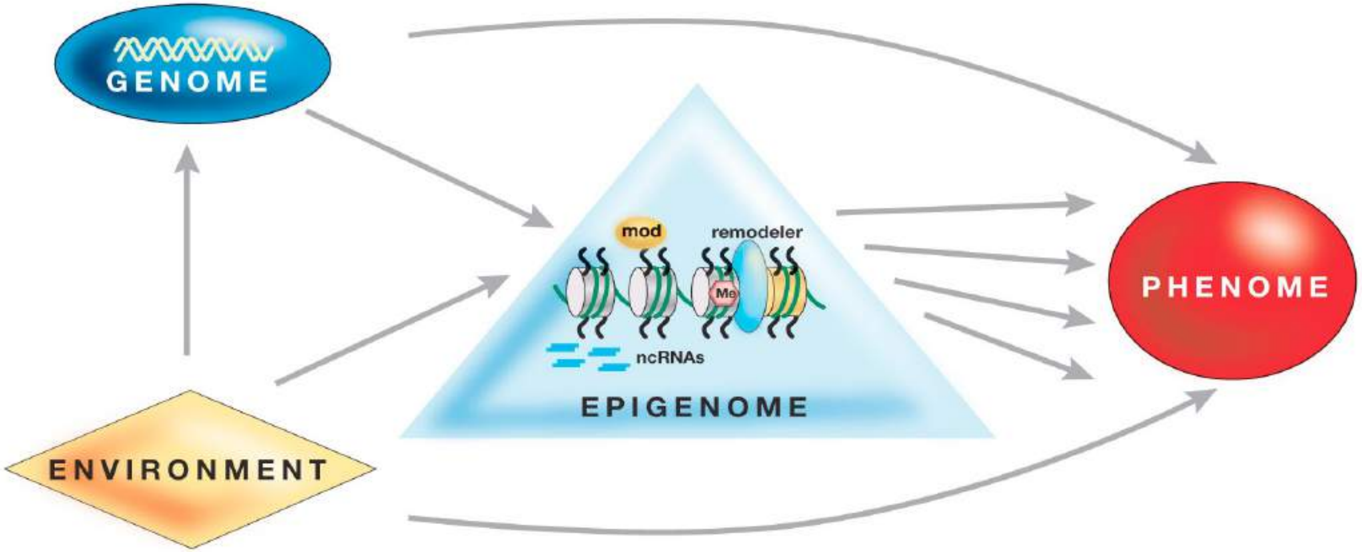
DNA mutations and Epigenetic modifications



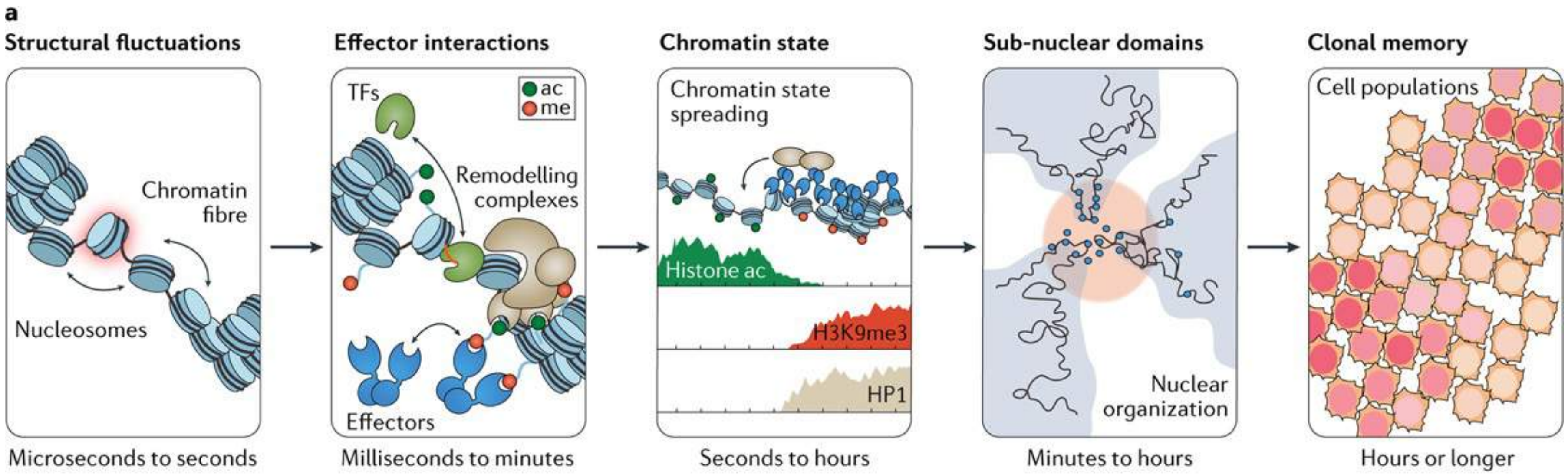
Primary nucleotide sequence is seminal	DNA-based modifications, post-translational modifications of histones, non-coding RNA
Mendelian inheritance	Responsive to environment
Strong evolutionary conservation	Rapid evolutionary divergence
Identical in all cell types	Differs between cell types
Highly conserved during mitosis and meiosis	Semi-conserved during mitosis and meiosis

Epigenomes as Integrators of the Environment



Thus the "Phenome" or phenotypic output can defined by DNA sequence (genetics), chromatin regulation (epigenetics and cellular memory) and environmental variables (e.g. nutrition), and their interactions

Epigenetic Modifications



Chromatin: the physiological template of the genome

Transcriptional activation or repression via DNA-sequence binding transcription factors (TFs), Chromatin Remodellers and Chromatin Modifiers

Chromatin spreading

Nuclear compartments of active and inactive chromatin

Epigenetic memory systems such as:

Polycomb (PRC)
HP1 and Suv39
DNA methylation

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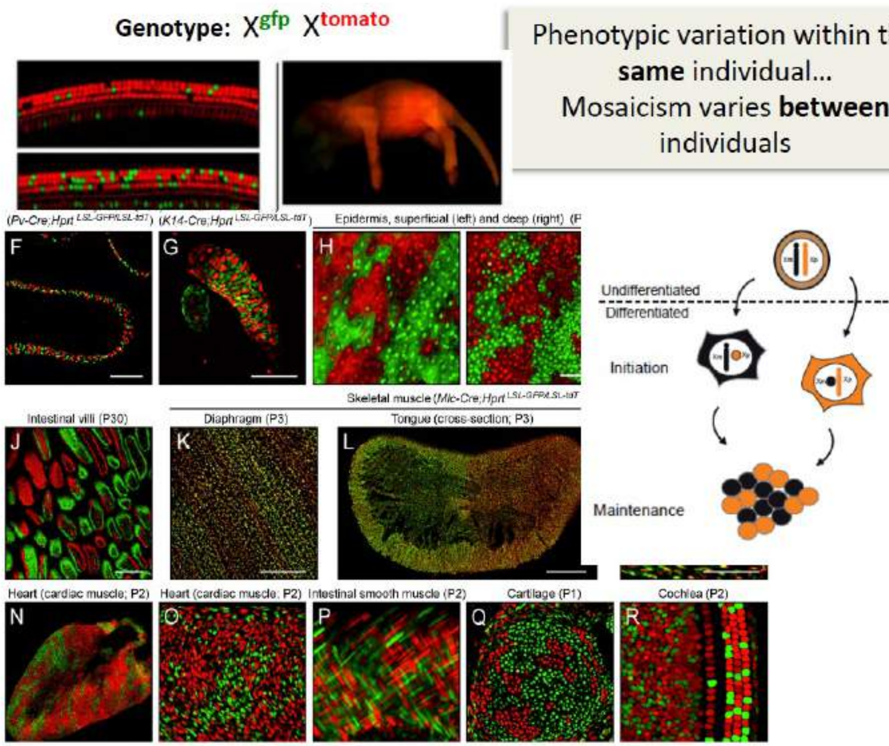
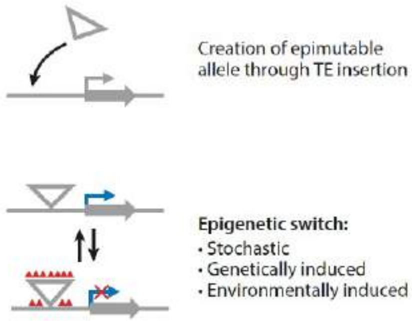
Phenotypic variation within and between individuals

DNA – the genome - remains the blueprint for an individual organism, but epigenetic modifications are important in development, adult physiology, phenotypic plasticity, and can account for variation both *within* and *between* individuals, including individuals that are genetically identical.



Wu et al (2014) "Cellular Resolution Maps of X Chromosome Inactivation: Implication for Neural Development, Function, and Disease." *Neuron* 81, 103–119



TE-containing alleles of genes can become epimutable due to epigenetic silencing mechanisms

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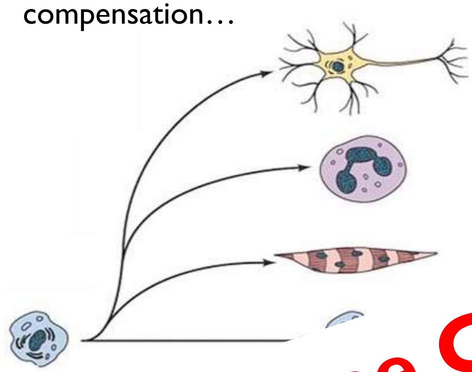
Phenotypic variation within and between individuals

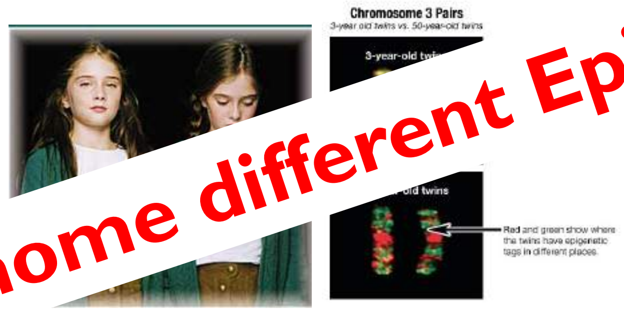
DNA – the genome - remains the blueprint for an individual organism, but epigenetic modifications are important in development, adult physiology, phenotypic plasticity, and can account for variation both *within* and *between* individuals, including individuals that are genetically identical.

