CHAIRE ÉPIGÉNÉTIQUE ET MÉMOIRE CELLULAIRE

Année 2018-2019:

"Épigénétique, Environnement et Biodiversité"

6 Novembre 2018

Cours I

Biodiversité – du génotype aux phénotypes: la place de l'épigénétique

COLLÈGE DE FRANCE 1530

Biodiversity

It is interesting to contemplate a tangled bank, clothed with manyplants of many kinds, with birds singing on the bushes, with various insects flitting about, and with worms crawling through the damp earth, and to reflect that these elaborately constructed forms, so different from each other, and dependent upon each other in so complexa manner, have all been produced by laws acting around us. »

Charles Darwin, Origin of Species, 1859;

Il est intéressant de contempler un rivage luxuriant, tapissé de nombreuses plantes appartenant à de nombreuses espèces abritant des oiseaux qui chantent dans les buissons, des insectes variés qui voltigent çà et là, des vers qui rampent dans la terre humide, si l'on songe que ces formes si admirablement construites, si différemment conformées, et dépendantes les unes des autres d'une manière si complexe, ont toutes été produites par des lois qui agissent autour de nous.

Biodiversity

- Biodiversity is the variety of life on Earth, in all its forms and all its interactions.
- Biodiversity is a measure of the health of any ecosystem, of the planet. Every organism is part of an ecosystem (biome), relying on other organisms and the physical environment.
- Biodiversity describes how much <u>variety</u> an ecosystem has, in terms of *resources* and *species*, and also *genetically* and *epigenetically* within species.
- The more diverse an ecosystem is, the more resources it has to help it recover from famine, drought, disease and extinction of species.
- A species is made up of individuals. With the exception of twins or clones, each of these individuals has their own <u>unique combination of gene variants (alleles)</u>.
- If we destroy half of the individuals in each species, we will still have the same number of of species, <u>*but we lose 50 per cent of each species' genetic diversity*</u>.

Biodiversity can be within an individual, within species, between species, within ecosystems…

Biodiversity

- Biodiversity is comprised of several levels - genes, species, populations and individuals within them, communities of creatures, and entire ecosystems: forests or coral reefs, where life interplays with the physical environment.
- **These interactions have made Earth habitable for billions of years**.
- Biodiversity can also be considered as representing the knowledge learned by evolving species over millions of years about how to survive through the vastly varying environmental conditions Earth has experienced.

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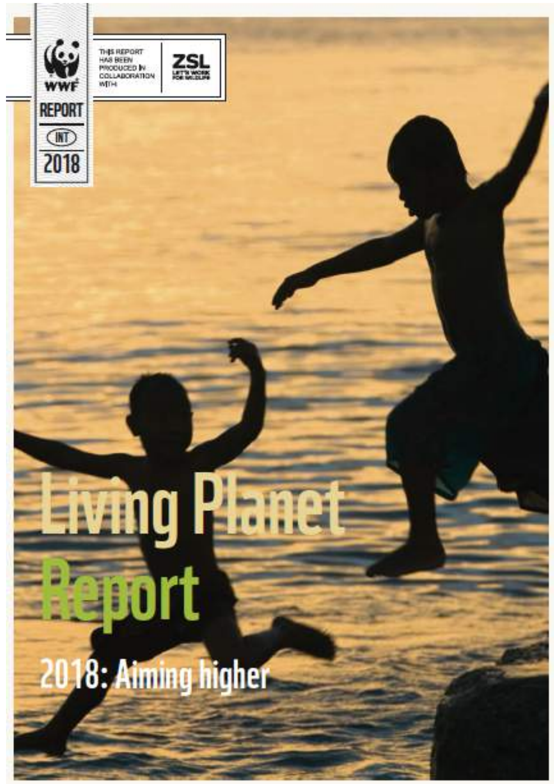
- Biodiversity can also be considered as representing the knowledge learned by evolving species over millions of years about how to survive through the vastly varying environmental conditions Earth has experienced.

- Humanity is currently « burning the library of life ». Man is destroying ecosystems on a massive scale: Accelerating pollution, deforestation, climate change and other manmade factors have created a **"mindblowing" crisis**
- (World Wildlife Fund, Living Planet Report 2018)

Biodiversity



- (World Wildlife Fund, Living Planet Report 2018)

- The number of animals living on the Earth has plunged by half since 1970
- 75% of genetic diversity of agricultural crops has been lost
- 75% of the world's fisheries are fully or over exploited
- 1/3rd of reef-building corals around the world are threatened with extinction
- Deforestation of closed tropical rain forests could account for the loss of as many as 100 species every day.
- We talk about the Earth's 6th mass extinction…

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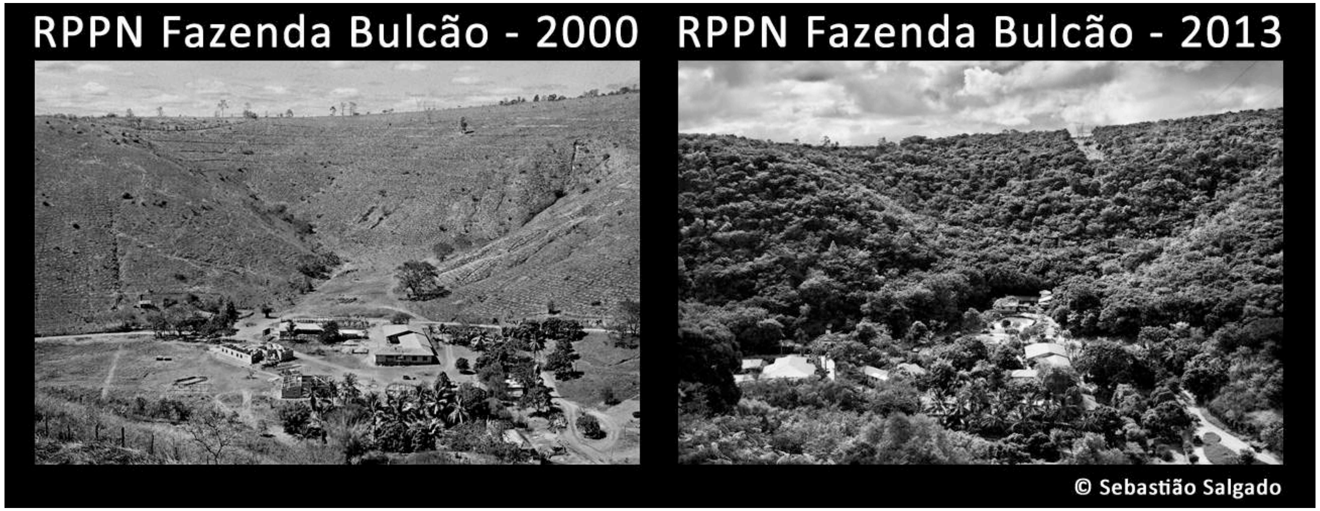
Biodiversity

- Disturbed ecosystems and reduced biodiversity can result in epidemics and disease…

Biodiversity

- The total numbers of more than 4,000 mammal, bird, fish, reptile and amphibian species declined rapidly between 1970 and 2014….

- The good news is that it is not too late to reverse this trend



Biodiversity

- The total numbers of more than 4,000 mammal, bird, fish, reptile and amphibian species declined rapidly between 1970 and 2014….
- The good news is that it is not too late to reverse this trend
- The bad news is that when we reduce the number of individuals in a species by half, we LOSE half of their genetic diversity – FOREVER…

> *We are the first generation of scientists with the tools to address the dimensions of biodiversity on Earth… and ironically we may be the last generation with the opportunity to discover and understand Earth's biodiversity before it is irrevocably changed or lost.*
>
> James Collins, February 13, 2009

Année 2018-2019:
"Épigénétique, Environnement et Biodiversité"

6/11/2018
COURS I Biodiversité – du génotype aux phénotypes: la place de l'épigénétique

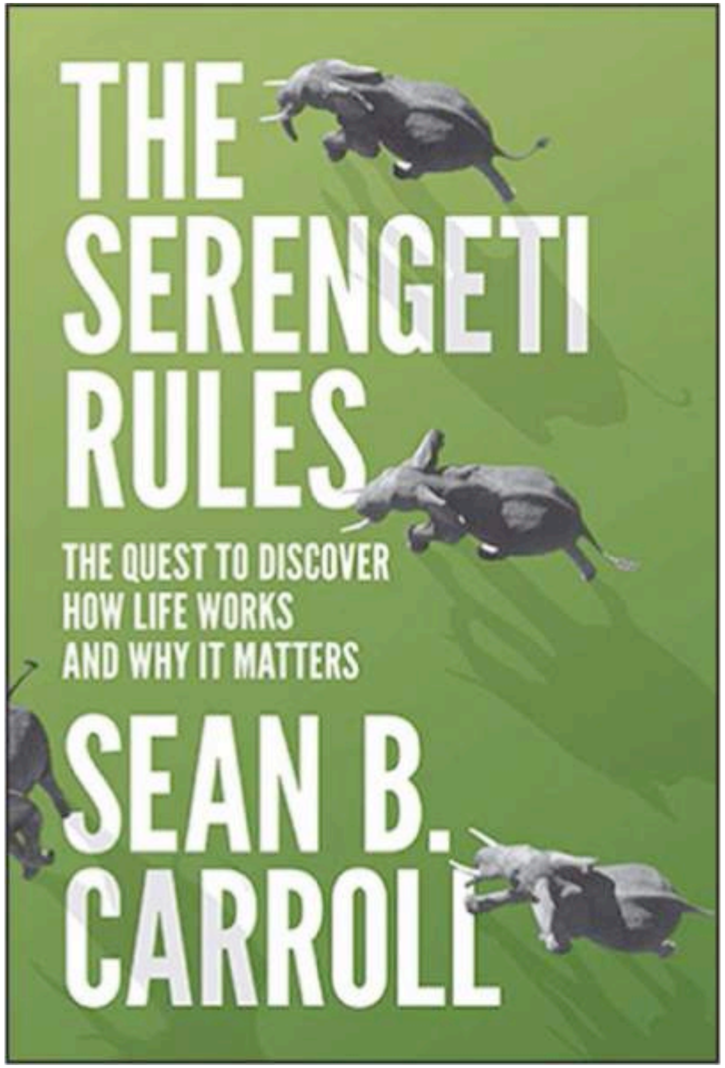
13/11/2018
COURS II La diversité génétique et épigénétique au sein d'un individu ou d'un écosystème

4/12/2018
COURS III Quelle est l'influence de l'environnement sur les modifications épigénétiques et leur transmission?

11/12/2018
COURS IV Le role de l'épigénétique dans la plasticité phénotypique et l'évolution des réponses adaptatives
SÉMINAIRE : **SEAN CARROLL**

8/04/2019
COURS V Colloque: Épigénétique, Environnement et Biodiversité »

Professor Sean B. Carroll
University of Wisconsin–Madison



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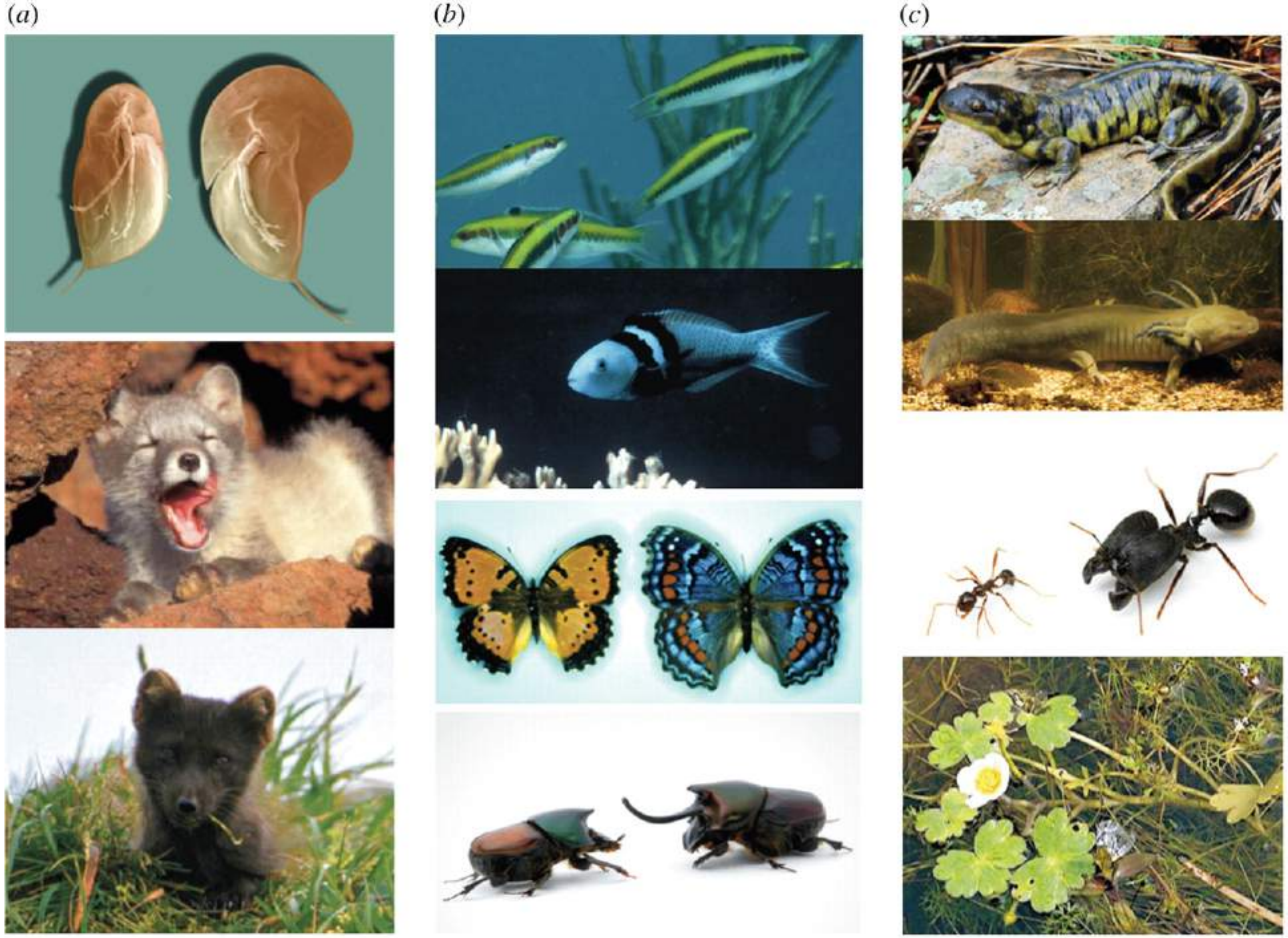
Biodiversity – from genotype to phenotypes : The role of epigenetics?

Same Genotype - very different Phenotypes
Environmentally induced before, during, or after development



Armin P. Moczek et al. Proc. R. Soc. B 2011;rspb.2011.0971

Epigenetics

Conrad H. Waddington
(1905-1975)
British geneticist, embryologist & philosopher

Original definition of **Epigenetics** by Waddington in 1942 was to help bridge the gap between genetics and experimental embryology:

- **Epigenetics**: The study of the mechanisms of development through which genes bring about phenotypic effects
- A need to establish **causal relationships between genotype & phenotype**, in order to understand development.
- **Epigenotype:** the processes linking genotype and phenotype
- This definition of Epigenetics corresponds to the discipline of 'Developmental Genetics' today

More recent definitions of epigenetics:

Holliday, Riggs (1970s-1980's)

The study of heritable changes (mitotic or meiotic) in gene function that cannot be explained by changes in DNA sequence

Today…?

