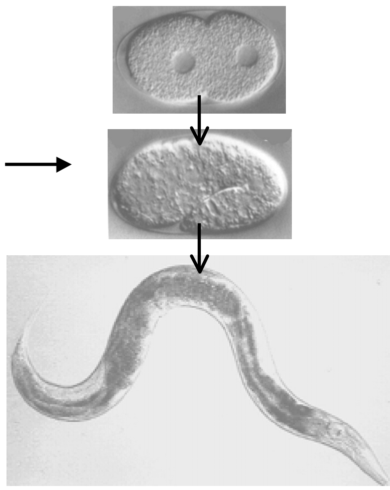
Evolution of development

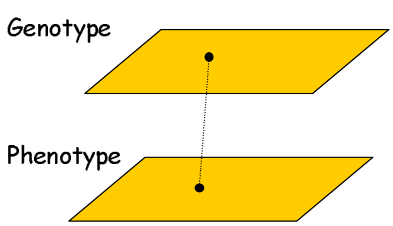
in evolution:

genotypic variations →

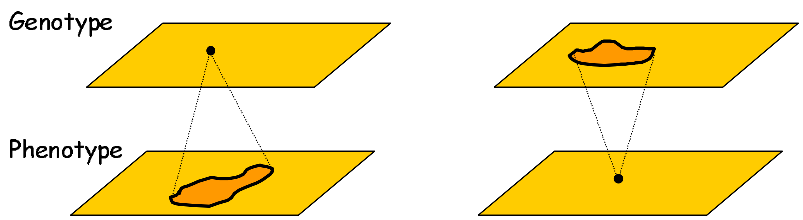


→ phenotypic variations

Correspondance between genotype and phenotype



Correspondance between genotype and phenotype



non-canalised/robust/buffered against internal or environmental noise

canalised/robust/buffered against genetic variations

- How stable are developmental processes when faced with internal/environmental/genetic variations ?
- What is the nature of genotypic changes that modify developmental processes?
- How do they propagate at the phenotypic level through the hierarchy of biological organisation?

Hierarchy of biological organization

DNA base
Molecule
my favorite module → **Cell**
Organism

… and some modularity inbetween all levels….

Modularity helps to describe morphological organization and developmental dynamics

How do these modules behave in evolution?

MODULAR ORGANIZATION OF DEVELOPMENT

(1) Supracellular modules — Organs; Interacting cells in development

(2) Modules of interacting molecules

MODULAR ORGANIZATION IN EVOLUTION

(3) Evolution of a supracellular network module - breakage

(4) Evolution of modules within the organism is facilitated by modularity of geneorganization

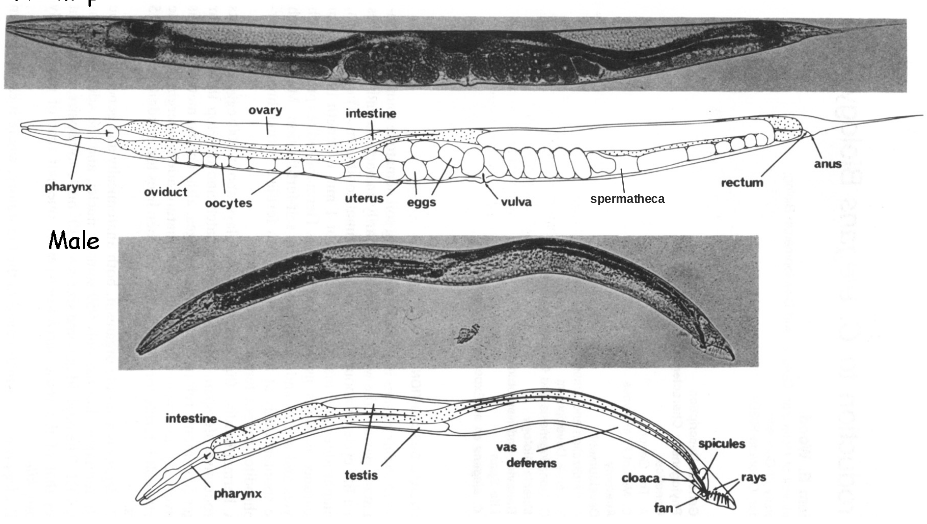
(5) Morphological evolution and the body plan

…and on nematode vulva evolution if time permits..