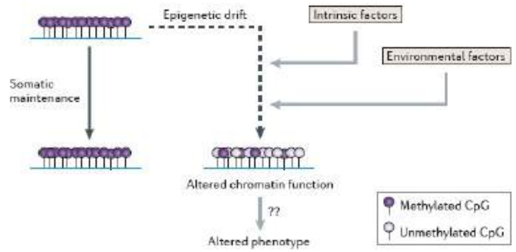
Differences can be established and influenced by STOCHASTIC events and by the ENVIRONMENT

Developmental epigenetics:
Development, sex chromosome dosage compensation…

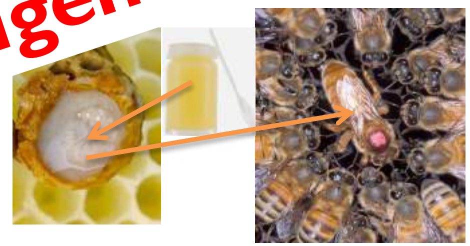


Stochastic epigenetic events:
Differences in twins, clones…
Disease « epimutations »





Exogenously / envir… entally programm… …cs :
Be…
…mperature/seasons



0 3 6
Weeks of vernalization (4°C)

Same Genome different Epigenomes

E. Heard

How does the environment influence phenotypes?

Phenotypic plasticity within a lifetime

Environmentally programmed phenotypes

Environmentally induced cross-generational parental phenotypes

Environmentally induced trans-generational phenotypes

Environmentally induced trans-generational bet-hedging / phenotypic plasticity

Environmentally plastic responses that pave the way for *permanent* adaptations

Impact of rapid and dramatic changes in environment on phenotypes: stress, survival, adaptation or extinction

Phenotypic Plasticity and Polyphenism

Developmental and Phenotypic Plasticity, Polyphenism

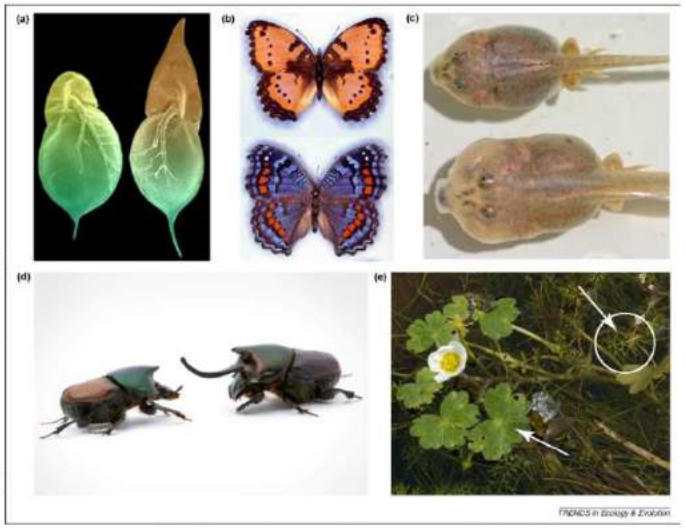
- Most species can display some degree of phenotypic plasticity – either distinctly stable « morphs » - or continuum of traits

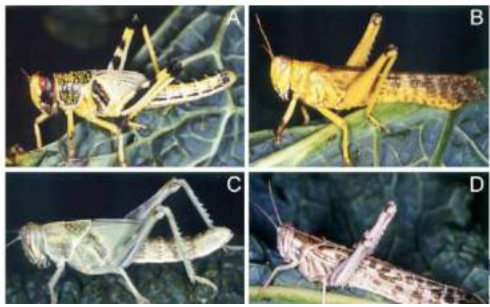
- It can be functional (and potentially adaptive), inevitable (neutral or deleterious)

- It can an be restricted to a few minutes, to a whole life time, or to many generations

- How one genotype can give rise to different phenotypes through environmental effects is clearly an EPIGENETICS question

- Back to Waddington's original definition – but actual mechanisms are still elusive





E. Heard

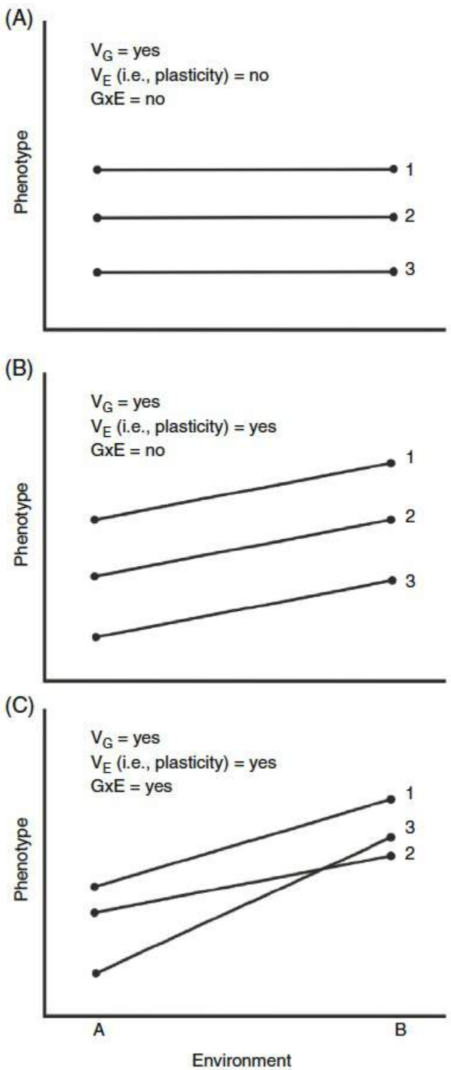
Voir COURS 2018-2019

Phenotypic Plasticity

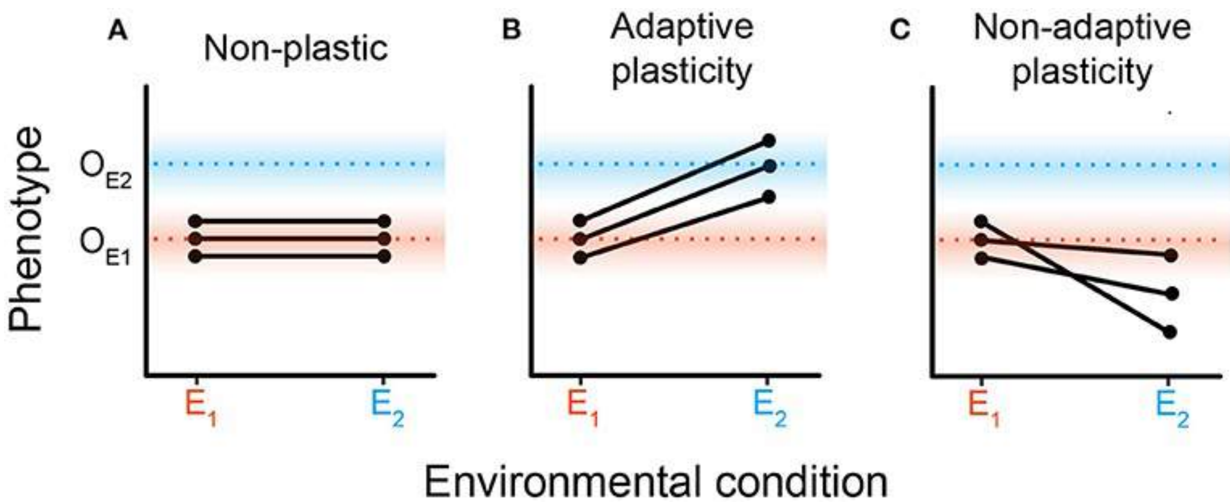
- One genotype can produce more than one phenotype when exposed to different environments
- The modification of developmental events by the environment
- Ability of an individual organism to alter its phenotype in response to changes in environmental conditions.
- Whether plasticity aids **adaptive evolution** depends on how it improves the fitness of individuals.
- Predator avoidance, insect wing polymorphisms, timing of metamorphosis in amphibians, osmoregulation in fishes, reproductive tactics in male vertebrates all appear to be adaptive.
- A plastic response is said to be ‘adaptive’ when it allows genotypes to express phenotypes more close to the environmental optimum, and it is called ‘maladaptive’ otherwise
- Plasticity may be maladaptive under extreme environments, unless genetic correlations are strong between extreme and non-extreme environmental states, and the optimum phenotype changes smoothly with the environment.

Pristimantis mutabilis skin texture transformation
Juan Guayasamin (2015) The Zoological Journal of the Linnean Society

Phenotypic Plasticity Revisited



- Genotypes may differ phenotypically within one environment, differ phenotypically in yet another environment, but all show the same basic developmental or physiological response to this environmental variation.
- In such a case, these genotypes are phenotypically plastic—that is, they exhibit "reaction norms" of non-zero slope—for the trait of interest, but the reaction norms are all parallel.
- The environmentally induced phenotypic differences within each genotype are often referred to as "non-genetic" or "environmental" differences.



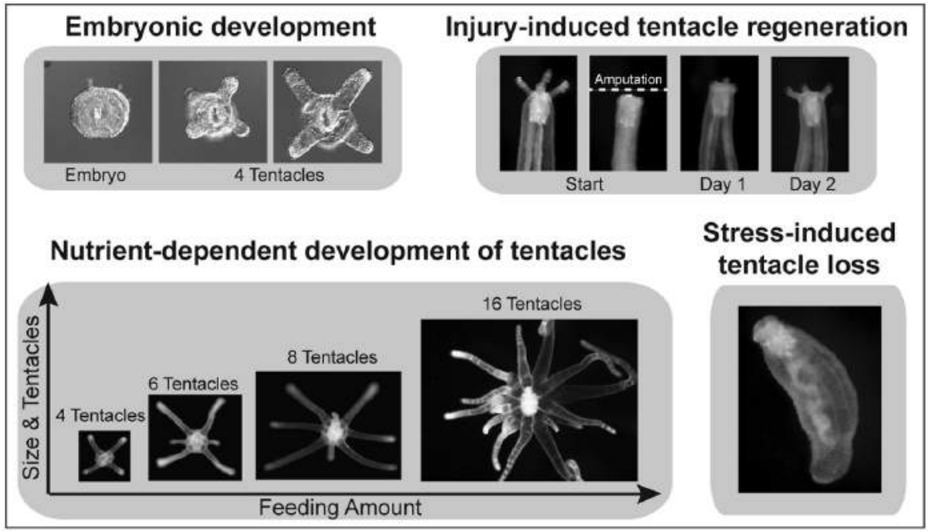
How does the nutritional environment influence phenotypes?