Chromosome changes that affect genome function

Environmentally induced phenotypic changes (molecular or physiological)

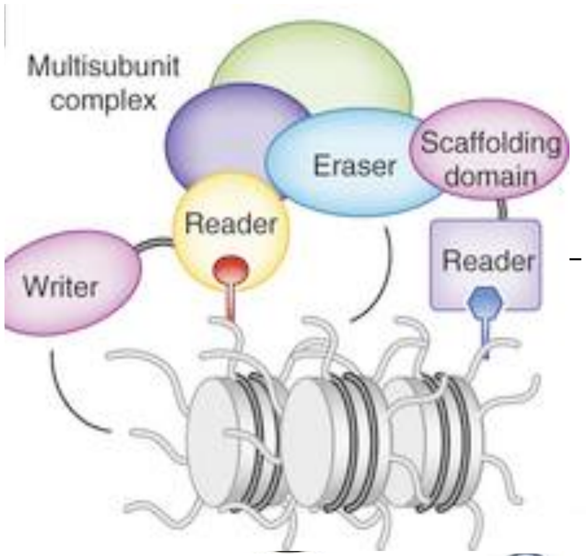
(=Gene regulation?)

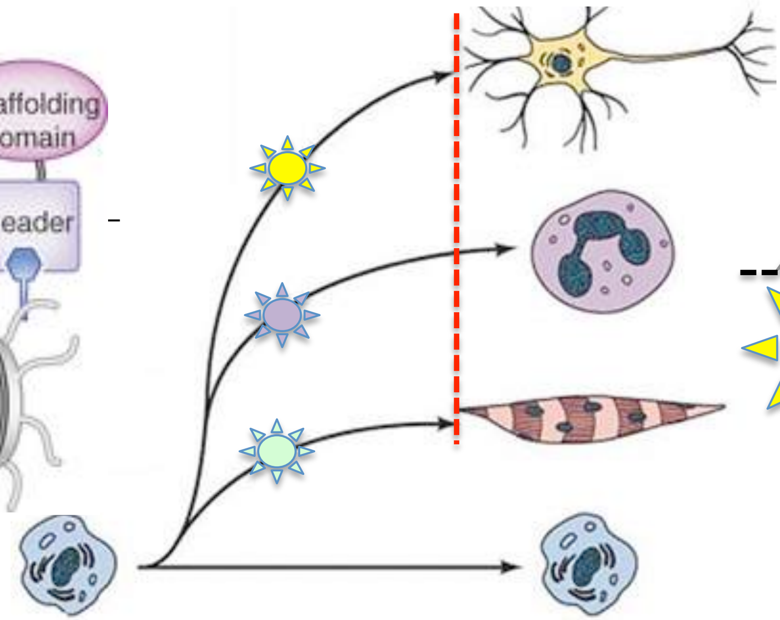
Gene Regulation & Epigenetics in Eukaryotes

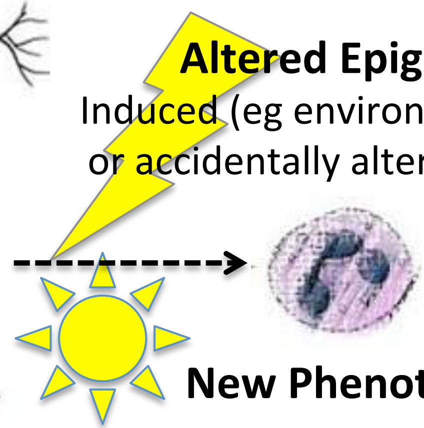
Chromatin as a barrier and facilitator
Epigenetic memorisation of gene activity states

Heritable (somatic) states

(Epigenetic "Barriers")







Altered Epigenome

Induced (eg environment, stress,)
or accidentally altered (eg aging)

New Phenotypes ?

Adaptive
Inevitable
Deleterious

One Genome

Multiple Epigenomes

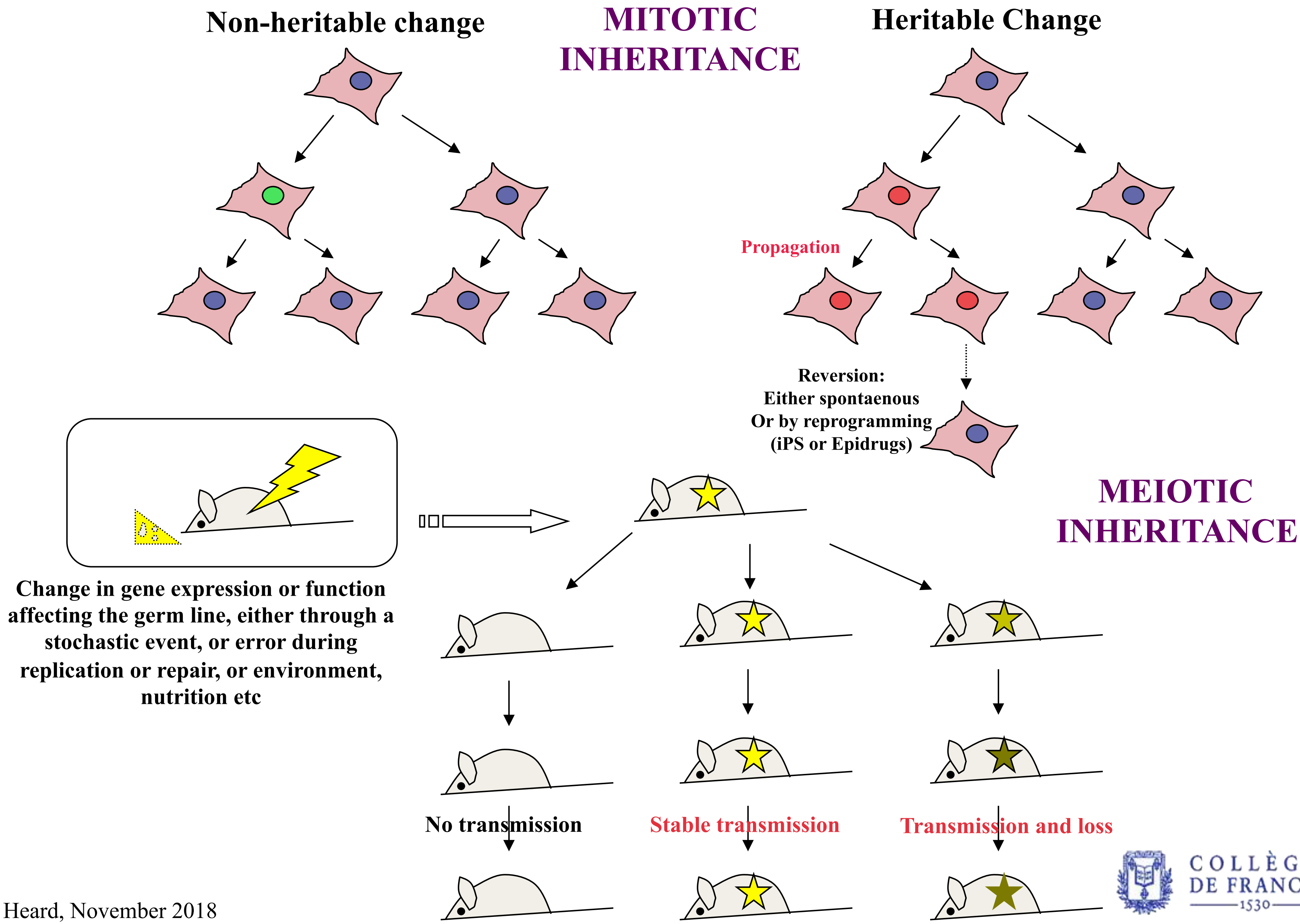
gene expression & chromatin states

Different Cell Identities

DNA sequence-specific Transcription Factors
& Signalling pathways

(positional information, cell-cell contacts, growth factors, etc
(to establish cell type, patterning, morphogenesis)

Mitotic and Meiotic Epigenetic Heritability

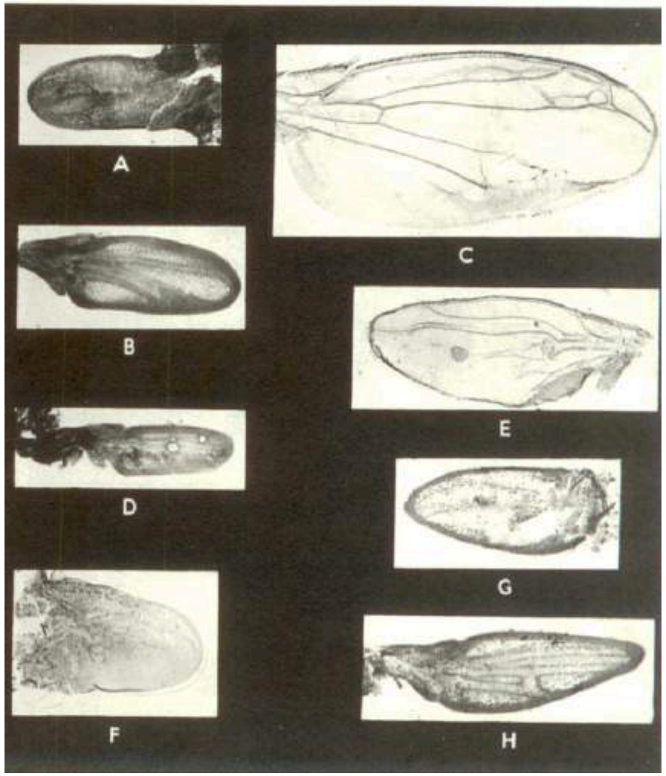


E. Heard, November 2018

Returning to Waddington's Epigenetics

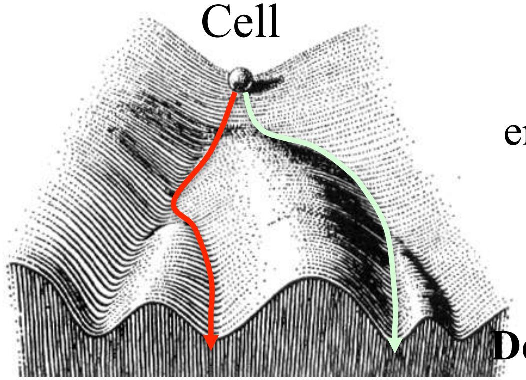
"Epigenetics is a landscape in which a cell can go down different pathways and have a different fate according to the interactions between **genes** and their **environment**"

Drosophila wing development – affected by 30 loci.
In first 48h after larva enters pupa, wings undergo at least 15 different processes, each of which is affected by a known gene

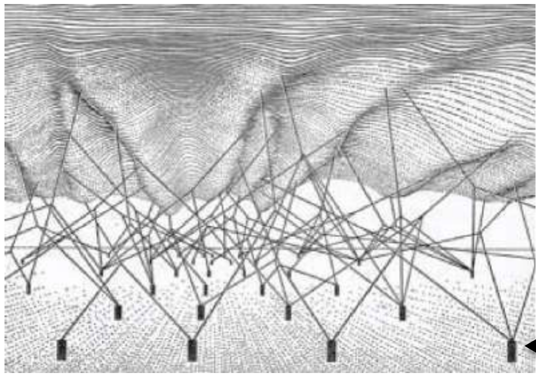


Conrad H. Waddington (1957)
The strategy of the genes (London: Allen and Unwin)

Cell



Different cell fates



← Genes

Buffering (canalization):
Up to a certain threshold, genetic or environmental variation will not affect the pathway

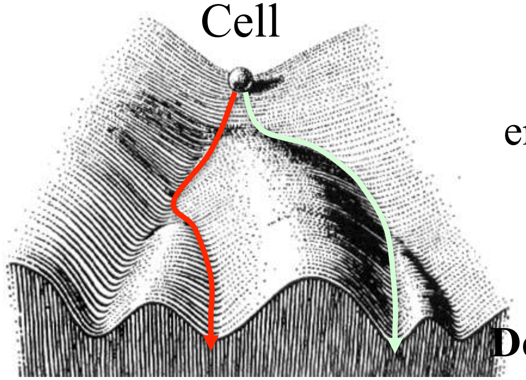
Developmental and phenotypic plasticity:
Alternative pathways
Same genotype
different phenotypes
& different epigenotypes

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

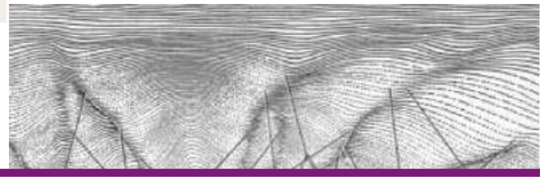
Returning to Waddington's Epigenetics

"Epigenetics is a landscape in which a cell can go down different pathways and have a different fate according to the interactions between **genes** and their **environment**"

EPIGENETIC FORCES SHAPE PHENOTYPES AT THE CELLULAR AND ORGANISMAL LEVEL, BEFORE DURING AND AFTER DEVELOPMENT…



Different cell fates



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Reconciling the Definitions

Cells and organisms need to **stabilize phenotypic responses** to changing environments. Some of these phenotypic states must **persist after the initial stimulus has subsided**, often for long period of time, and, on occasion, must be reestablished after cell division and/or organismal reproduction.

Conrad H. Waddin
The strategy of the

E. Heard, November 2018

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Waddington's Epigenetics Revisited

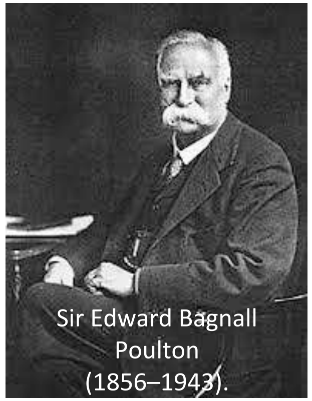
Biodiversity : *within* and *between* individuals of the same species

Phenotypic variation with the same genotype:
within a cell population
within an organism
within a species

Developmental and phenotypic plasticity

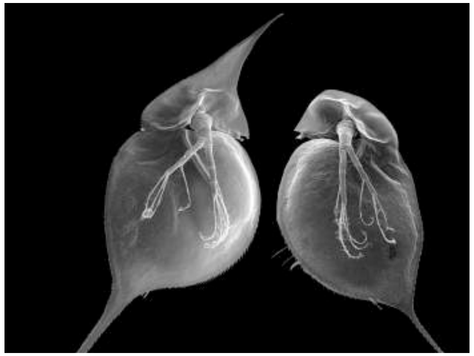
How does environment influence phenotypes within individuals and populations

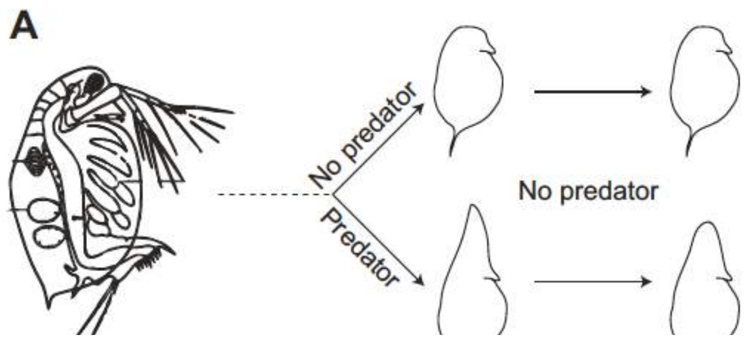
Phenotypic variations



- In late 1800s, August Weismann in Freiburg and Edward Poulton at Oxford had shown influence of environmental cues to change the phenotype in moths and butterflies (mimicry)
- Darwin's « species » were much criticised - Poulton supportively argued that species were reproductively isolated populations.
- Alfred Russel Wallace (1865) described varieties *below the species level*

- 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





Can grow as parthenogenotes => « clones », exposed to different envrionments
Eg chemical signals from predators, induce protective cranial structures « *Helmets* » (*casques*)
Phneotype can be transmitted to subsequent generation in absence of predator signal
But only to F2? Inter- rather than trans-generational?
Wonderful « eco-devo » model for testing epigenetic impact and to detect toxins…

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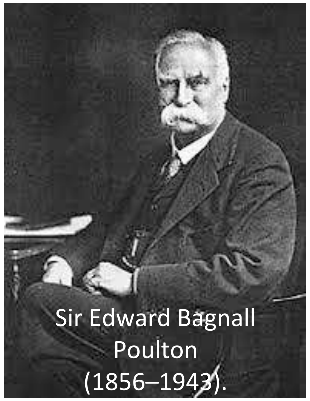
Sir Edward Bagnall Poulton (1856–1943).