Caenorhabditis elegans

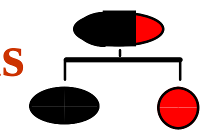
Hermaphrodite

Male



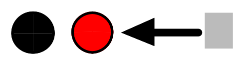
CELL SPECIFICATION MECHANISMS IN DEVELOPMENT

Segregation of determinants at mitosis



Visualization:
asymmetric cell size
segregation of determinant
(P granules, PAR-1, etc.)

Intercellular signaling



The specification of cell fates during *C. elegans* development is the result of **asymmetric cell divisions** and **cell interactions**.

Its **cell lineage is invariant** because of stereotyped asymmetric cell divisions, but also because the cell interactions are reproducible.

Is there a supracellular level of description of *C. elegans* development/morphology?

1. Modularity in the final result
(the structure in a broad sense)

A tissue
A body part

Not necessarily built in a modular fashion!

2. Modularity in the building process
(the mechanism of development)

Lineage
Cell interactions

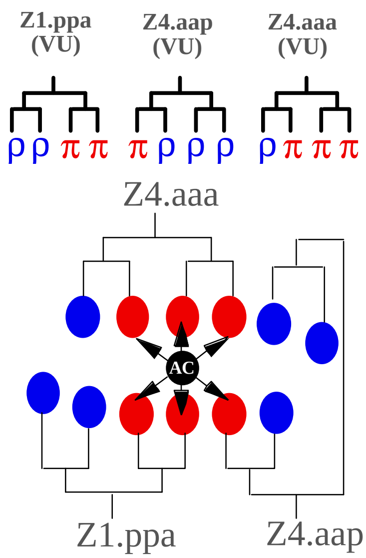
MODULAR SPECIFICATION BY LINEAGE

E → all intestinal cells and only intestinal cells

P4 → all germ line and only germ line

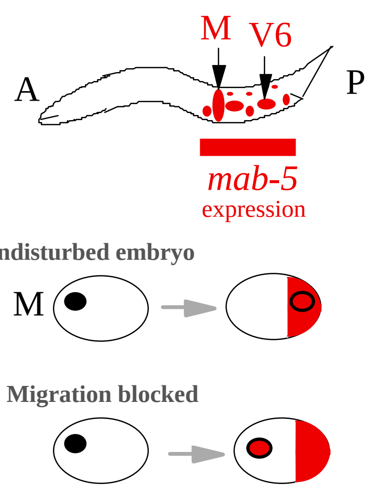
Sulston et al. 1983

MODULAR SPECIFICATION BY CELL INTERACTIONS



Newman and Sternberg, 1995

NON-MODULAR SPECIFICATION: PIECEMEAL RECRUITMENT



Expression of *mab-5* in the M cell is independent of its final position

Cowing and Kenyon, 1996

Cell groups may be specified

A. in a modular fashion by:

i. shared lineage

ii. shared cell interactions

'Independent' cell interaction networks
Often used in the development
of coherent final structures (ex: limb bud)

B. in a non-modular fashion
by piecemeal recruitment
« perverse assignments »
(J. Sulston et al.)

MODULAR ORGANIZATION OF DEVELOPMENT

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(2) Modules of interacting molecules