Organism-environment interactions and development

https://doi.org/10.1038/s41467-020-18133-0 OPEN

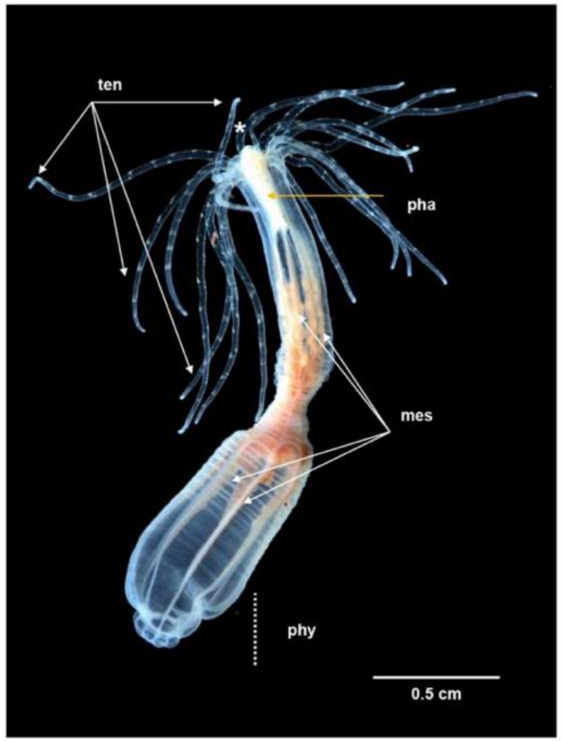
Feeding-dependent tentacle development in the sea anemone *Nematostella vectensis*

Aissam Ikmi[1,2], Petrus J. Steenbergen[1], Marie Anzo[1], Mason R. McMullen[2,3], Anniek Stokkermans[1], Lacey R. Ellington[2] & Matthew C. Gibson[2,4]



Cnidarians, show remarkable developmental plasticity.

B. *Nematostella* morphology



E. Heard

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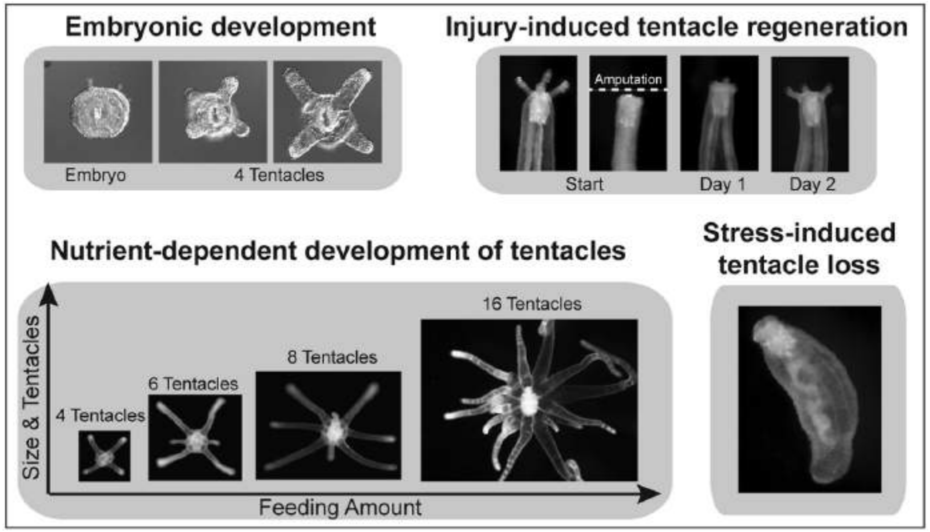


Cnidarians, show remarkable developmental plasticity.

How do they cope with fluctuations of food availability?

- Use the *tentacles* of the sea anemone Nematostella vectensis as an experimental paradigm for developmental patterning across distinct life history stages.
- By analyzing over 1000 growing polyps, we find that tentacle progression is stereotyped and occurs in a feeding-dependent manner.
- Using genetic, cellular and molecular approaches, find that crosstalknbetween Target of Rapamycin (TOR) and Fibroblast growth factor receptor b (Fgfrb) signaling in ring muscles defines tentacle primordia in fed polyps.
- Fgfrb-dependent polarized growth is observed in polyp but not embryonic tentacle primordia.
- Unexpected plasticity of tentacle development, and link post-embryonic body patterning with food availability.

How does the environment influence phenotypes?

Phenotypic plasticity within a lifetime

Environmentally programmed phenotypes

Environmentally induced cross-generational parental phenotypes

Environmentally induced trans-generational phenotypes

Environmentally induced trans-generational bet-hedging / phenotypic plasticity

Environmentally plastic responses that pave the way for *permanent* adaptations

Impact of rapid and dramatic changes in environment on phenotypes: stress, survival, adaptation or extinction

Environmentally programmed phenotypes

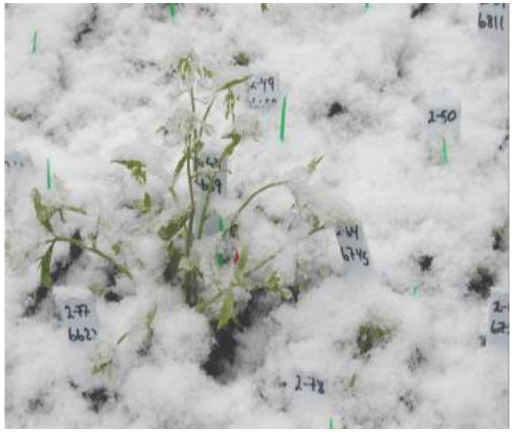
In nature, environment and timing are crucial…

• Correct timing of flowering is key to reproductive success

• Eg to ensure that reproductive development and seed production occurs in spring and summer, not autumn

• Multiple pathways have evolved to mediate different environmental and endogenous cues

• Eg. Longer days as well as cold temperatures are required for winter **wheat** plants to go from the vegetative to the reproductive state (*VRN1*, *VRN2*, and *FT* (*VRN3*) genes)

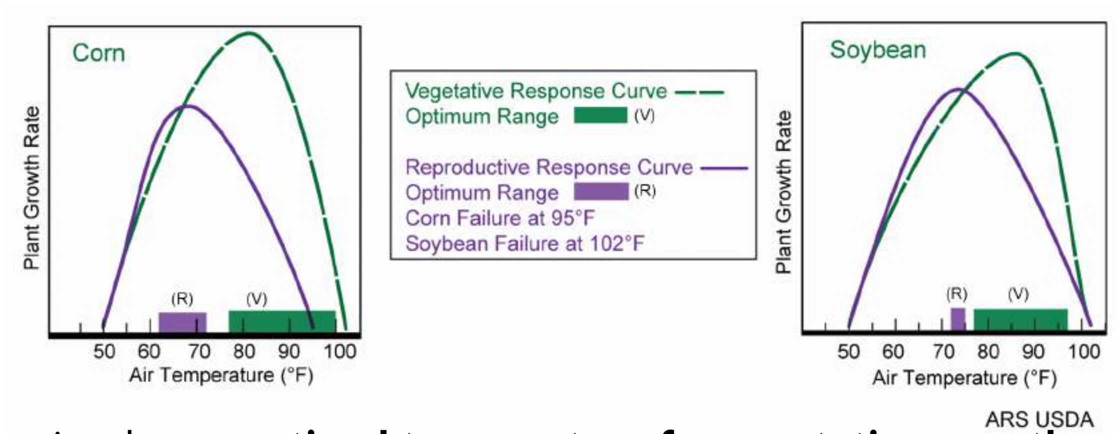


J. Stinchcombe

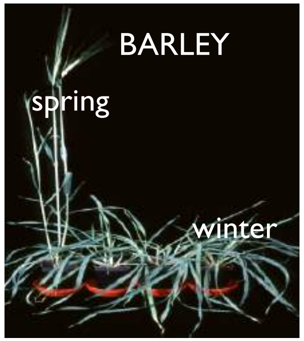
Courtesy of C. Dean

COLLÈGE DE FRANCE 1530

Temperature programmed phenotypes in Plants



Every plant variety has an **optimal temperature for vegetative growth**, and a **specific range of temperatures at which a plant will produce seed**. Outside of this range, the plant will not reproduce. Eg corn will fail to reproduce at temperatures above 95 °F (35 °C) and soybean above 102 °F (38.8 °C).



Many plants are completely dependent on subtle aspects of the weather to survive Eg **Vernalization** – a period of cold required for appropriate flowering timing

Plants that need to be vernalised include important food species such as sugar beet and wheat, which feed millions and provide much-needed income globally.

Phenotypic Plasticity and the evolutionary success of Insects

- **Polyphenisms are thought to be a major reason for the success of the insects.**
- They can deploy the same genome to produce developmentally and environmentally alternative phenotypes in order to:
  - Partition life history stages (feeding larval stages versus reproducing, dispersing adults)
  - Adopt phenotypes that best suit predictable environmental changes (seasonal morphs)
  - Adopt phenotypes that best suit 'predictably unpredictable' environmental shifts such as the transformation of desert environments after unpredictable rain or the degradation of an environment by overcrowding.
  - Partition labour within social groups: eusocial insects.