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• However, in the 1900s the rise of genetics and the fact that **environmentally induced phenotypic plasticity** could be taken for « Lamarckism », meant it was ignored in favour of "more useful and precise" study of genetic polymorphisms, in which phenotypic variants are produced by different rather than the same genotype (Mayr 1963).

• The **Genotype** was seen as a **self-contained internal developmental « programme »** that specifies a single, determinate phenotypic outcome

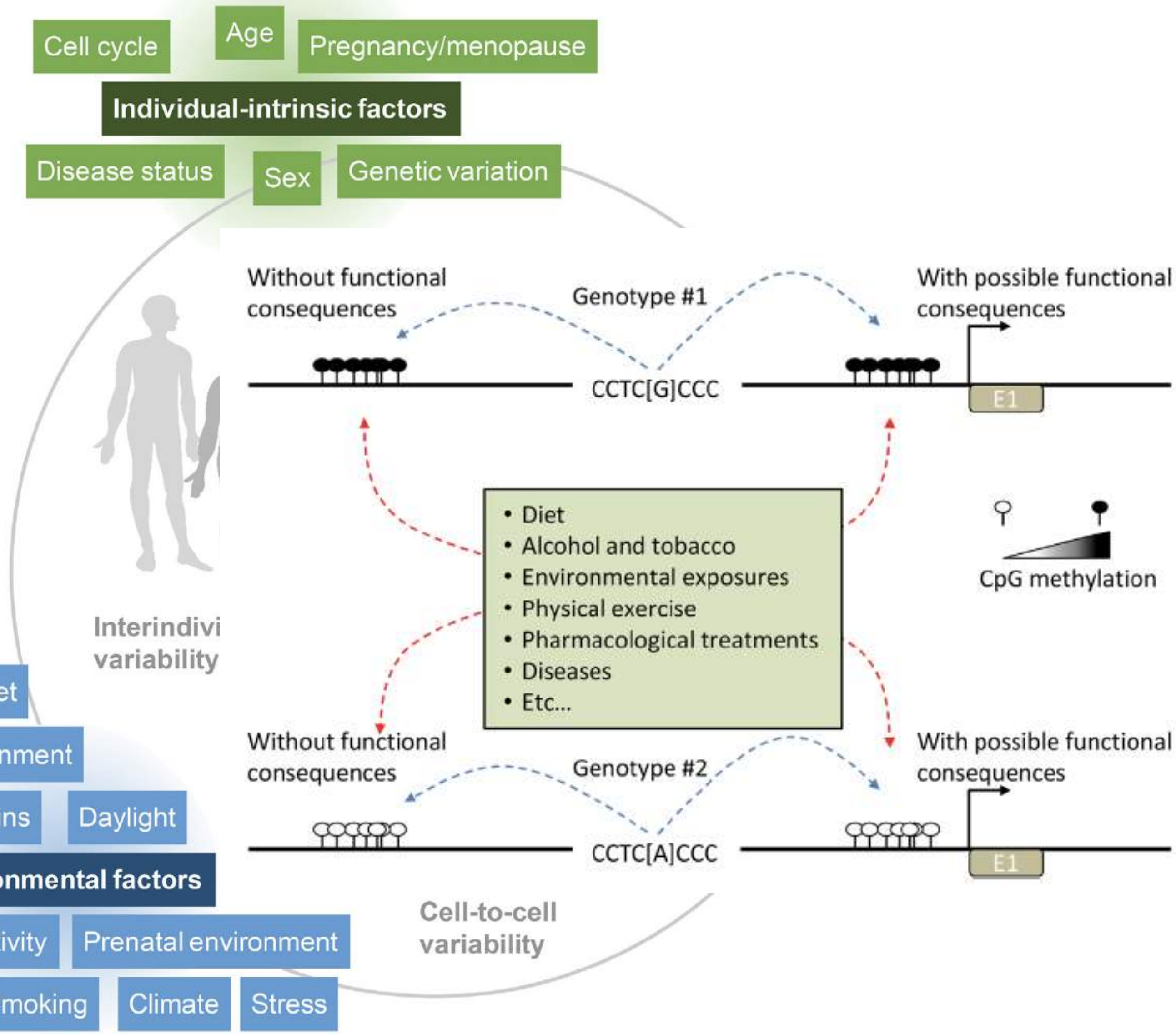
 See Review by Simpson, S. et al (2011) Current Biology 21, R738–R749

Revisiting Genotype to Phenotype

- The « GENETIC PROGRAMME » was (and still is) a deeply embedded metaphor for both developmental & evolutionary processes : one gentope = one phenotype
- Whereby genotype dictates phenotype and it is possible to know what an organism's features will be just by knowing its DNA sequence
- It is in this context that Epigenetics re-emerged in the late 20th C - with realisation that phenotypic variation could be found within and between individuals of same genotype
- Different phenotypes arise before, during and after development from same genotype
- Phenotypes can be stable (morphs) or plastic – and can be *functional*, *inevitable* or *accidental*

Role of the environment: a renaissance for Waddington's definition of epigenetics

Genotype to Phenotype Revisited



Adapted from Ecker et al, Bioessays 2018

E. Heard, November 2018

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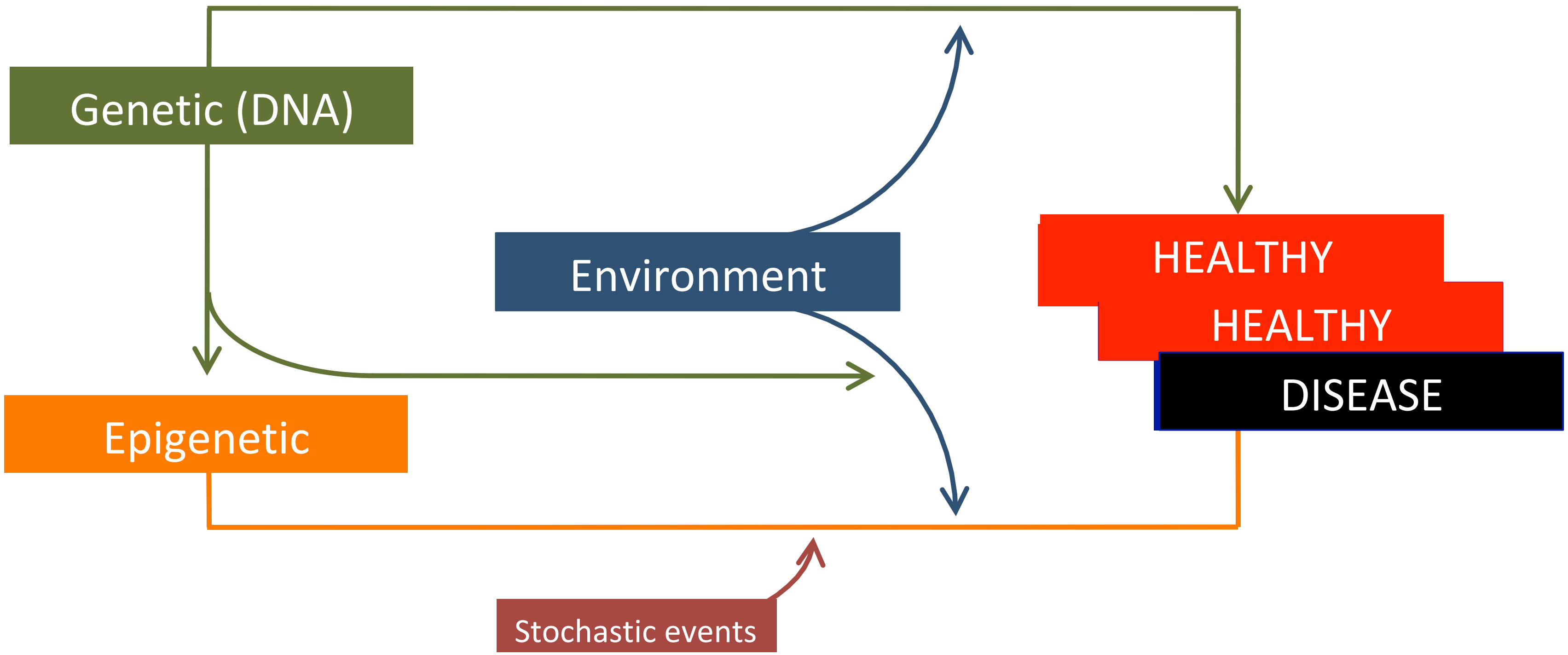
How to define the nature and extent of the epigenetic components in environmentally-induced phenotypic changes?



<u>Most lab models in the past :</u>

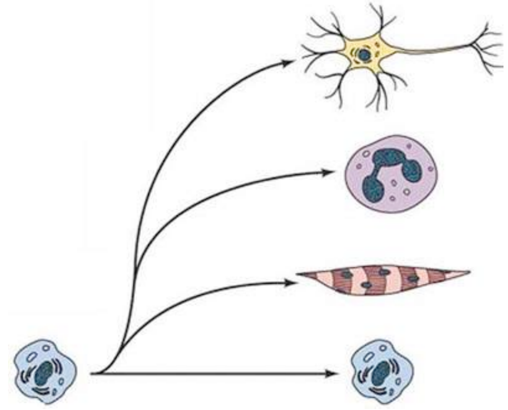
- Fixed environment + Genetic variation => phenotypes?

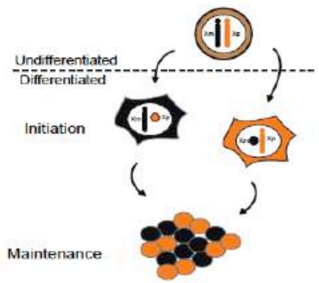
<u>To test impact of penvironment:</u>

- Genetically identical => *uniform* genetic information
- Can identify specific effects of different environmental influences
- Can identify the precise time at which sensitivity to the environment may occur
- Can identify the extent to which stochastic events contribute to phenotypic change

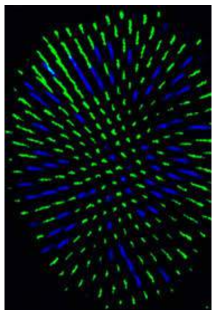
Epigenetics underlying biodiversity *within* species

- **Endogenously programmed epigenetics:**
  Development, X inactivation, imprinting…

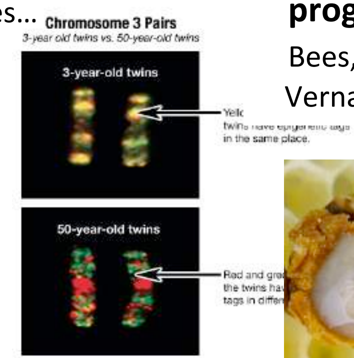


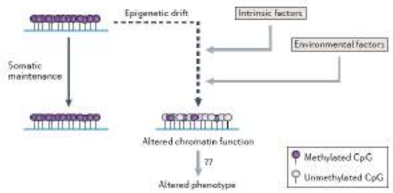


- **Developmental « noise »**
  Stochastic choice eg Drosophila eye development

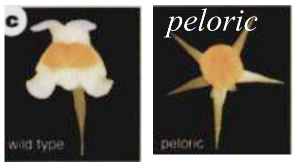


- **Stochastic epigenetic events:**
  Differences in twins, clones…

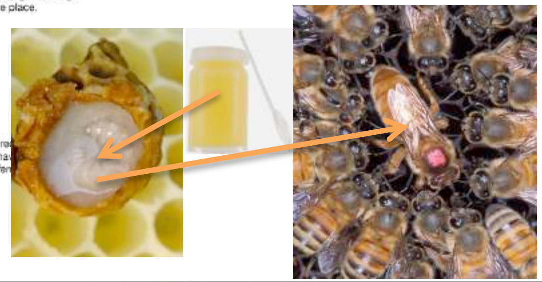


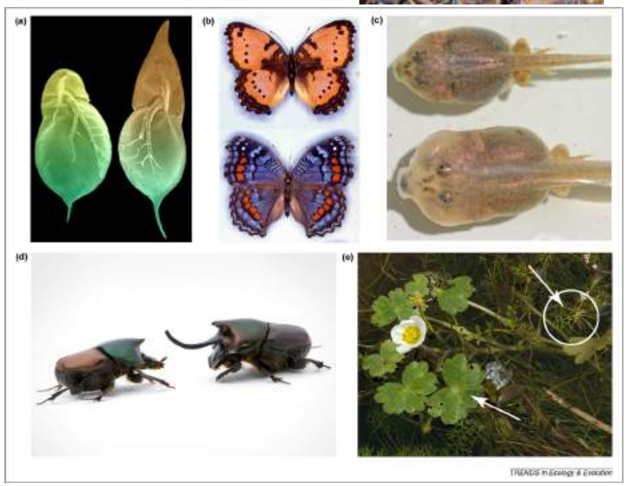


- **Heritable epigenetic variants:**
  Transgenerational epimutations
  Often due to transposons
  +/- Environmentally sensitive



- **Environmentally programmed epigenetics :**
  Bees, ants - nutrition
  Vernalisation in plants - climate