The developmental stages of insects provide some of the most striking examples:

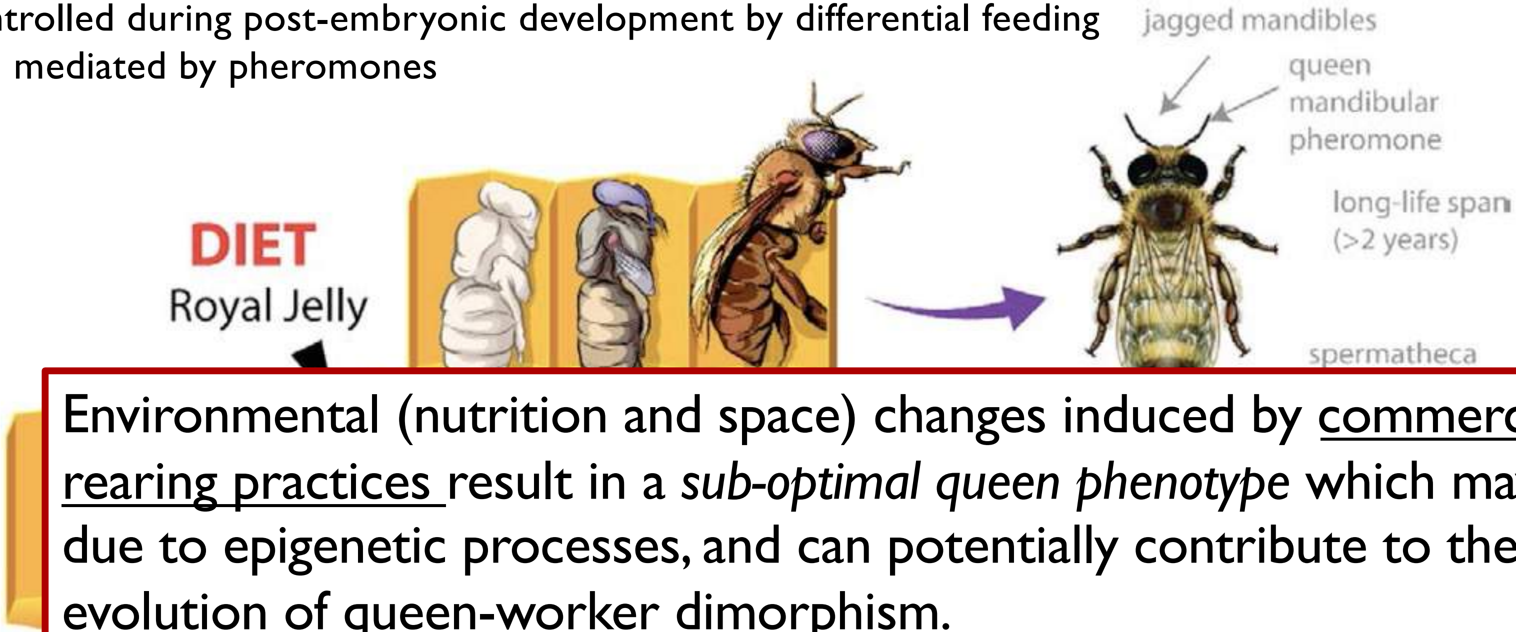
- the transition from larva to pupa to adult in holometabolous (discontinuously developing) insects such as the Lepidoptera (moths and butterflies), Coleoptera (beetles), Hymenoptera (ants, bees and wasps) and Diptera (true flies).

Seasonal morphs are exemplified by the aphids and Lepidoptera
Density-dependent phenotypes (locusts)
Plastic sexually selected phenotypes (horned beetles),
Diet-mediated phenotypes (some caterpillars and in the castes of social insects)

What kinds of sensory cues trigger shifts in phenotype?
What are the neurochemical and hormonal pathways that mediate the transformation?
What are the molecular genetic and epigenetic mechanisms involved in initiating and maintaining the polyphenism?
In a rapidly altered environment, can phenotypic plasticity in fact be maladaptive?

Nutritionally programmed phenotypes in Bees

Queen–worker morphological and reproductive divide is environmentally controlled during post-embryonic development by differential feeding and mediated by pheromones



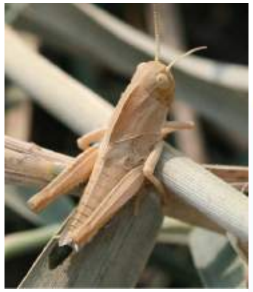
Environmental (nutrition and space) changes induced by <u>commercial rearing practices</u> result in a *sub-optimal queen phenotype* which may be due to epigenetic processes, and can potentially contribute to the evolution of queen-worker dimorphism.

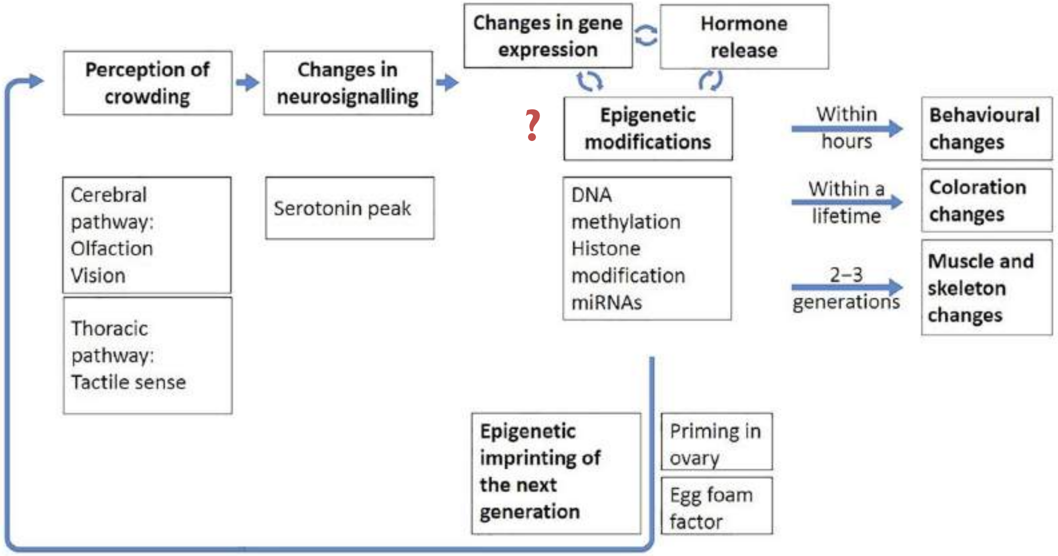
This has probably contributed to the global increase in honeybee colony failure rates.

Climate change is also impacting bees forcing them north to cooler climates and causing spring flowers to bloom earlier than normal leaving less time for the bees to pollinate them.

E. Heard,

Epigenetic and Phenotypic Plasticity in Locusts





Initiation of phase transition

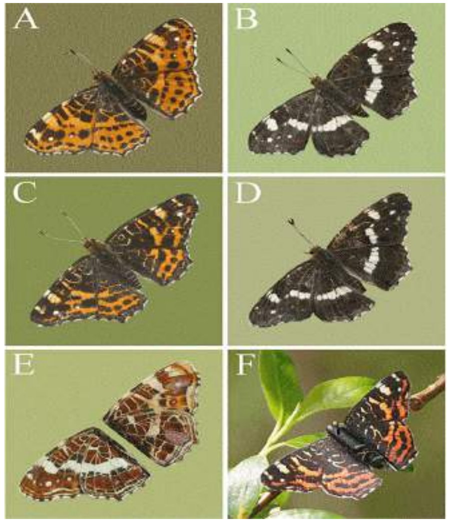
Visual, olfactory and/or mechanosensory information (hindlegs or antennae)

- Tactile information of degree of crowding experienced by the mother directly influences the colour of hatchlings in S. gregaria and L. migratoria => maternal factor (Maeno et al., 2011).
- An alkylated L-DOPA analogue isolated from egg foam, can induce gregarious behaviour in nymphs hatched from treated eggs deposited by solitarious females (Islam, 2013; Miller et al., 2008).

Juvenile hormone (JH) in conjunction with corazonin (*undecapeptide*) account for body colour polyphenism – but cannot induce phase transition.

Seasonally programmed phenotypes in Insects

Seasonal Polyphenism in Butterflies and Moths



Seasonal Morphs

The European map butterfly Araschnia levana:
A, spring female; B, summer female;
C, spring male; D, summer male;
E, ventral side of the wings of a spring female (top) and a summer female (bottom); F, a spring male dummy attacked by a bird in the field.

Response to climate change in the seasonal polyphenism of Colias eurytheme butterflies

« Unfortunately, anthropogenic climate change poses an extra challenge for organisms which use photoperiod as a cue. Photoperiod can be used as a cue for seasonal conditions because of a consistent historical relationship between time of year and temperature… contemporary photoperiods no longer predict the same temperatures that they once did, creating a mismatch between the cue (photoperiod) and selective environment (temperature). This would lead organisms to produce the wrong seasonal morph for at least some of the year. »

Matt Nielsen https://www.lep-net.org/4

E. Heard

Seasonally programmed phenotypes in Insects

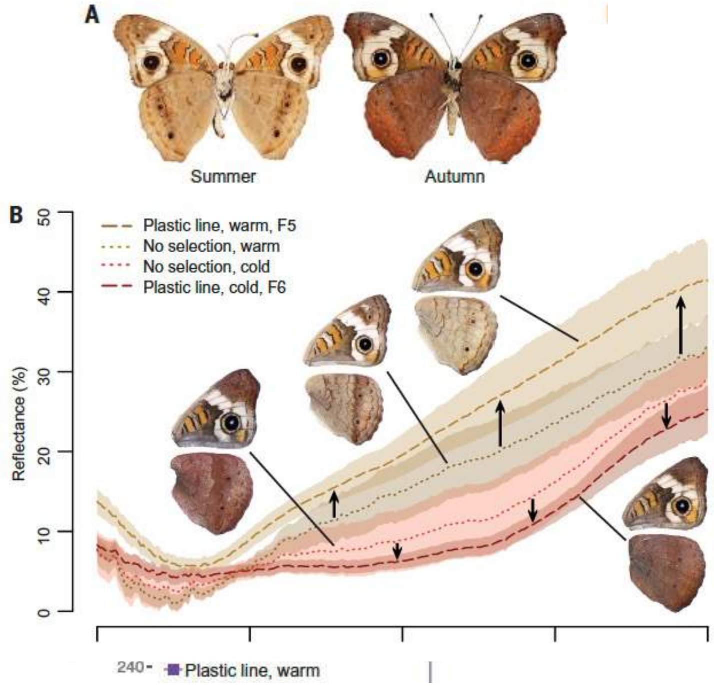
ECOLOGICAL GENOMICS

Genomic architecture of a genetically assimilated seasonal color pattern

Karin R. L. van der Burg[1*], James J. Lewis[1,2], Benjamin J. Brack[1], Richard A. Fandino[1], Anyi Mazo-Vargas[1], Robert D. Reed[1*]

Untangling the genetics of plasticity

- The common buckeye butterfly, *Junonia coenia*, exhibits plastic coloration; it has two color morphs, light tan and dark red, that depend on day length and temperature.
- By selecting for more and less color plasticity (similarly to Waddington's alternate selection regime) van der Burg *et al.* generated butterfly lines that were used to map the genetic variants that underlie differential coloration.



A) Seasonal morphs of J. coenia.
B) Wing color response differences after six generations of selection for increased plasticity (warm = 27°C and 16 hours of light, cold = 19°C and 8 hours of light).

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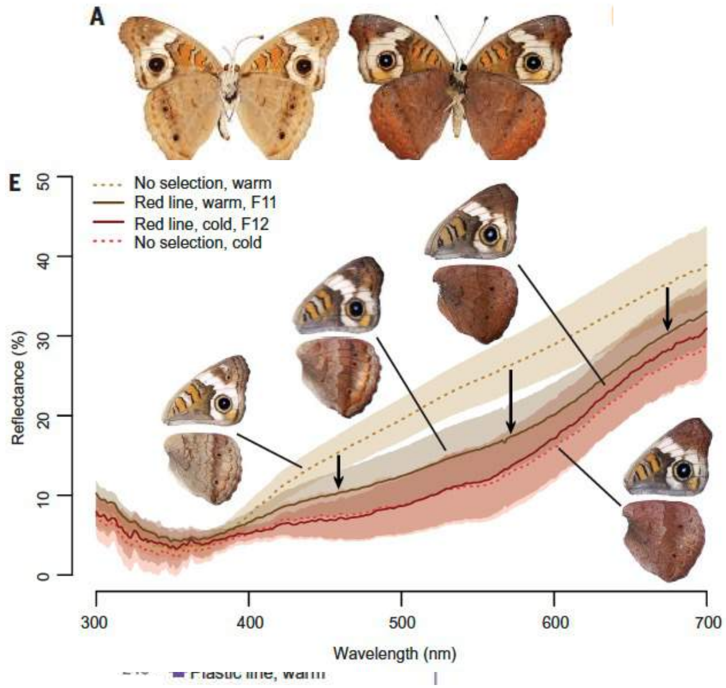

A) Seasonal morphs of J. coenia.
B) Wing color response differences after six generations of selection for <u>increased plasticity</u>
E) Wing color response differences after 12 generations of selection for <u>reduced plasticity.</u>

Seasonally programmed phenotypes in Insects

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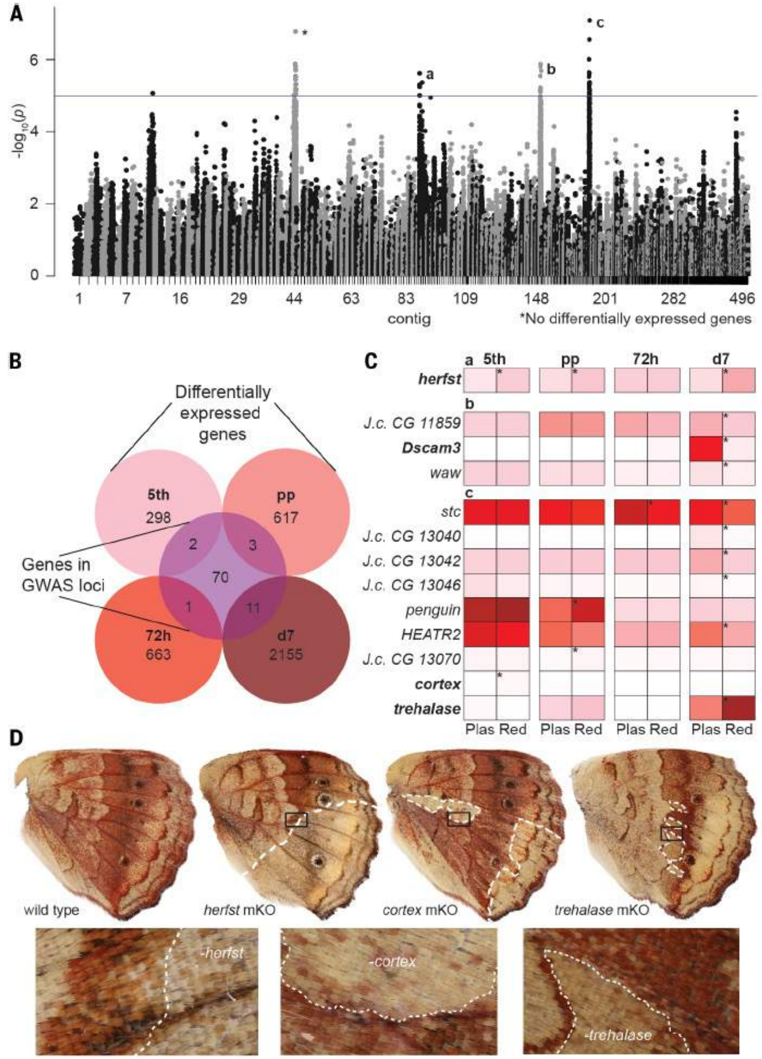

- Genome-wide analysis and RNA sequencing identified the genes most likely to be associated with the differences in color plasticity.
- Inactivation of genes with CRISPR–Cas9 identified three genes (*herfst*, *cortex*, and *trehalase*) that affected the red phenotype, and other techniques identified cis-regulatory, noncoding genomic variants that were correlated with coloration.
- From these results, the authors were able to model how genetically encoded plasticity and assimilation of the plastic trait likely evolved.

E. Heard

Seasonally programmed phenotypes in Insects

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- Theoretical model where assimilation occurs by the appearance of a genetic cue that replaces the environmental cue to induce a phenotype. In J. coenia, differential expression of three genes across wing development, independent of endocrine signaling, can underlie the genetic cue through which assimilation of wing color evolves.

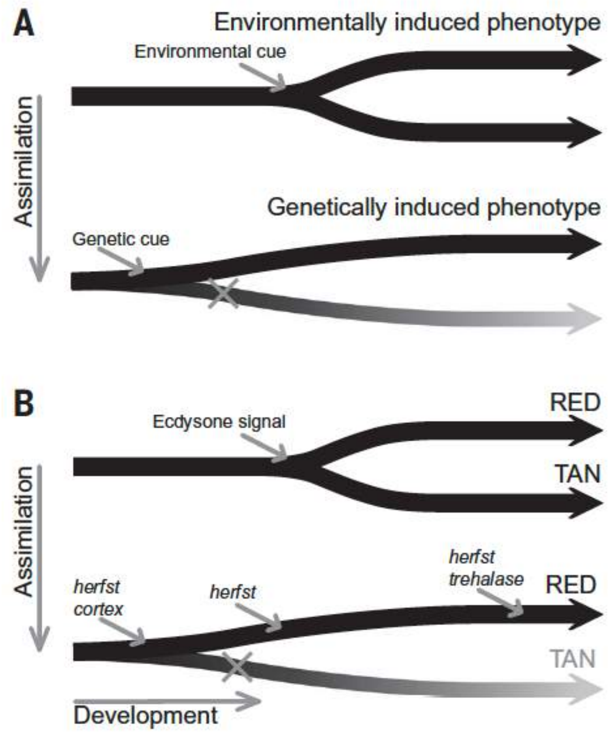

Fig. 4. Multigenic evolution of genetic assimilation. (**A**) Theoretical model where assimilation occurs by the appearance of a genetic cue that replaces the environmental cue to induce a phenotype. (**B**) In *J. coenia*, differential expression of three genes across wing development, independent of endocrine signaling, can underlie the genetic cue through which assimilation of wing color evolves.

Seasonally programmed phenotypes in Insects

ECOLOGICAL GENOMICS

Genomic architecture of a genetically assimilated seasonal color pattern

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More Next Week!

Surprise RNA paints colorful patterns on butterfly wings

Understudied means of regulating genes is likely widespread in butterflies—and perhaps other animals

By Elizabeth Pennisi

A mutant butterfly for sale on eBay has helped upend naturalists' picture of how butterfly wings acquire their intricate variety of red, yellow, white, and black stripes. It and recent research into other butterflies show how visible traits in many animals may be controlled by an underexplored genetic regulatory mechanism, based not on proteins, but on RNA.

In 2016, geneticists thought they had pinned much of the wing-pattern variation on a protein-encoding gene called *cortex*. But three teams have now proved that a different gene, previously missed because it overlaps with *cortex*, is the key. Its final product is not protein, but RNA that regulates genes responsible for the pigmentation patterns of black and other hues on the wings. One team also showed the RNA is broken down into a smaller RNA that fine-tunes the production of the colors. "They solved a puzzle that had left everyone in the community wondering," says Nicolas Gompel, a developmental biologist at the

being sold on eBay. When they sequenced dozens of these so-called ivory mutants, they found a deletion in the region of the *cortex* gene. They then realized the missing DNA included a sequence encoding an lncRNA that no one had ever closely examined. Working with painted lady butterflies (*Vanessa cardui*), which have colorful wings and are easy to breed in the lab, they used the gene editor CRISPR to disable just the lncRNA's gene. The edit yielded white-winged painted ladies, just like the ivory *Heliconius*, they reported on 12 February in a preprint on bioRxiv. Disabling *cortex* had no effect.

Moreover, Livraghi's team found this same lncRNA also controls black and other

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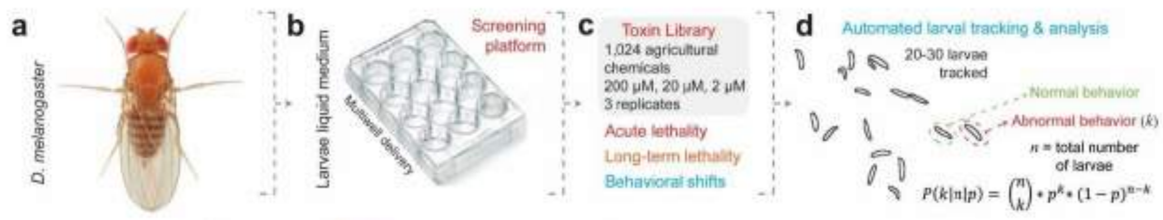
Impact of Pesticides on Insect Phenotypes

Pervasive sublethal effects of agrochemicals as contributing factors to insect decline

Pervasive sublethal effects of agrochemicals as contributing factors to insect decline

Gandara, Lautaro[1*]; Jacoby, Richard[1]; Laurent, François[2,3]; Spatuzzi, Matteo[1]; Vlachopoulos, Nikolaos[1]; Borst, Noa O[1]; Ekmen, Gülina[1]; Potel, Clement M[1]; Garrido-Rodriguez, Martin[1]; Böhmert, Antonia L[4]; Misunou, Natalia[1]; Bartmanski, Bartosz J[1]; Li, Xueying C[1]; Kutra, Dominik[1]; Hériché, Jean-Karim[1]; Tischer, Christian[1]; Zimmermann-Kogadeeva, Maria[1]; Ingham, Victoria[4]; Savitski, Mikhail M[1]; Masson, Jean-Baptiste[2,3]; Zimmermann, Michael[1]; Crocker, Justin[1*].