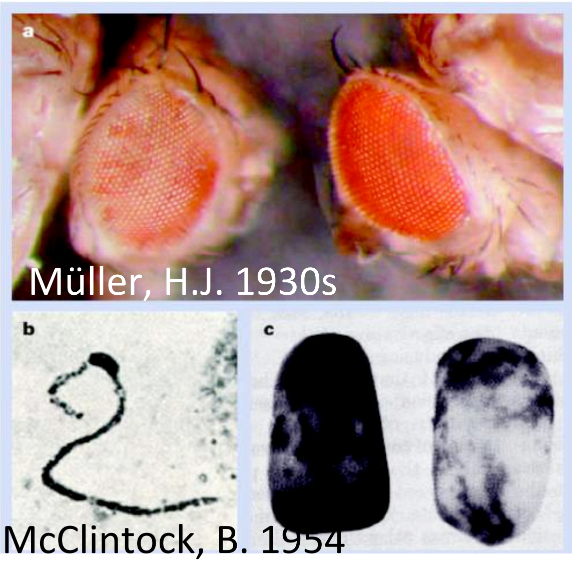


- **Developmental Plasticity**
  Polyphenism

COURS III et IV

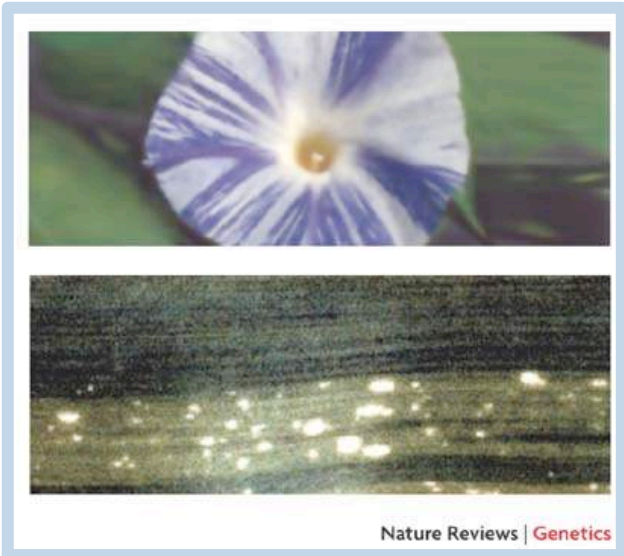
Epigenetics underlying diversity *within individuals* (or cell populations) **COURS II**

- Variation in phenotype and gene expression observed <u>within the same cell type in a single</u> individual
- Clonal, alternate activity states leading to cellular phenotypic mosiacism
- Associated with heterochromatin formation and sometimes with metastable states



Müller, H.J. 1930s

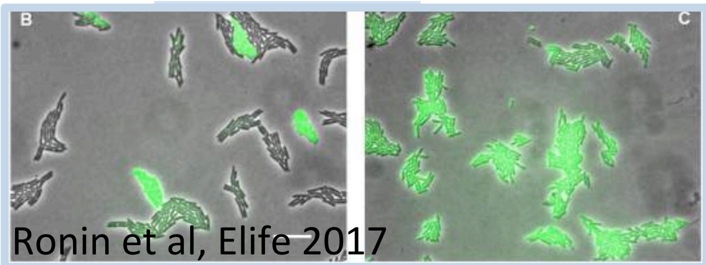
McClintock, B. 1954



From reviews by Lippman and Martienssen, 2004; Schotta et al, 2003

Lyon, M. 1961

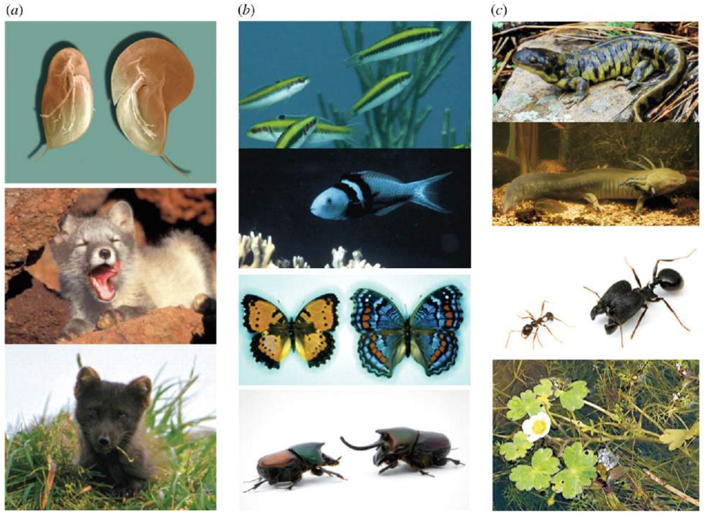
A. Klar; R. Allshire 1990's



Ronin et al, Elife 2017

E. Heard, November 2018

Phenotypic Plasticity and Polyphenism



Environmentally dependent polyphenism in various taxa.

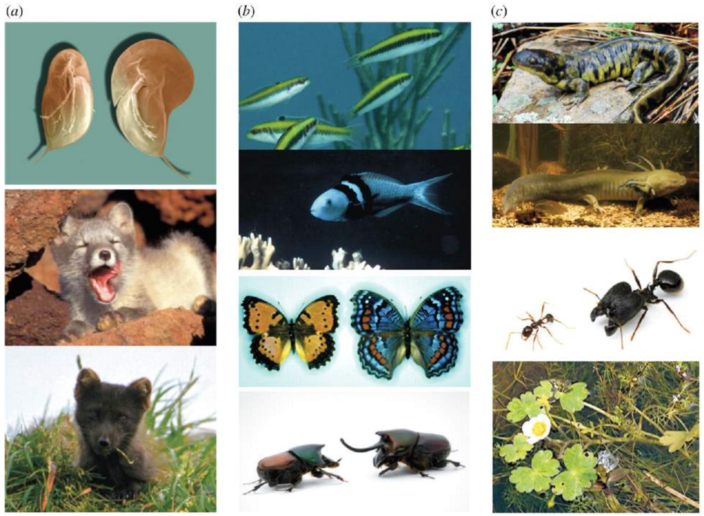
Phenotypic Plasticity:

- One genotype can produce more than one phenotype when exposed to different environments
- The modification of developmental events by the environment,
- The ability of an individual organism to alter its phenotype in response to changes in environmental conditions.

Phenotypic plasticity may be a powerful means of *adaptation*

- predator avoidance, insect wing polymorphisms, timing of metamorphosis in amphibians, osmoregulation in fishes, reproductive tactics in male vertebrates.
- in humans, examples of plasticity include results of exercise, training and/or dieting on human morphology and physiology.

Phenotypic Plasticity and Polyphenism



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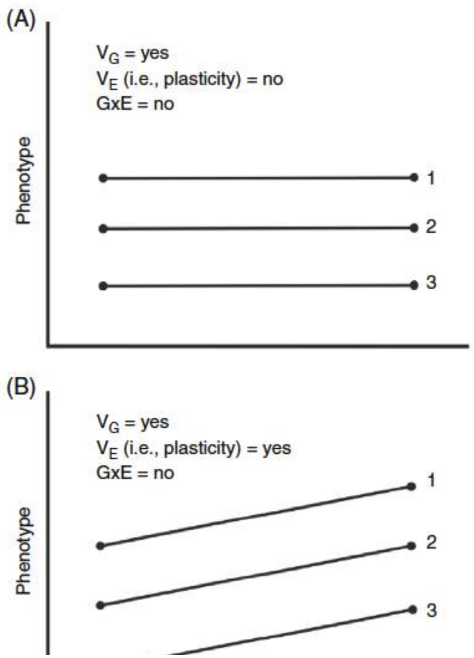
Phenotypic plasticity can be passive, anticipatory, instantaneous, delayed, continuous, discrete, permanent, reversible, beneficial, harmful, adaptive or non-adaptive, and generational.

Phenotypic plasticity, through its ecological effects, can facilitate evolutionary change and speciation
(COURS IV)

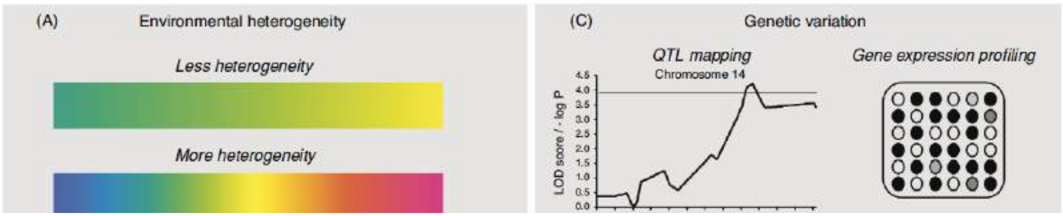
Natural populations of snowshoe hares exposed to 3 y of widely varying snowpack
Show plasticity in the rate of the spring white-to-brown molt
But not in the initiation dates of color change
Nor in the rate of the autumn brown-to-white molt.

NB Climate change may lead to increased mortality due to camouflage mismatching…

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 all phenotypically plastic —that is, they exhibit "reaction norms" of nonzero slope—for the trait of interest, but the reaction norms are parallel. The environmentally induced phenotypic differences within each genotype are often referred to as "nongenetic" or "environmental" difference.



HOW do organisms integrate environmental cues with inherited biological information to guide development or adult transformation?

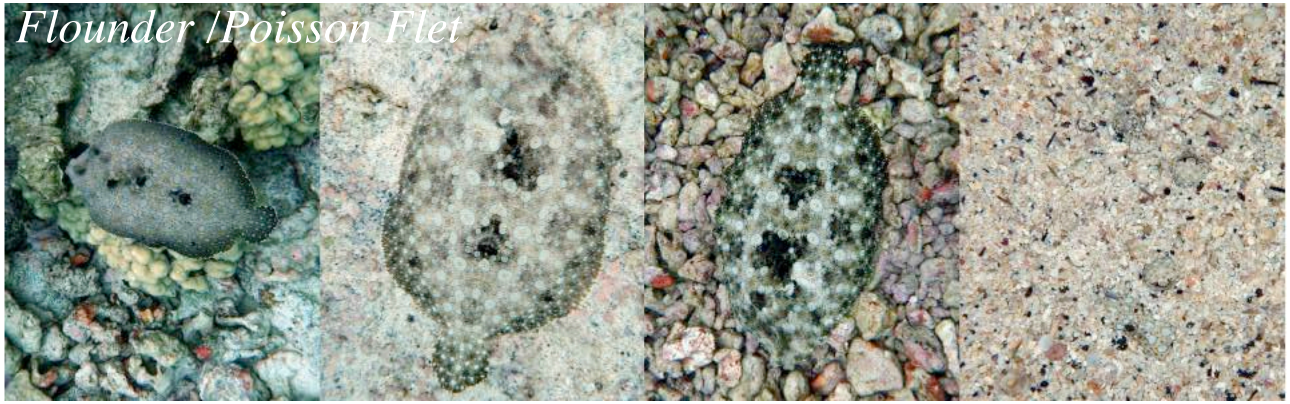
When transmitted across generations, this information can include more than genes alone, because organisms also inherit environmentally induced developmental factors from their parents, such as altered provisioning of resources to the embryo and epigenetic modifications of genetic material…

What is the nature of these inherited developmental effects and what are their <u>transmission mechanisms</u>?

COURS III and IV

Phenotypic Plasticity

Camouflage



Peacock Flounder, Bothus mancus displaying its active camouflage abilities, changing colors depending on the colors of its surroundings. All frames are of the same fish taken few minutes apart.

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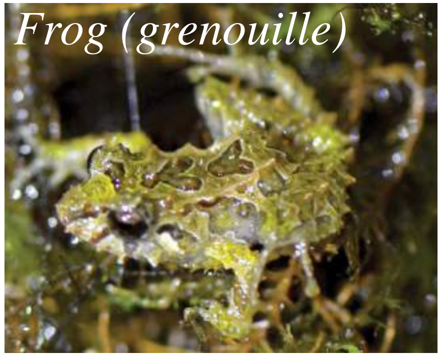
Phenotypic Plasticity

Pristimantis mutabilis skin texture transformation



Pristimantis mutabilis skin texture transformation

Over the course of 330 seconds, the skin of the mutable rain frog (Pristimantis mutabilis) from Ecuador changed from highly textured and rough to smooth

Juan Guayasamin (2015) The Zoological Journal of the Linnean Society

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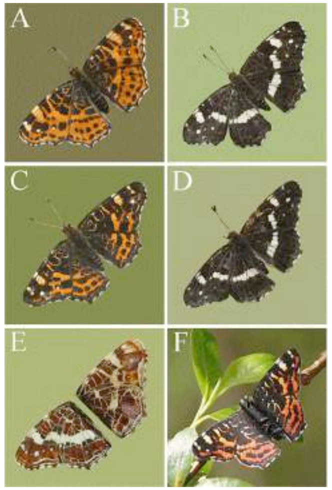
Phenotypic Plasticity

Mimicry: Diet-induced Polyphenism of *Nemoria* moth caterpillars

The catkin (left) and twig (right) morphs in caterpillars of the moth Nemoria arizonaria (photo courtesy of Erik Greene).

Phenotypic Plasticity

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.

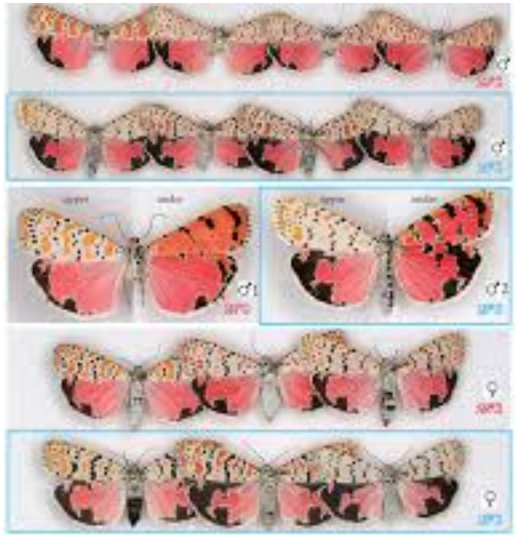


Fig. 1. Example of cold-induced reaction norm (decrease of orange/red on forewing, increase of melanic markings on the hindwings) in *Utetheisa ornatrix bella* (sample female specimens from Trial 2 (see Supplementary materials)).

Sourakov, 2015:

Natural variability in siblings | **Cold-induced variability in siblings**

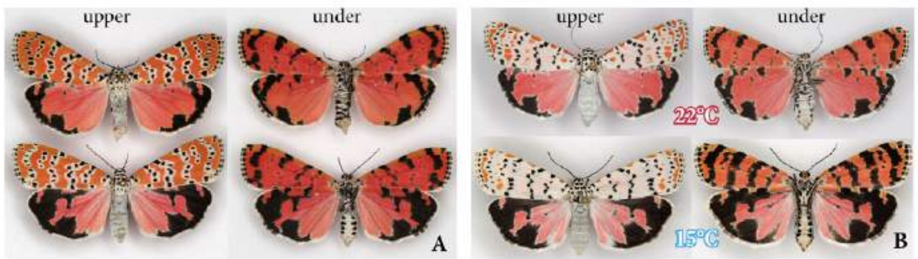


Fig. 3. Comparison of black marking variation in *Utetheisa ornatrix bella* found naturally among siblings (A) and induced by temperature (B). Natural variation can be confined to a single wing pair (in this case, hindwing), while induced variation affects simultaneously both wing pairs.