Fig.1: Agrochemicals alter larval development and behavior at sublethal concentrations



https://doi.org/10.1101/2024.01.12.575373 doi: bioRxiv preprint

More Next Week!

E. Heard

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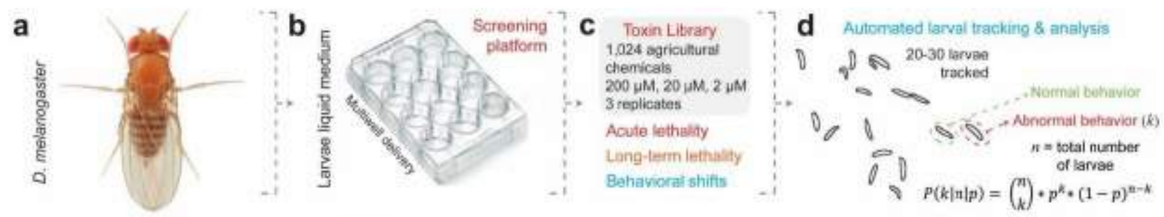
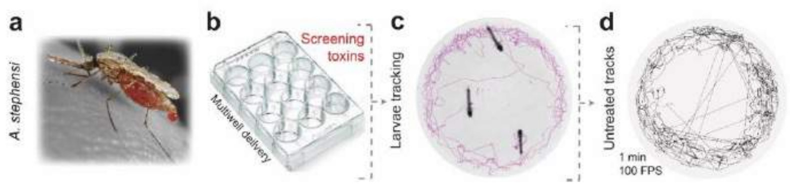
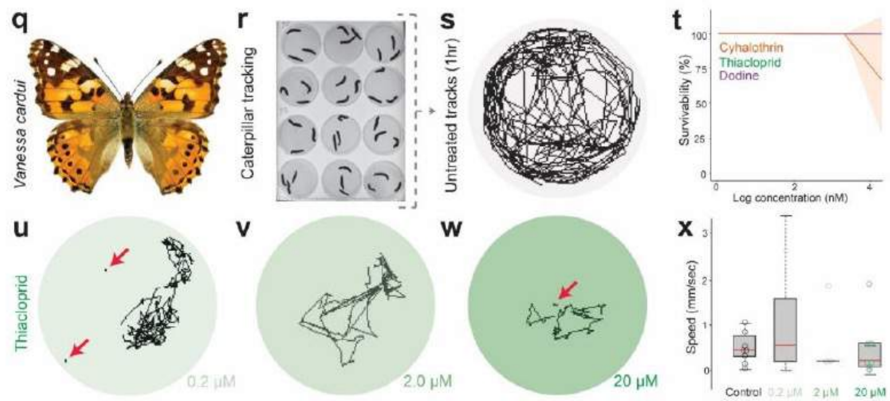


Long-term exposure to pesticide mix reveals changes in life-history traits

Sublethal effects of pesticides impact the behaviour of mosquitoes and butterflies





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More Next Week!

E. Heard

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Environmentally induced trans-generational bet-hedging / phenotypic plasticity

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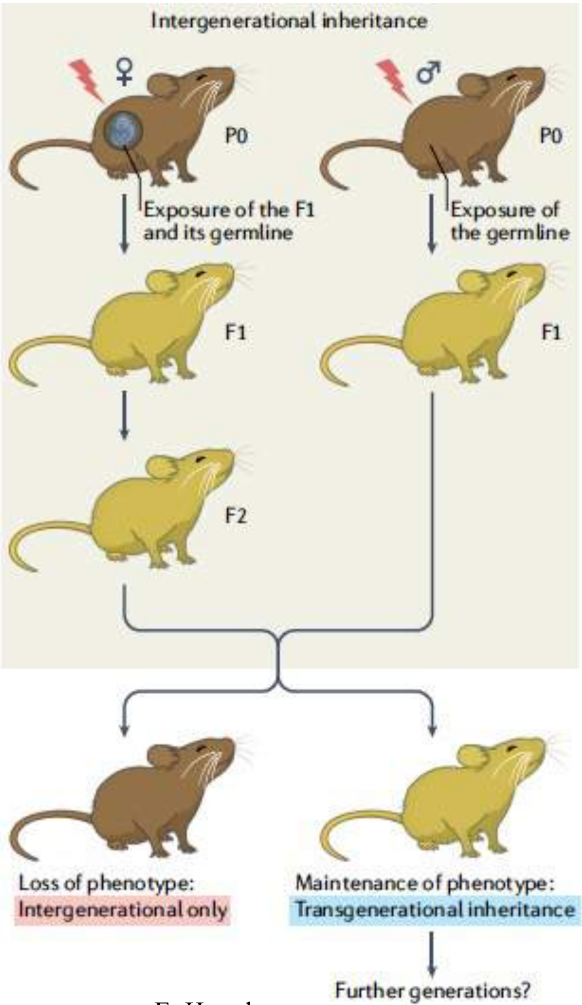
Impact of rapid and dramatic changes in environment on phenotypes: stress, survival, adaptation or extinction

Environmentally induced inter and trans-generational phenotypes in mammals and plants



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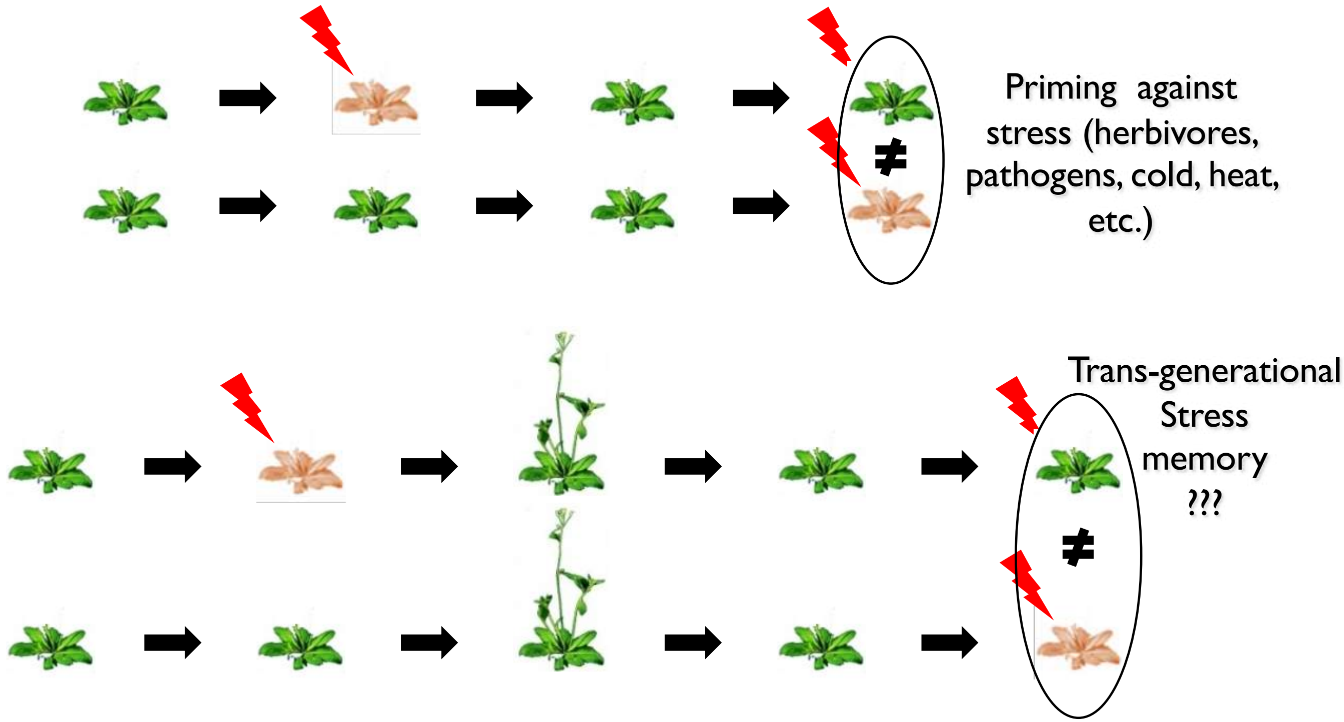
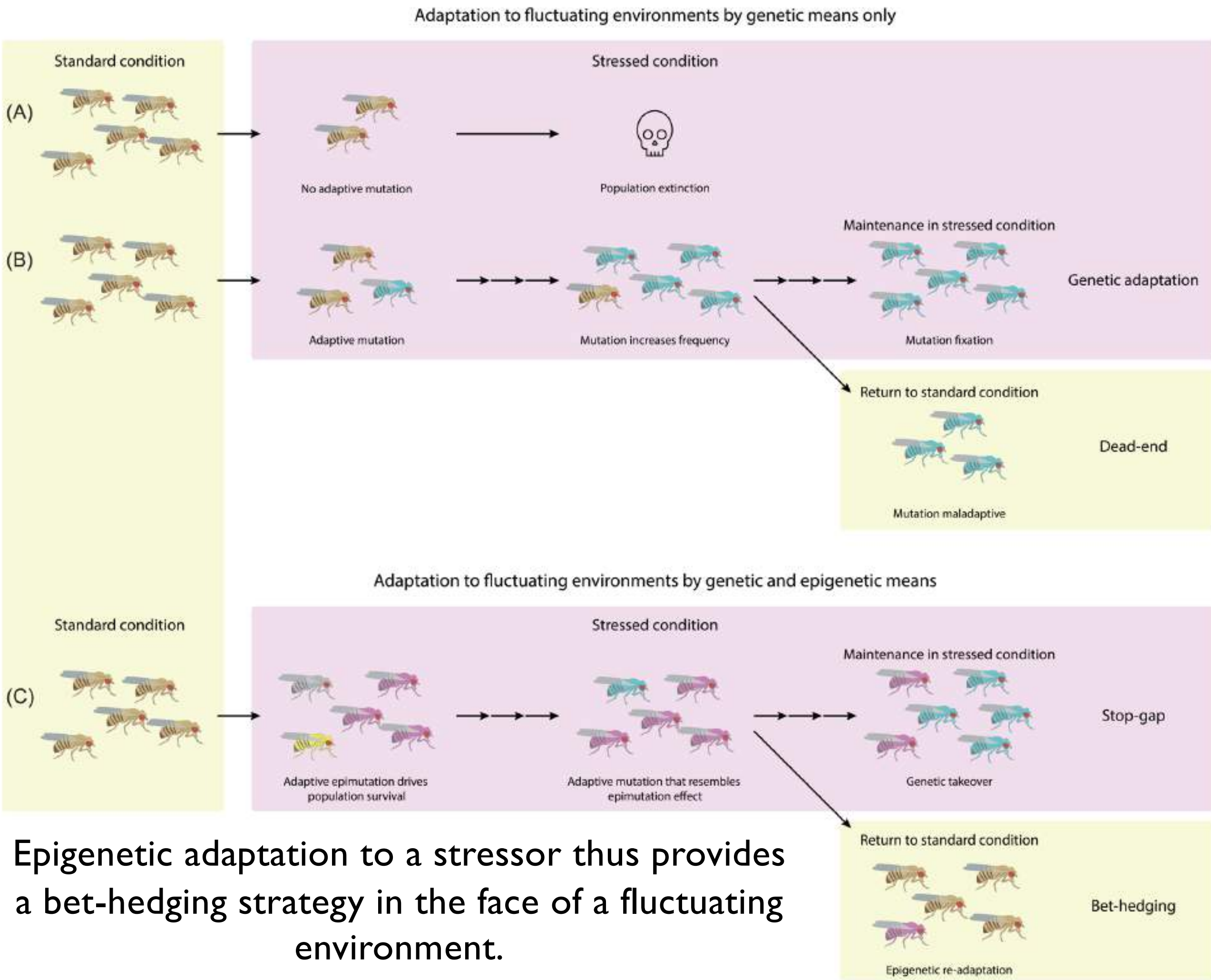