Cool Spring Form | Warm Summer Form

Evolution in response to climate change in the seasonal polyphenism of Colias eurytheme butterflies

Matthew Nielsen:

« 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. » https://www.lep-net.org/

Phenotypic Plasticity

© 2016. Published by The Company of Biologists Ltd | Journal of Experimental Biology (2016) 219, 354-363 doi:10.1242/jeb.131714

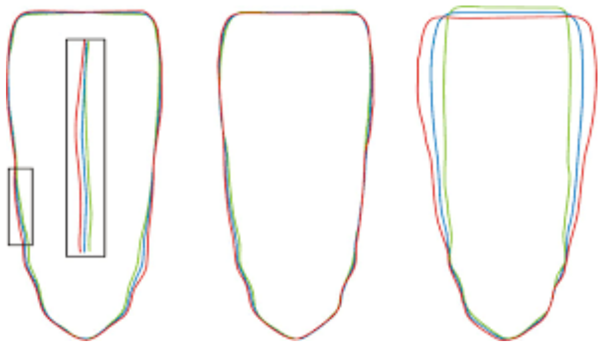
RESEARCH ARTICLE

Diet-induced phenotypic plasticity in European eel (*Anguilla anguilla*)

Jens De Meyer*, Joachim Christiaens and Dominique Adriaens

Two phenotypes are present within the European eel population: broad-heads and narrow-heads. The expression of these phenotypes has been linked to several factors, such as diet and differential growth. The exact factors causing this dimorphism, however, are still unknown. In this study, we performed a feeding experiment on glass eels from the moment they start to feed. Eels were either fed a hard diet, which required biting and spinning behavior, or a soft diet, which required suction feeding. We found that the hard feeders develop a broader head and a larger adductor mandibulae region than eels that were fed a soft diet, implying that the hard feeders are capable of larger bite forces. Next to this, soft feeders develop a sharper and narrower head, which could reduce hydrodynamic drag, allowing more rapid strikes towards their prey. Both phenotypes were found in a control group, which were given a combination of both diets. These phenotypes were, however, not as extreme as the hard or the soft feeding group, indicating that some specimens are more likely to consume hard prey and others soft prey, but that they do not selectively eat one of both diets. In conclusion, we found that diet is a major factor influencing head shape in European eel and this ability to specialize in feeding on hard or soft prey could decrease intra-specific competition in European eel populations.

Diet induced plasticity in Fish



This study shows that diet can already affect head shape early after the glass eels start to feed.

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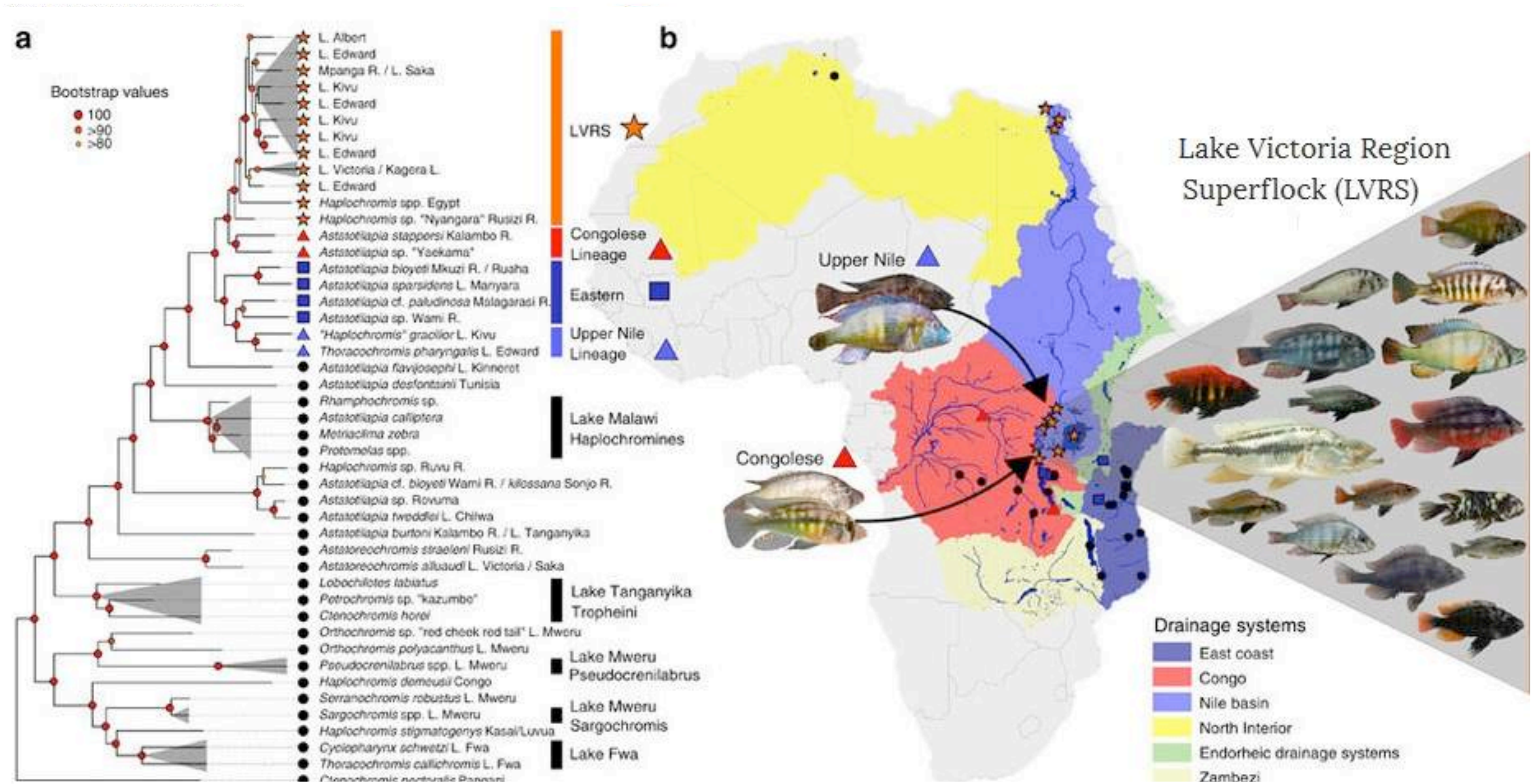
Phenotypic Plasticity and Rapid Speciation in Cichlids



Rapid, convergent radiations of cichlid fish in East African Lakes may have been facilitated by morphological plasticity, and its fixation as regulatory networks degenerate.

"The cichlids of Africa's lakes impress us mightily with what evolution can do in a short space of time", wrote Richard Dawkins in The Greatest Show on Earth (Bantam Press, 2009). https://natureecoevocommunity.nature.com/users/24561-richard-buggs/posts/13977-phenotypic-plasticity-drives-cichlid-radiations

E

Epigenetic and Phenotypic Plasticity in Insects

- **Polyphenisms are a major reason for the success of the insects.**
- 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.

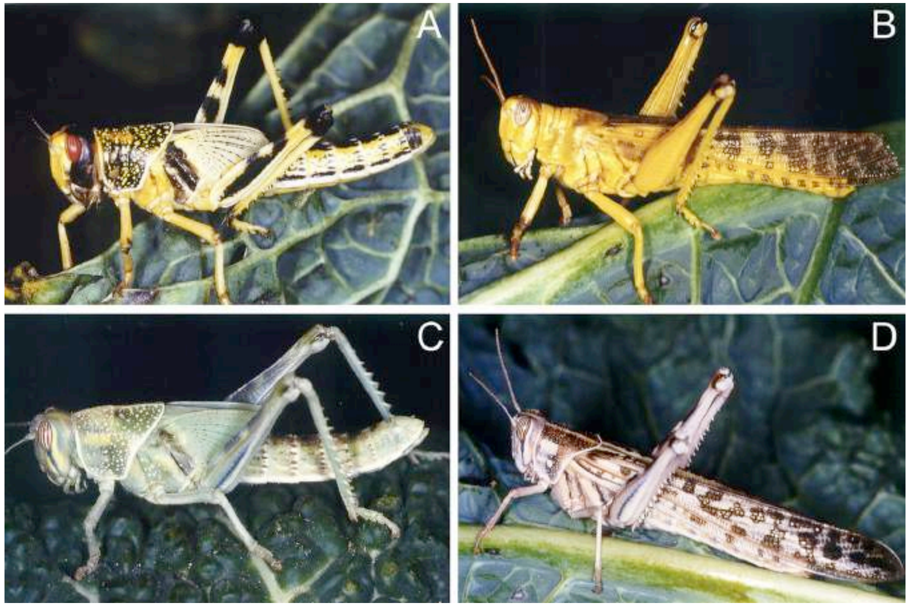
The developmental stages of insects provide some of the most striking examples:

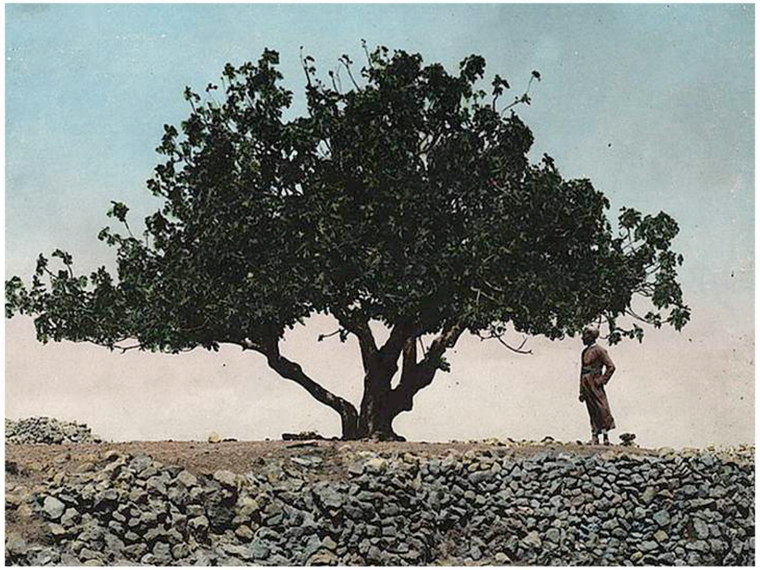
- the transition from larva to pupa to adult in holometabolous (discontinuously developing) insects such as the Lepidoptera (moths and butterflies), Coleoptera (beetles), Hymenoptera (ants, bees and wasps) and Diptera (true flies).

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?

Epigenetic and Phenotypic Plasticity in Locusts

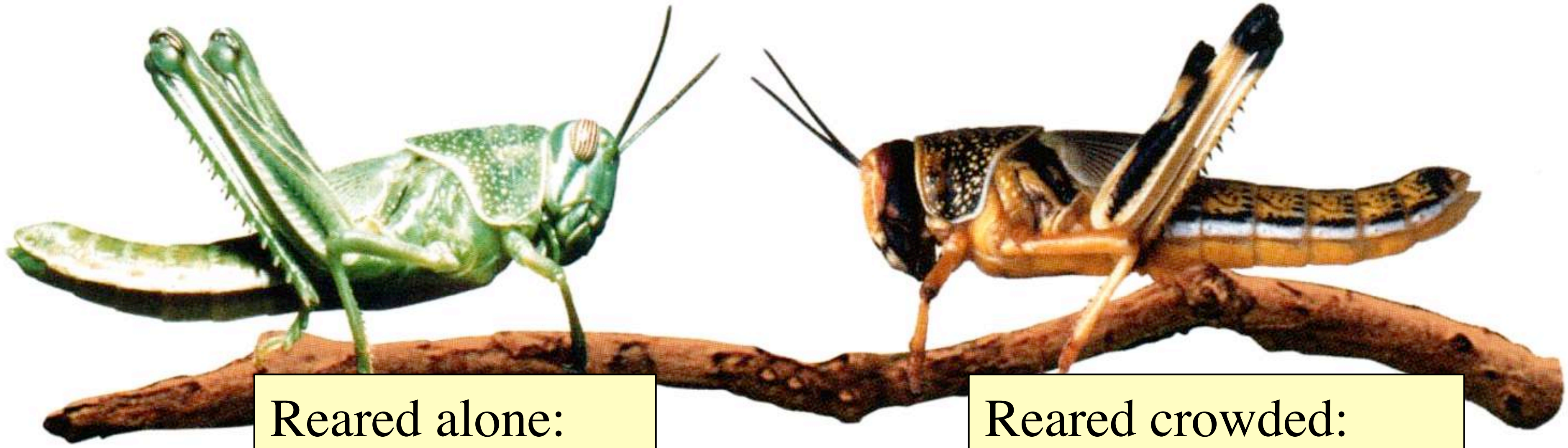




- Migratory locust swarms fly distances up to 1000 km.
- Swarms of the desert locust flew across the Atlantic Ocean in 1988, covering 5,000 km in 6 -10 days.
- Swarm sizes can cover areas up to 800 km2 and contain up to 40 billion locusts (largest terrestrial congregation of animals on Earth)…
- Swarms may contain 50 million adults per km2
- A moderate size 10km2 swarm can consume 1000 tons of fresh vegetation daily…

Epigenetic and Phenotypic Plasticity in Locusts

Two animals packed within the same genome



Reared alone:

phase *solitaria*

Reared crowded:

phase *gregaria*

- Phase transition induces a broad range of differences in **anatomy** (size, colour), **physiology** (lifespan, metabolism, immune responses, endocrinology and reproduction) & **behaviour** (solitary vs gregarious with population density increase)
- Gregarious morphs exhibit a wider dietary range, display increased locomotory activity, and fly during daytime, in contrast to isolated locusts, which generally fly at night

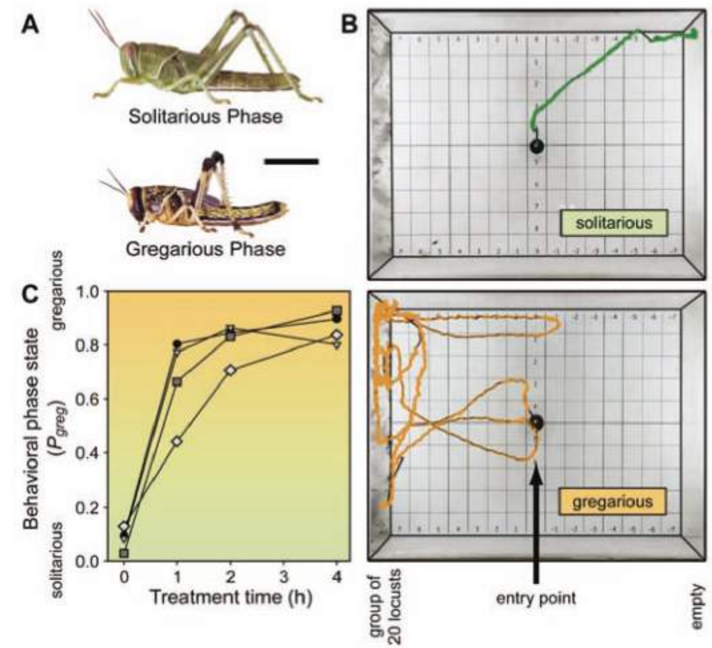
Courtesy of Stephen Simpson

Epigenetic and Phenotypic Plasticity in Locusts

Serotonin Mediates Behavioral Gregarization Underlying Swarm Formation in Desert Locusts

Michael L. Anstey,[1]* Stephen M. Rogers,[1,2]*† Swidbert R. Ott,[2] Malcolm Burrows,[2] Stephen J. Simpson[1,3]

Desert locusts, *Schistocerca gregaria*, show extreme phenotypic plasticity, transforming between a little-seen solitarious phase and the notorious swarming gregarious phase depending on population density. An essential tipping point in the process of swarm formation is the initial switch from strong mutual aversion in solitarious locusts to coherent group formation and greater activity in gregarious locusts. We show here that serotonin, an evolutionarily conserved mediator of neuronal plasticity, is responsible for this behavioral transformation, being both necessary if behavioral gregarization is to occur and sufficient to induce it. Our data demonstrate a neurochemical mechanism linking interactions between individuals to large-scale changes in population structure and the onset of mass migration.