COURS 3 et 4

COLLÈGE DE FRANCE 1530

Epigenetic Inheritance can be important for Fast Adaptation to Fluctuating Environments: Bet Hedging



(A) Failure to adapt to the stressor leads to a decline in the population which, if it persists or is taken to extremes of severity, can eventually lead to its extinction

(B) a (rare) de novo mutation arises in the population that provides resistance to the stressor. Mutation will gradually spread through the population depending on degree of advantage. Eventually, if the stressed condition persists, the mutation will become fixed (completely penetrate the population), However, if conditions revert back to standard, those individuals bearing the mutation may find themselves at a disadvantage in an environment to which they are now maladaptive, compared to others that were never subject to stressed conditions. A mutation response to stress may lead to adaptation, but also to an evolutionary dead-end.

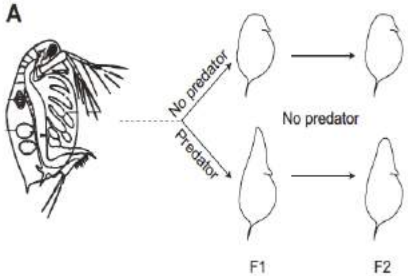
(C) An epimutation conferring a resistance phenotype can arise. While this epigenetic adaptation might be less stable than a genetic one, its advantages are (i) if stressed conditions are long-lasting, the epimutation can serve as a stop-gap - a temporary solution ensuring short-term survival until a more robust mutation arises and eventually replaces it; epimutation "buys time"(ii) if stressed conditions are transient, the epimutation allows for easy readaptation as it is more easily reversed than a DNA seq mutation and so does not represent an evolutionary dead-end.

Epigenetic adaptation to a stressor thus provides a bet-hedging strategy in the face of a fluctuating environment.

Taken from Sabaris et al, 2023
DOI: 10.1111/nyas.14992

Epigenetic Inheritance can be important for Fast Adaptation to Fluctuating Environments

- In early 1900s, Richard Woltereck working on helmet length (cyclomorphosis) in clones of Daphnia (*les daphnies – petits crustacés*), introduced the term 'reaktionsnorm' (**reaction norm**) to describe how the phenotype of an individual depends on the interaction between its genotype and environmental cues



Chemical signals from predators, induce protective cranial structures « Helmets » (casques)

This phenotype can be transmitted to subsequent generation in the <u>absence</u> of predator signal.

Daphnia magna (*D. magna*) is a <u>keystone species</u> in aquatic ecosystems, and a standard model species in the fields of ecology and ecotoxicology.

(Effertz et al., 2015; Le et al., 2013; Silvestre et al., 2012).

Due to its inherent phenotypic plasticity, well-known ecological background, and sensitivity to a range of aquatic biotic and/or abiotic factors, *D. magna* is used as important model organism for the understanding of interactions between it and its environment. (next slide)

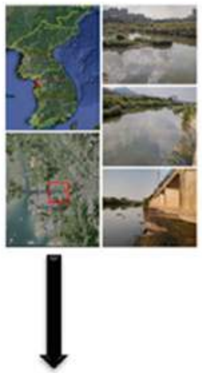
Potential adaptive potential of <u>environmentally induced epigenetic variation</u> and <u>inheritance</u> in natural populations, was recently demonstrated in the crustacean *Daphnia pulex*.

Epigenetic Inheritance can be important for Fast Adaptation to Fluctuating Environments

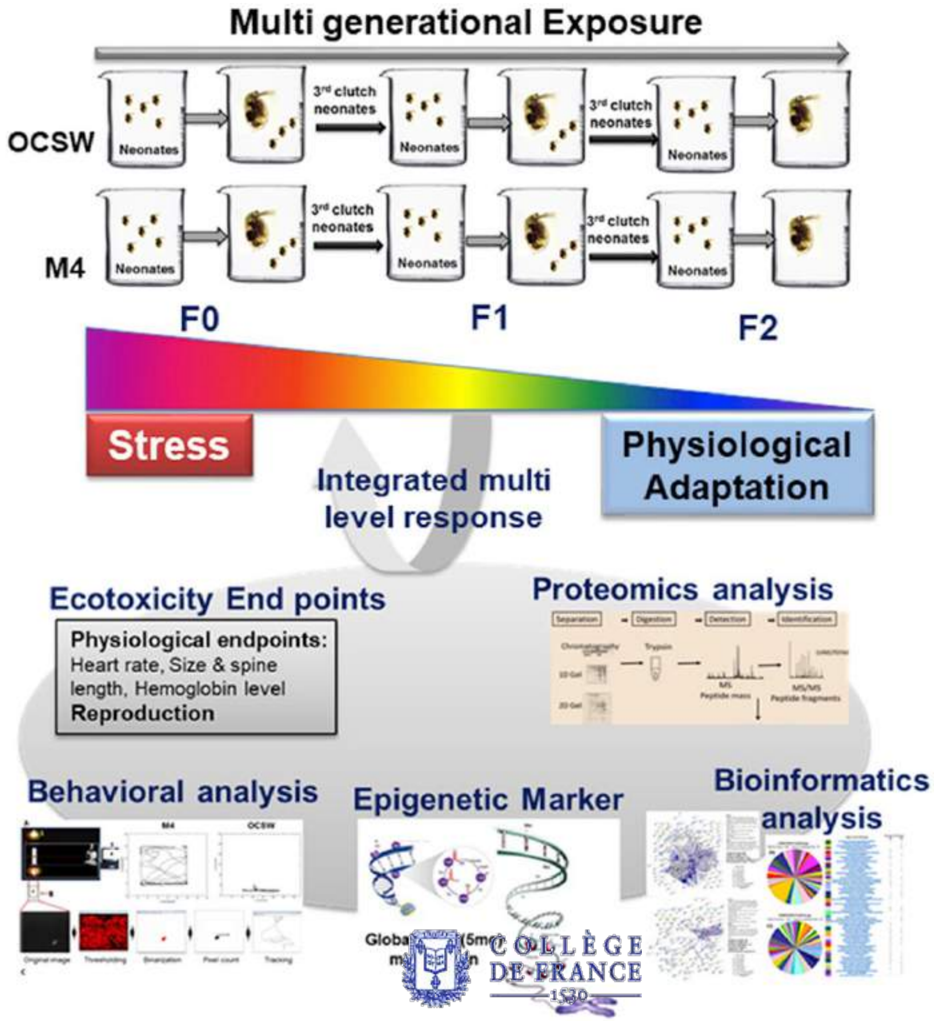
Multi-generational impacts of organic contaminated stream water on *Daphnia magna*: A combined proteomics, epigenetics and ecotoxicity approach

Multigenerational exposure effect in field stream water (fecal coliform contaminated) showed perturbations in physiology (increased size, hemoglobin etc.), reproduction, swimming behavior, and global DNA hypermethylation in *D. magna*, specifically in the first two generations (F0 and F1).

The role of the DNA methylation changes when exposed to fecal coliform and any link with the induced physiological adaptation and/or reproductive changes are unknown.



Contaminated Stream water collection



Chatterjee et al, 2019
https://doi.org/10.1016/j.envpol.2019.03.028

Epigenetic Inheritance can be important for Fast Adaptation to Fluctuating Environments

doi:10.1002/evl3.273

Pollution induces epigenetic effects that are stably transmitted across multiple generations

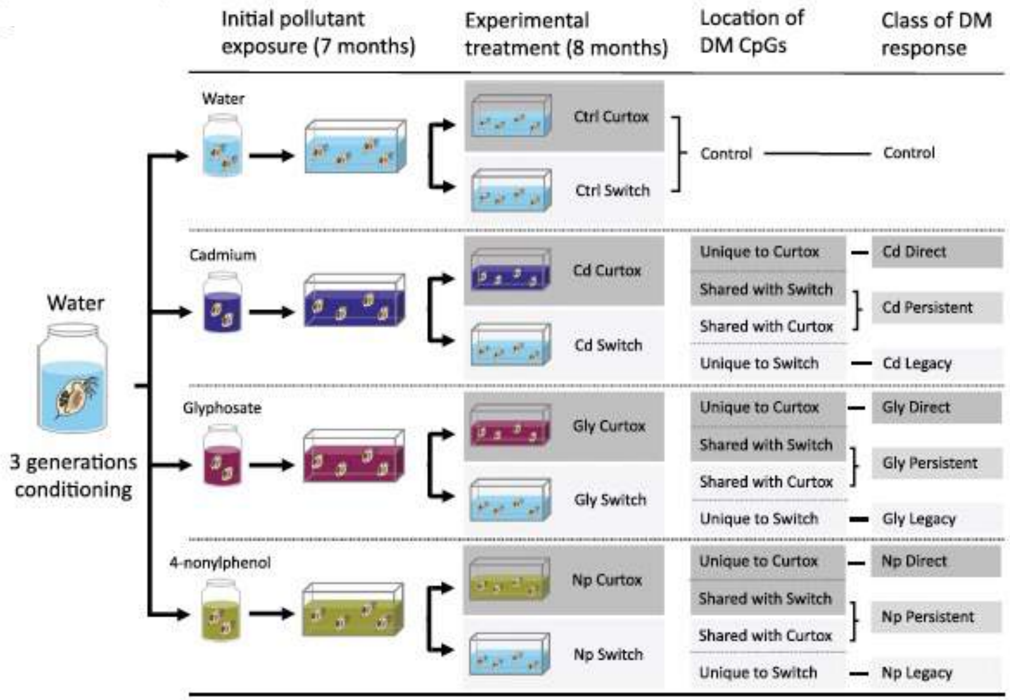
Ewan Harney,[1,2,3,*] Steve Paterson,[1,4,*] Hélène Collin,[1] Brian H.K. Chan,[1,5] Daimark Bennett,[6] and Stewart J. Plaistow[1,7]

Changes in the epigenome were found in response to three common environmental pollutants (**cadmium, glyphosate,** and **4-nonylphenol**) in genetically homogeneous populations.