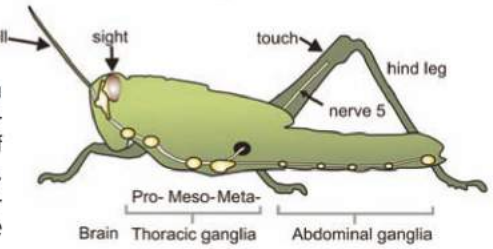
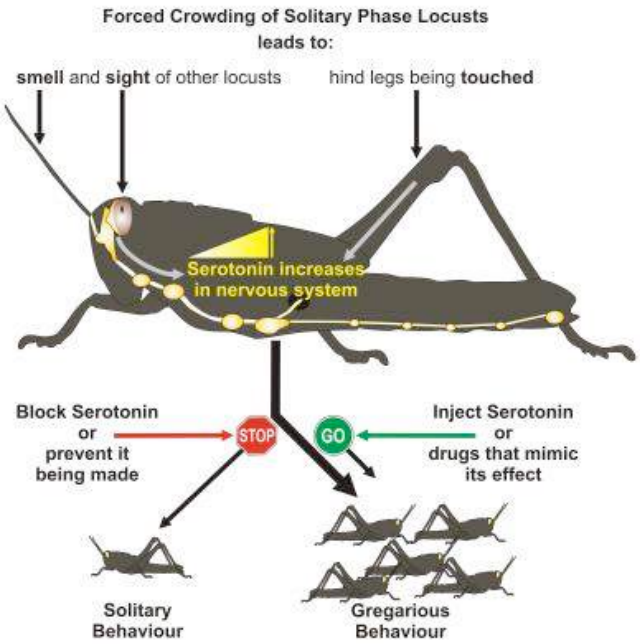


Fig. 1. (**A**) Final larval instar solitarious and gregarious locusts. Scale bar, 1 cm. (**B**) Trajectories (over 500 s) of a solitarious (upper) and gregarious (lower) locust in the behavioral arena. A group of 20 long-term gregarious-phase locusts was placed behind a clear partition on the left. (**C**) Solitarious locusts undergo rapid behavioral gregarization with appropriate stimulation; median P_{greg} of locusts treated for 0 to 4 hours by either forced crowding with gregarious locusts (circles), stroking a hind femur (squares), electrically stimulating the principal hind-leg nerve (diamonds), or exposure to the sight and smell of other locusts (triangles). See SOM text for analysis. (**D**) The CNS of a locust consists of the brain, which receives olfactory and visual information, and a chain of segmental ganglia linked by paired connectives. The three thoracic ganglia receive direct mechanosensory and proprioceptive inputs from the legs.

- Only serotonin shows a substantial increase during the critical 1–4 h window during which gregarious behaviour is established. Blocking the action of serotonin or preventing its synthesis prevents behavioural gregarization.
- Applying serotonin or its agonists induces gregarious behaviour even in locusts that have never encountered other locusts.
- Behavioural changes can rely on short-term neuronal plasticity to alter circuit activity and function

Serotonin, a brain chemical and neurotransmitter influences moods in humans.

Serotoninergic nerve cells control swarming behaviour

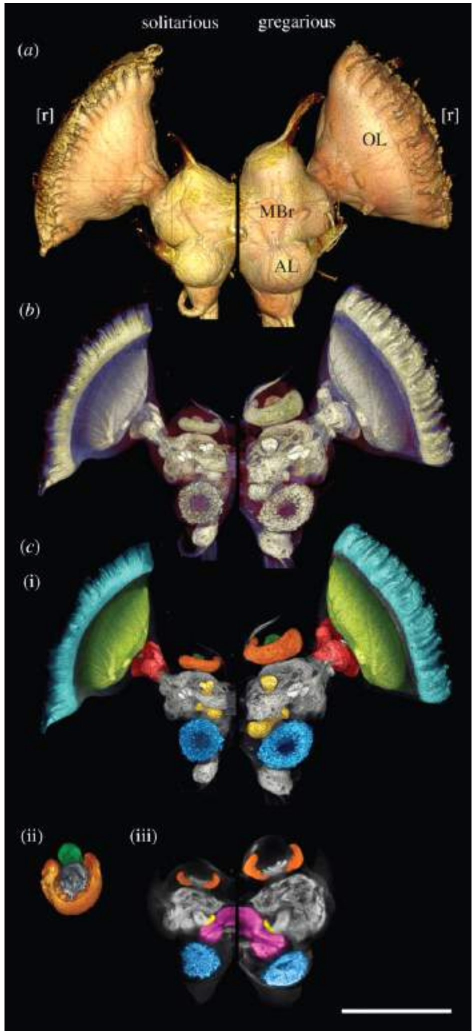


Anstey, M.L., Rogers, S.M., Ott, S.R., Burrows, M. & Simpson, S.J. (2009) *Science* 323, 627-630.

Courtesy of Stephen Simpson

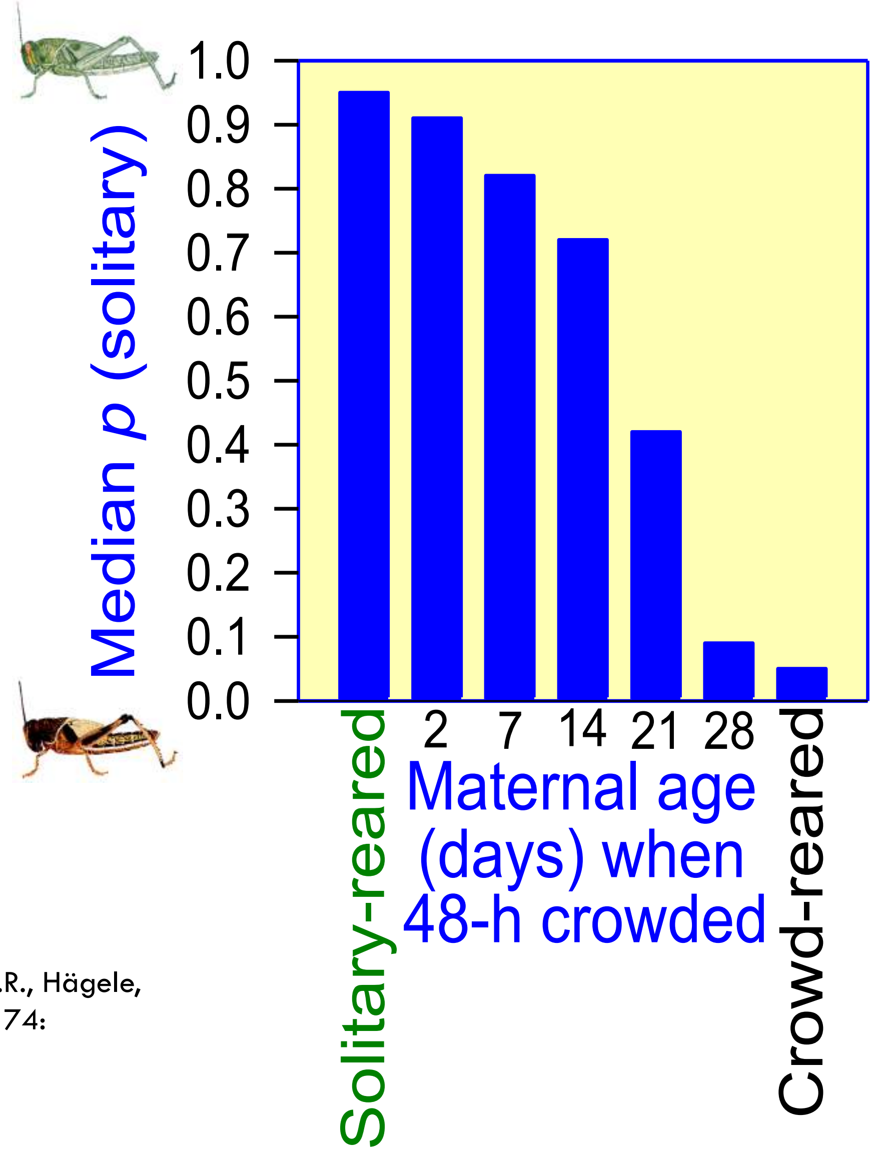
Brain morphology changes

Half-brains of a solitarious locust (left) and gregarious locust (right) in frontal view to the same scale (scale bar, 1 mm).



Swidbert R. Ott, and Stephen M. Rogers Proc. R. Soc. B 2010;277:3087-3096

Phase state is transmitted epigenetically: the mother has a memory of being crowded, which she translates to her offspring



Courtesy of Stephen Simpson

The older she is when crowded the more effectively she transmits the crowiding behaviour to her offspring

Simpson, S.J., McCaffery, A.R., Hägele, B. (1999 *Biological Reviews* 74: 461-480.

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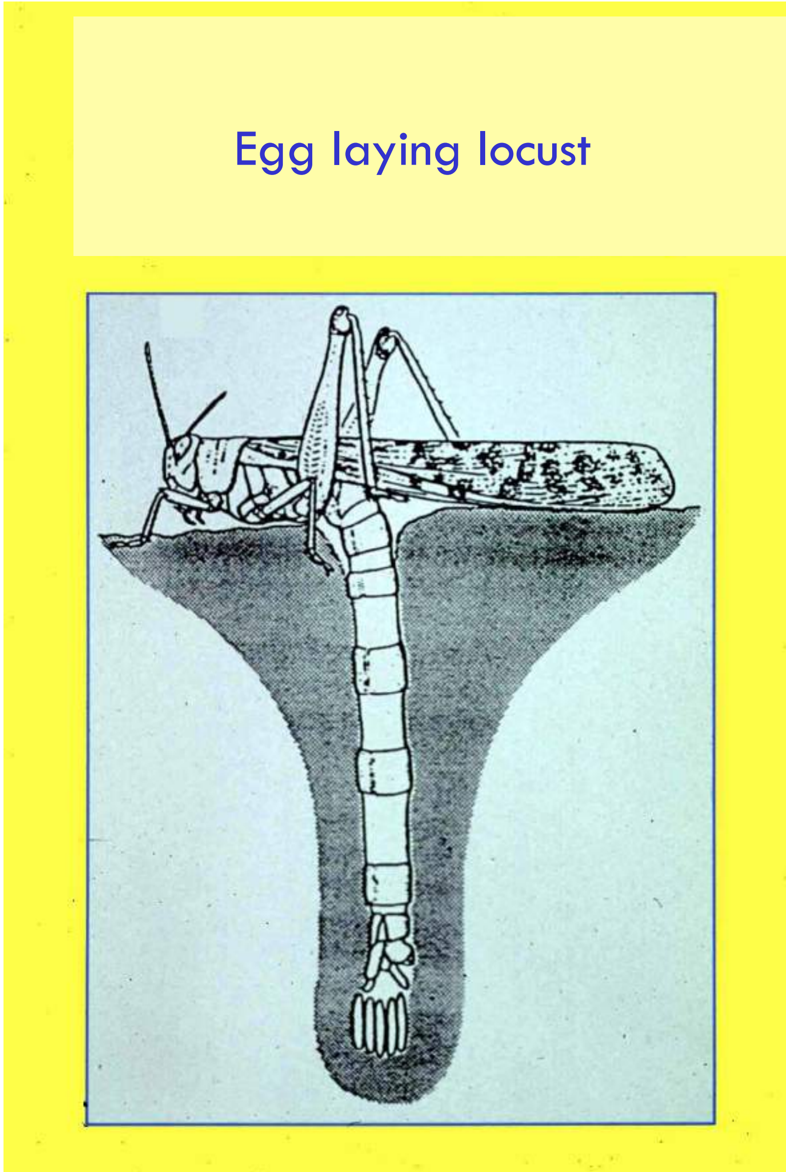
She influences hatchling phase-state by adding a chemical to the egg foam when laying a pod of eggs



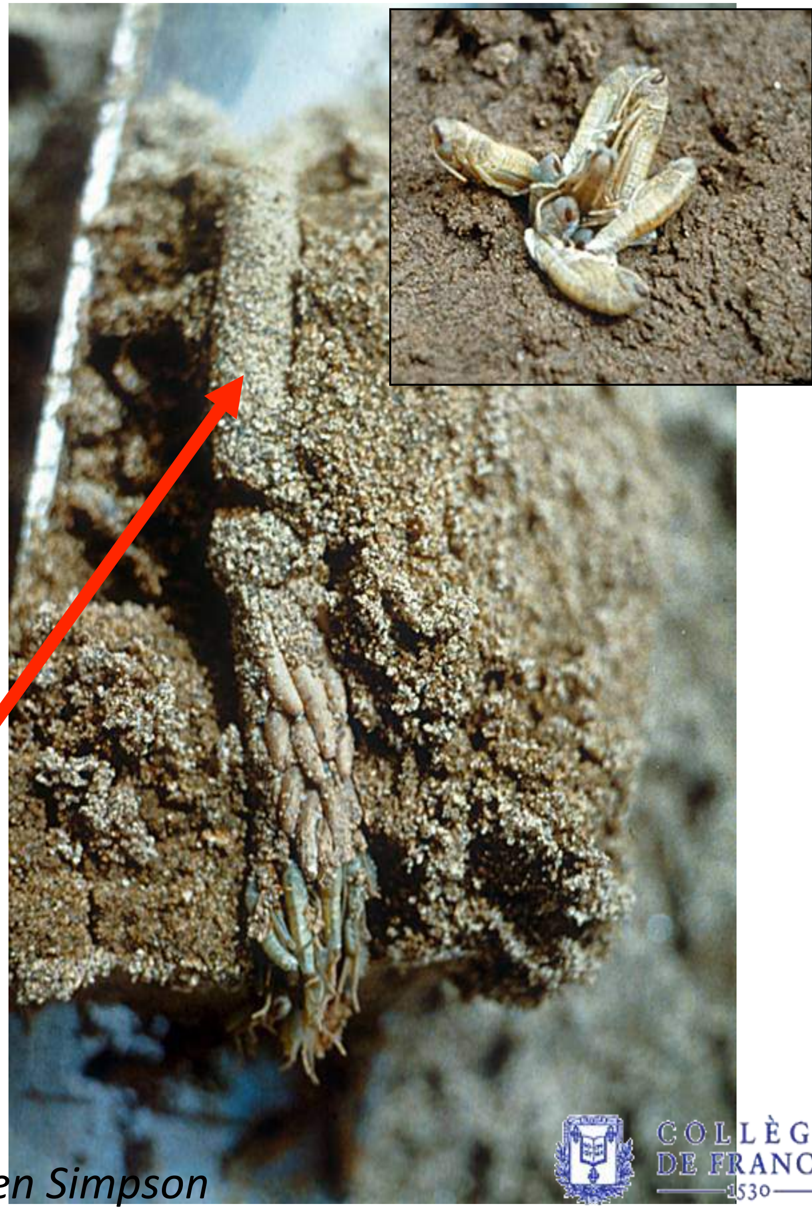
- Water soluble: some activity in ethanol extracts, none in hexane (therefore not C8 ketones as suggested by Malual et al., 2001)

- Originate in female accessory glands (Haegele, B., McCaffery, A.R., Oag, V., Bouaichi, A. & Simpson, S.J. (2000) *Journal of Insect Physiology*, 46, 275-280)

- Only effective within a few hours of the eggs being laid

Courtesy of Stephen Simpson

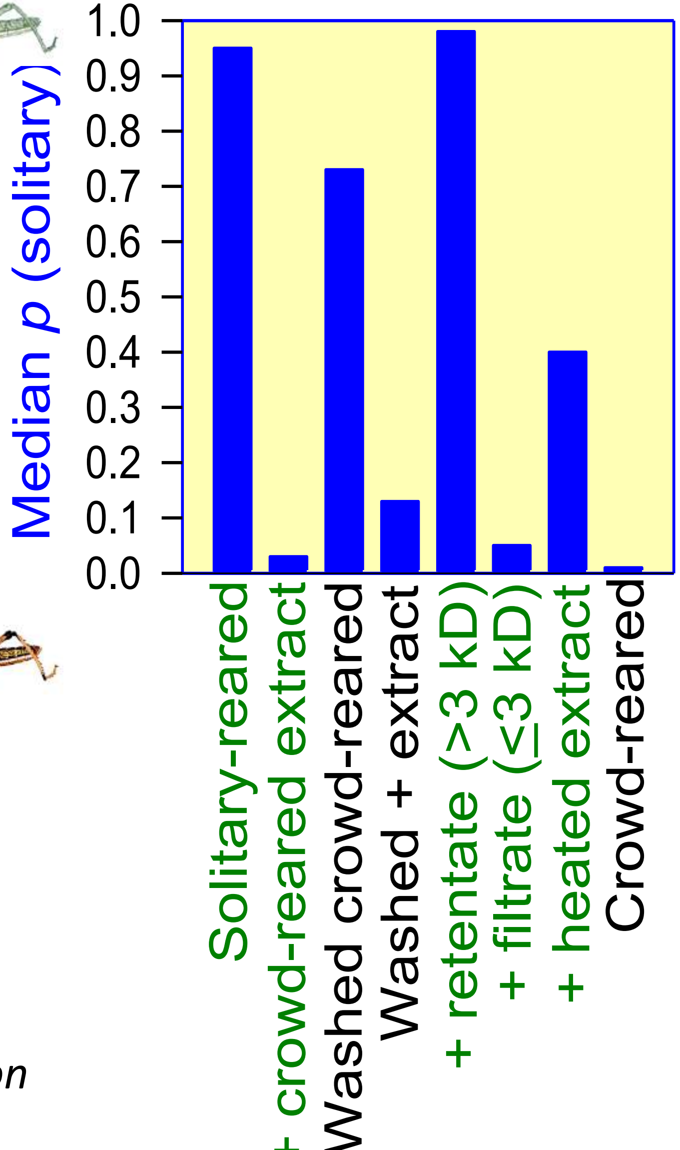
She influences hatchling phase-state by adding a chemical to the egg foam when laying a pod of eggs



Egg foam

Courtesy of Stephen Simpson

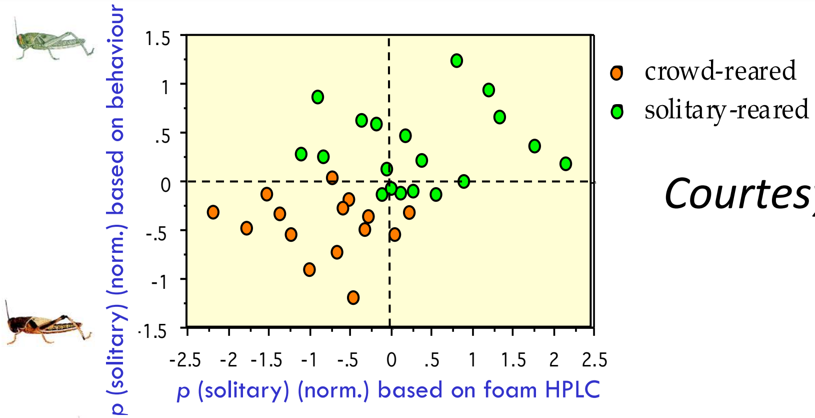
Maternally deposited chemical in egg foam is responsible for gregarious behaviour



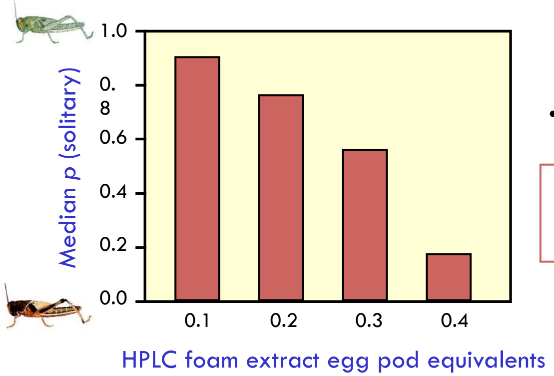
Courtesy of Stephen Simpson

McCaffery, A.R., Simpson, S.J., Islam, M.S. & Roessingh, P. (1998) *Journal of experimental Biology*, 201, 347-363.

Foam chemistry correlates with hatchling behaviour



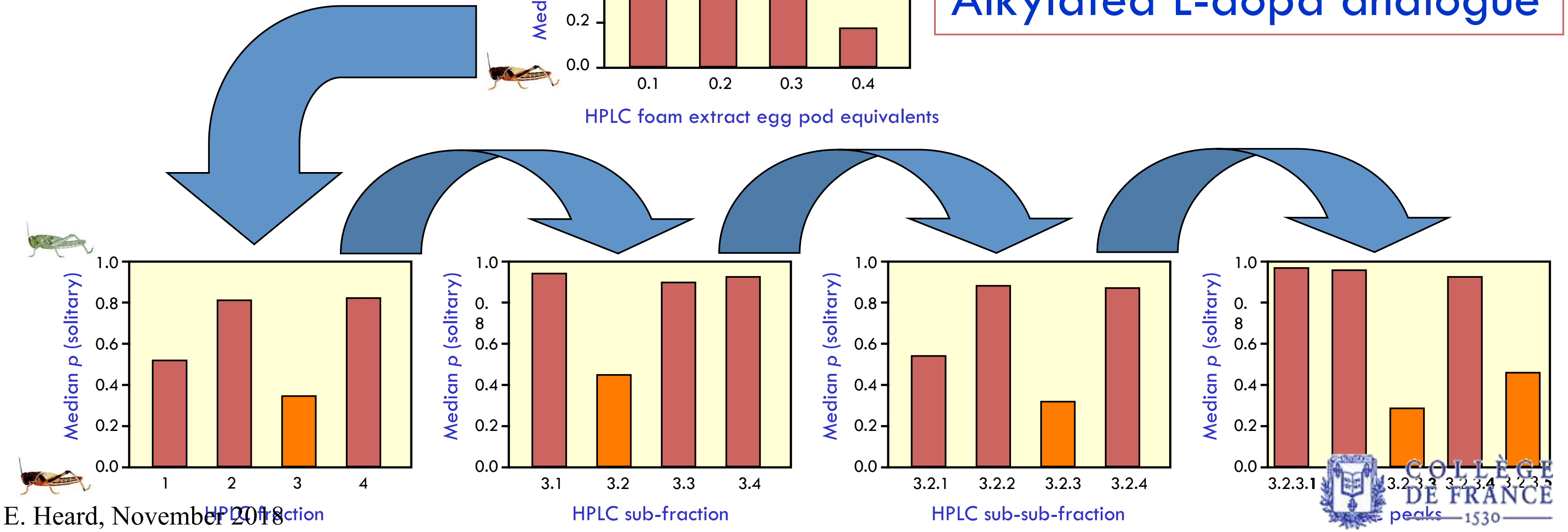
Courtesy of Stephen Simpson



..in a dose-dependant manner

Alkylated L-dopa analogue

Fractionation

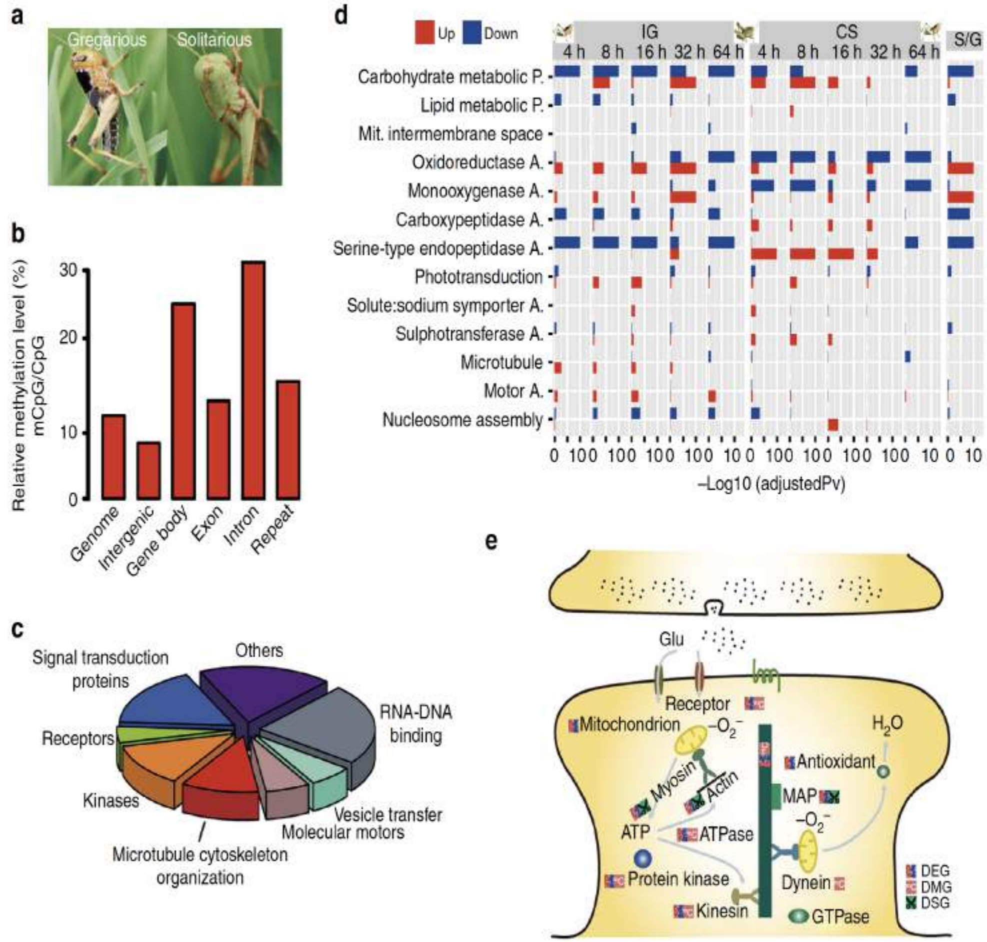


The Genome/Epigenomes of Solitarious vs Gregarious Locusts

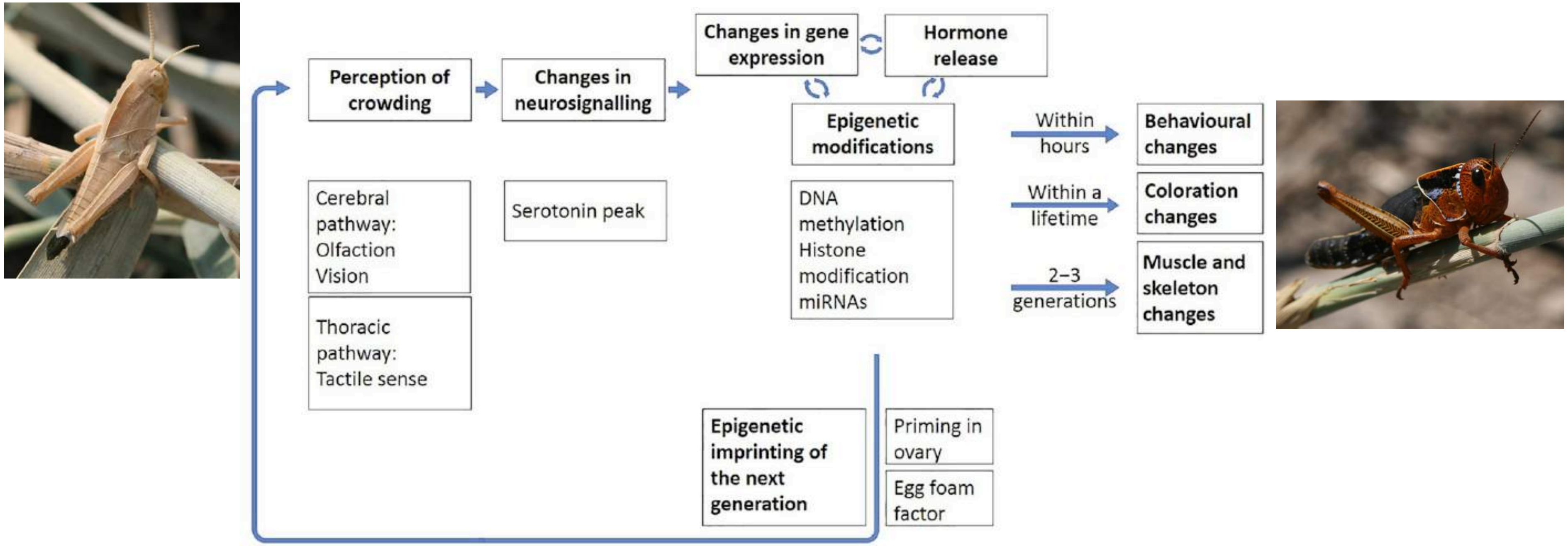
ARTICLE
Received 6 Aug 2013 | Accepted 19 Nov 2013 | Published 14 Jan 2014 DOI: 10.1038/ncomms3957 OPEN

The locust genome provides insight into swarm formation and long-distance flight

- Twenty-five significantly expanded gene families in the L. migratoria genome were mainly involved in detoxification, chemoreception, chromosome activity and nutritional metabolism, indicating unique adaptation features of the L. migratoria genome
- A massive number of repetitive elements (at least 60%) in the L. migratoria genome and their rates of loss are lower than those in other insect species
- 90 differentially methylated genes
- 4,893 differentially expressed genes in at least one of the time points during both processes (28.3% of gene sets)
- During locust crowding (ie S to G) : increased expression of genes associated with synaptic transmission, carbohydrate metabolism and nucleosome assembly, decrease for genes associated with oxidoreductase and antioxidase, microtubule and motor activity.