Individuals were exposed for over 15 generations to the pollutants and then either continued for a similar period of time in polluted water or moved to clean water.

Exposure to all three pollutants alters global patterns of DNA methylation compared to individuals maintained throughout in clean water

Different fitness traits were compromised in the F3 progeny of treated animals after being returned to clean water, suggesting that the transmitted epigenetic information may correspond to phenotypic variation and have a role in short-term adapative evolution



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Epigenetic Inheritance can be important for Fast Adaptation to Fluctuating Environments

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Original Article
OXFORD

Phenotypic plasticity in the monoclonal marbled crayfish is associated with very low genetic diversity but pronounced epigenetic diversity

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Handling editor: Adriana Bellati

- In the last decade, the apomictic parthenogenetic marble crayfish, Procambarus virginalis, has been developed as a model to investigate the relationships between phenotyp plasticity and genetic and epigenetic diversity in detail.
- This crayfish originated about 30 years ago by autotriploi from a single slough crayfish Procambarus fallax.
- As a result of human releases and active spreading, marbl crayfish has established numerous populations in very diverse habitats in 22 countries- tropics to cold temperate regions.
- Studies in the laboratory and field revealed considerable plasticity in coloration, spination, morphometric parameters, growth, food preference, population structure, trophic position, and niche width.

The laboratory specimens of marbled crayfish also had significantly different body proportions (relatively longer pleons and broader carapaces) when compared to equal-sized specimens from Lake Moosweiher. Interestingly, the adult offspring of specimen that was transferred from Lake Moosweiher to the laboratory and reproduced there 1 year later had total length/carapace length ratios similar to the wild population and their mother, but carapace length/carapace width ratios more similar to the laboratory population suggesting partial acclimatization to the new conditions.

Epigenetic Inheritance can be important for Fast Adaptation to Fluctuating Environments

Rapid Epigenetic Adaptation in Animals and Its Role in Invasiveness

Vitor Coutinho Carneiro and Frank Lyko [1]
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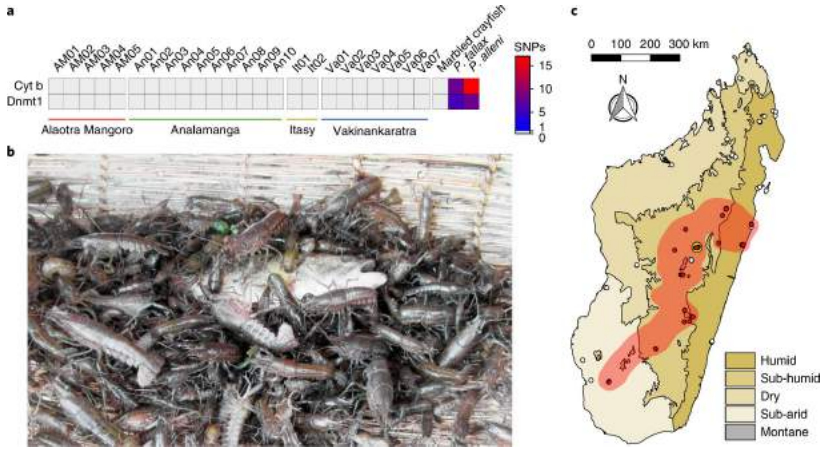
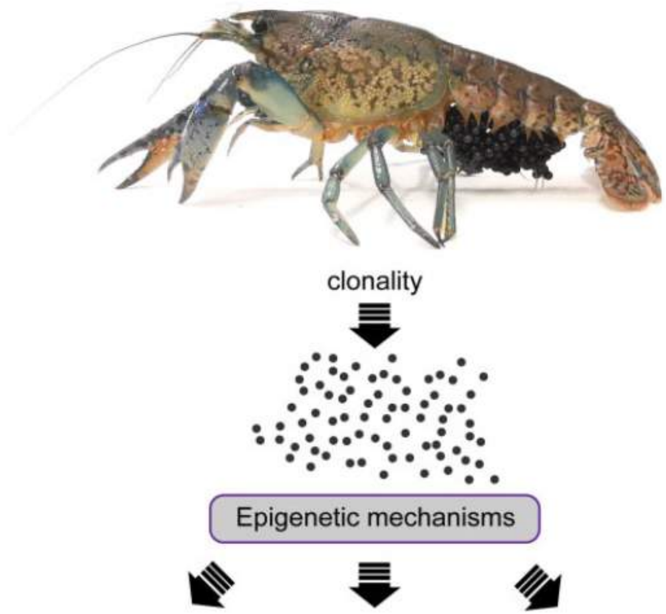




- Epigenetic mechanisms can produce phenotypic variation from the same DNA sequence.
- Epigenetic variation helps to cope with short- to medium-term environmental challenges.
- Epigenetic variation can produce different epigenetic ecotypes in genetically uniform organisms.
- Epigenetic variation likely underpins the general-purpose genotype.
- Epigenetic variation is suitable to explain the invasion paradox.
- Epigenetic variation may be the starting point of the evolution of species diversity in asexuals.
- Is transgenerational epigenetic inheritance involved in the production of epigenetic ecotypes?
- Can epigenetic ecotypes evolve into classical genetically based ecotypes, & finally, into different species?

Role of non-genetic information in adaptive evolution?

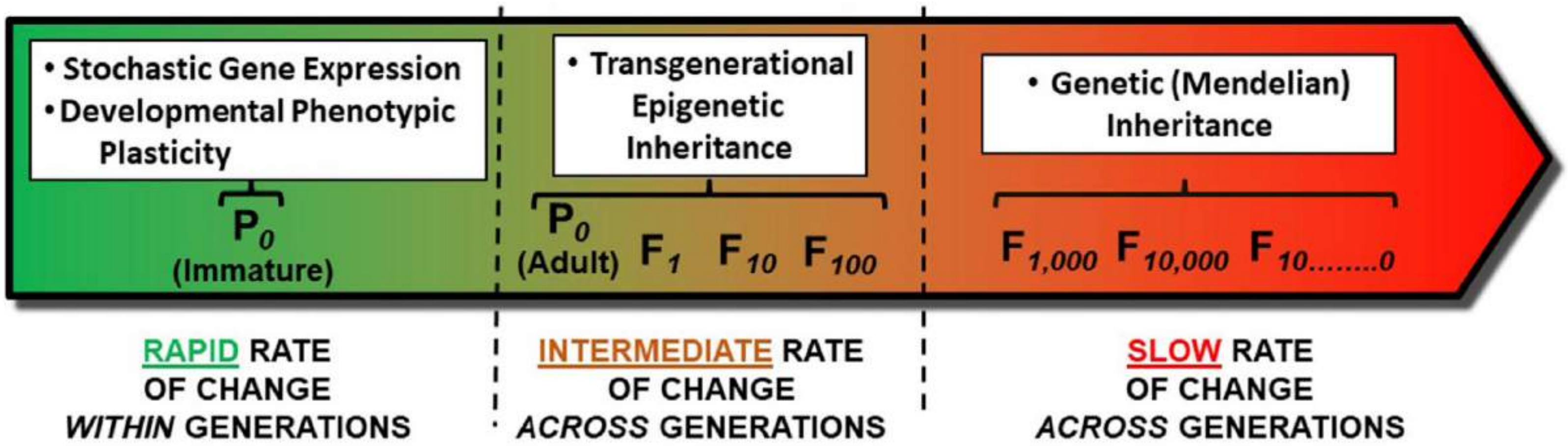
Epigenetic signals triggered by environmental stress can persist over very long timeframes, contributing to phenotypic changes in relevant traits upon which selection could act.

Epigenetic (or "extra-genetic"?) inheritance may play an important role in fast phenotypic adaptation to fluctuating environments, ensuring the survival of the organisms of a population under environmental stress in the short term while maintaining a "bet-hedging" strategy of reverting to the original state if the environment returns to standard conditions.

The role of non-genetic information in adaptive evolution will be further explored in the coming lectures

Environmentally induced cross- and trans-generational phenotypes

- **Stochastic phenotypic variation**, occurring from stochastic variation in gene transcription and translation, especially during development, that are not related to environmental cues;
- **Phenotypic plasticity** operates within the timeframe of an organism's entire life span, and involves the ability to alter phenotype through acclimatization (acclimation);
- **Transgenerational epigenetic inheritance** influences phenotype of a species over typically a few generations through changes in gene expression (but not sequence);
- **Classic Mendelian inheritance** acts over large number of generations–that is, evolutionary time–through permanent changes in gene sequence.



Burggren and Mendez-Sanchez, Frontiers in Physiology 2023 DOI 10.3389/fphys.2023.1245875

L'épigénétique à l'interface organisme-environnement

4 mars
Cours 1: Introduction

11 mars
Cours 2: Comment l'environnement influence-t-il les phénotypes ?

18 mars
Cours 3: Exemples d'impacts environnementaux sur le règne animal

25 mars
Cours 4: Exemples d'impacts environnementaux sur le règne végétal

E. Heard

CHAIRE ÉPIGÉNÉTIQUE ET MÉMOIRE CELLULAIRE

L'interface organisme-environnement

Colloque le 11-12 juin 2024

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