Epigenetic and Phenotypic Plasticity in Locusts



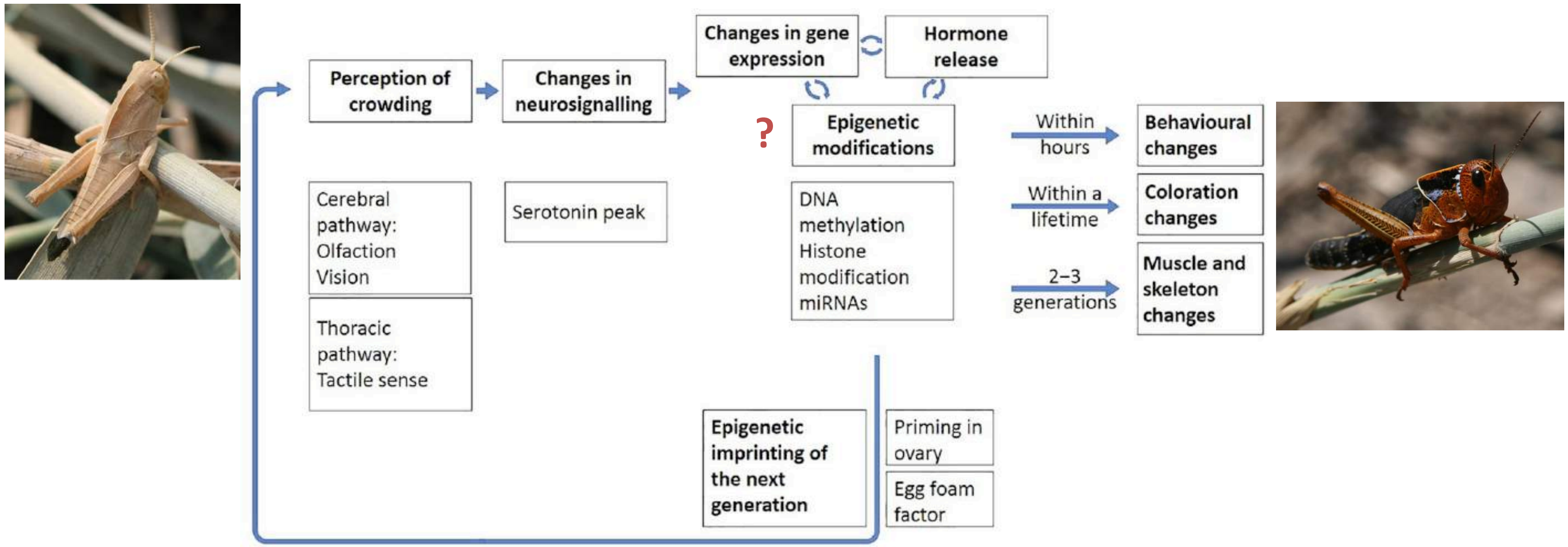
Initiation of phase transition

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

- Within hours - serotonin induces behavioural change
- Inducing neuronal plasticity to alter circuit activity and function?
- Across generations - tactile information of degree of crowding experienced by the mother directly influences the **colour** of hatchlings in S. gregaria and L. migratoria => via maternal factor
- 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 behaviour…

Epigenetic and Phenotypic Plasticity in Locusts

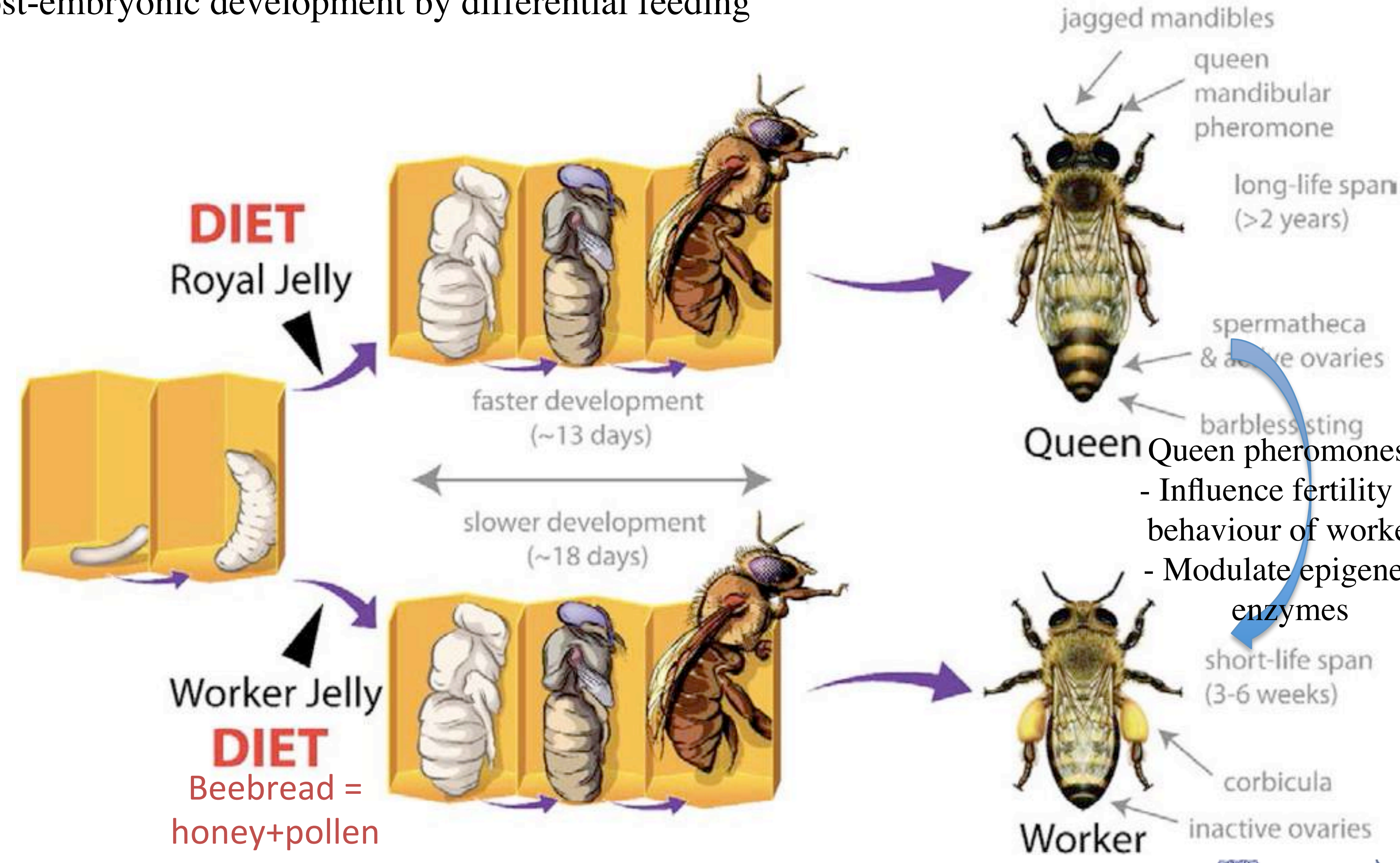


Propagation of phase transition

- 6 kDa Phase-related peptide (Clynen et al., 2002) is present in much higher concentrations in the haemolymph of gregarious (up to 0.1 mmol l–1) compared to solitarious locusts – goes down progressively (generations) when gregarious locust put into solitude
- Higher concentrations of this peptide are found in the eggs of gregarious *S. gregaria* (Rahman et al., 2002, 2003
- 90 differentially methylated genes; 4,893 differentially expressed genes in at least one of the time points during both processes (28.3% of gene sets)
- During locust crowding (ie S to G) : increased expression of genes associated with synaptic transmission, carbohydrate metabolism and nucleosome assembly, decrease for genes associated with oxidoreductase and antioxidase, microtubule and motor activity.
- 105 retro-elements in migratory locust: some show a differential expression in solitarious and gregarious phase at the fifth instar and in adults (Jiang et al., 2012)

Epigenetic and Phenotypic Plasticity in Social Insects

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



Queen pheromones –
- Influence fertility and behaviour of workers
- Modulate epigenetic enzymes

Beebread =
honey+pollen
Contains plant miRNAs

Epigenetic and Phenotypic Plasticity in Social Insects

Queen pheromones modulate DNA methyltransferase activity in bee and ant workers

Luke Holman[1], Kalevi Trontti[2,3] and Heikki Helanterä[3,4]

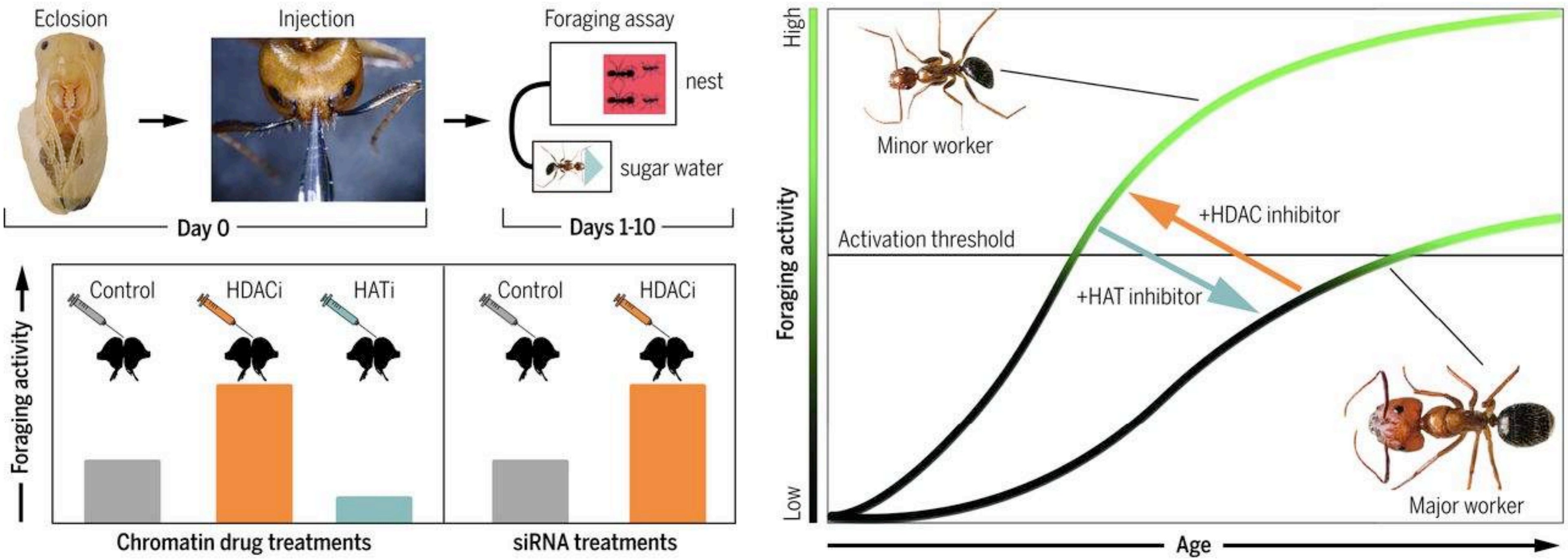
[1]Division of Ecology, Evolution & Genetics, Research School of Biology, Australian National University, Canberra, Australian Capital Territory 2601, Australia
[2]Department of Biosciences, Division of Genetics, University of Helsinki, Helsinki 00014, Finland
[3]Centre of Excellence in Biological Interactions, Department of Biosciences, University of Helsinki, PO Box 65, Helsinki 00014, Finland
[4]Tvärminne Zoological Station, J. A. Palménin tie 260, Hanko 10900, Finland

DNA methylation is emerging as an important regulator of polyphenism in the social insects. Research has concentrated on differences in methylation between queens and workers, though we hypothesized that methylation is involved in mediating other flexible phenotypes, including pheromone-dependent changes in worker behaviour and physiology. Here, we find that exposure to queen pheromone affects the expression of two DNA methyltransferase genes in *Apis mellifera* honeybees and in two species of *Lasius* ants, but not in *Bombus terrestris* bumblebees. These results suggest that queen pheromones influence the worker methylome, pointing to a novel proximate mechanism for these key social signals.

- Queen pheromones = chemical signals that characterize queens and other reproductive individuals
- Multiple important functions, and likely exist in all eusocial insects [14].
- Queen pheromones have long-lasting ‘primer’ effects on recipients’ physiology, such as rendering them sterile
- Primer effects might involve epigenetic changes, allowing individuals that have detected queen pheromone to record this
- Information and express a long-lasting transcriptomic response…
- => Does queen pheromone stimulate DNA methyltransferase activity in workers?
- Queen pheromone treatment
- - *lowered* DNMT1 expression in A. mellifera honeybees,
- - *elevated* expression in Lasius niger and L. flavus ants
- - had *no effect* on expression in B. terrestris bumblebees.

Epigenetic and Phenotypic Plasticity in Ants

- Epigenetic (re)programming of caste-specific behavior in the ant Camponotus floridanus (Simola et al, Science 2016)



An epigenetic model for division of labor. Left: Workers were injected at eclosion and tested for foraging activity. HDAC inhibition (HDACi) with chromatin drugs or siRNA enhanced foraging; HATi suppressed foraging. Right: Minor and major workers express distinct behavioral ontogenies. Minors forage earlier in life and with greater intensity than majors. HDACi in majors stimulated minor-like foraging behavior, a gain of function suppressed by HATi treatment.

Epigenetic mechanisms in life phase transitions?

• **Water flea *Daphnia magna***, exposure to 5-azacytidine reduced overall DNA methylation as well as body length (Vandegehuchte et al., 2010). DNA hypomethylation pattern was transferred to two subsequent generations that were not exposed to the drug, demonstrating transgenerational epigenetic inheritance

The locust genome is more highly methylated than most known insect genomes

• Many retro-transposons are methylated – and may be differentially expressed in phase transition? (Kang lab)

• 90 genes are differentially methylated (at least four differentially methylated CpG sites) in gregarious versus solitarious locusts, including genes involved in cytoskeleton formation - involved in synaptic plasticity and, for the phase transition, point to a crucial role of microtubule dynamics control in locust brains

Despite the overwhelming indications for an important role of epigenetics in the regulation of phase transitions in insects, the direct evidence is relatively limited.

Honeybee

DNA methylation and histone modifications in:

(1) the irreversible differentiation of a female larva into a queen or worker phenotype (Kucharski et al., 2008)

(2) the reversible shift for worker bees from a temporal nurse subcaste to the forager subcaste (Herb et al., 2012; Lockett et al., 2012).

The differentiation into a queen or a worker has dramatic consequences: a honeybee queen lives several years, is much larger, highly fertile and also differs in many more morphological traits and behavioural characteristics from her sisters that developed into workers and have a life expectancy of only a few weeks (Winston, 1987).

• Induction of queen-like phenotypes in honeybees, *Apis mellifera*, by downregulating of DNA methyltransferase 3 (Dnmt3) (Kucharski et al., 2008; Li-Byarlay et al., 2013).

• Buff-tailed bumblebee, *Bombus terrestris*, experimental alteration of DNA methylation by feeding with 5-aza-20-deoxycytidine (decitabine) renders queenless worker bees more aggressive and more fertile (Amarasinghe et al., 2014).

SUMMARY: Epigenetics in life phase transitions

- For more than a century – biodiversity within species (phenotypic variation) was regarded with interest but some suspicion as genetic determinism prevailed…
- Today it is clear that most species can display some degree of phenotypic plasticity – either distinctly stable « morphs » - or continuum of traits (eusociality)
- It can be functional (and potentially adaptive), neutral, or deleterious
- Can be restricted to a few minutes, to a whole life time, or to many generations
  ⇒ Implications for evolutionary theory… the Modern Synthesis?
- Clearly such plasticity can be subject to Natural Selection (Eg insects are the most diverse kingdom because of their remarkable phenotypic plasticity)
- How one genotype can give rise to different phenotypes through environmental effects is clearly an EPIGENETICS question – firmly brings us back to Waddington's original definition – but actual mechanisms are still elusive
- New tools to explore both genomes and epigenomes, as well as genetic engineering strategies, and ecotrons are opening up a new era of research.
- Understanding this level of biodiversity will be key to understand life on our planet, and how it can (or cannot) adapt to the rapid, manmade changes we are imposing.

CHAIRE ÉPIGÉNÉTIQUE ET MÉMOIRE CELLULAIRE

Année 2018-2019:
"Épigénétique, Environnement et Biodiversité"

13 Novembre 2018

Cours II
La diversité génétique et épigénétique au sein d'un individu ou d'un écosystème