MODULAR ORGANIZATION IN EVOLUTION

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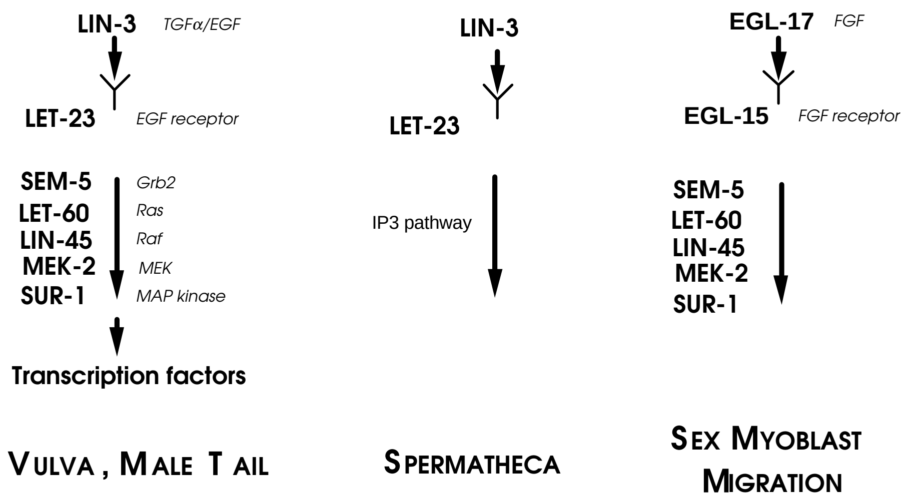
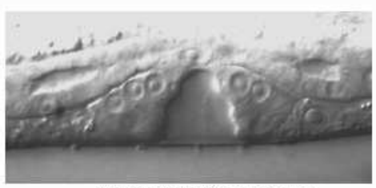
(5) Morphological evolution and the body plan



Reuse of molecular pathways in development - submodules



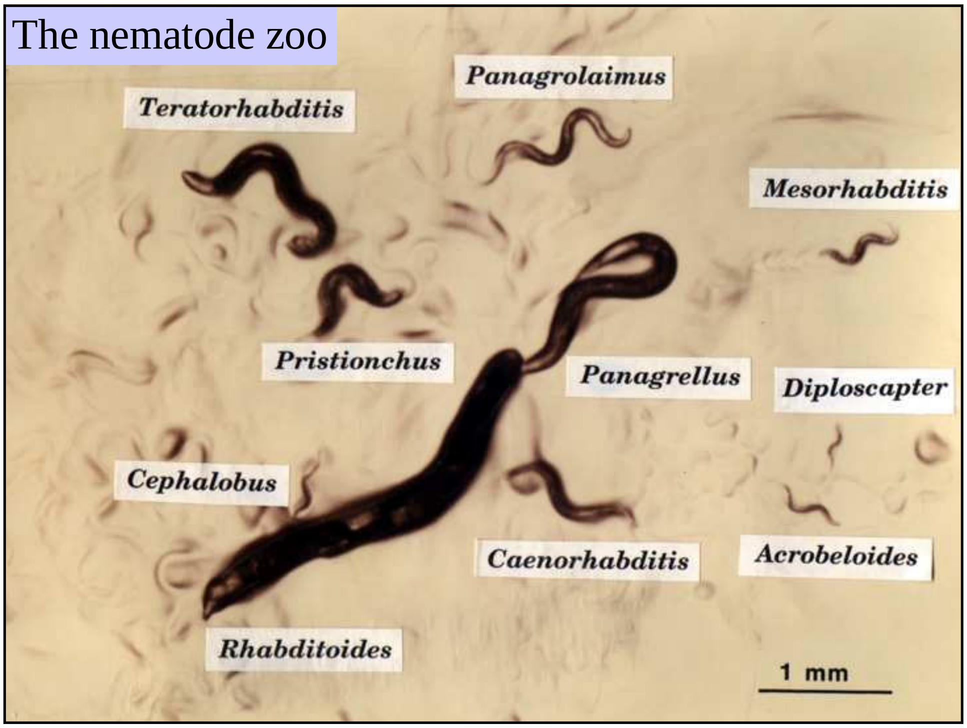
Caenorhabditis elegans
vulval induction
EGF-Ras-MAP kinase

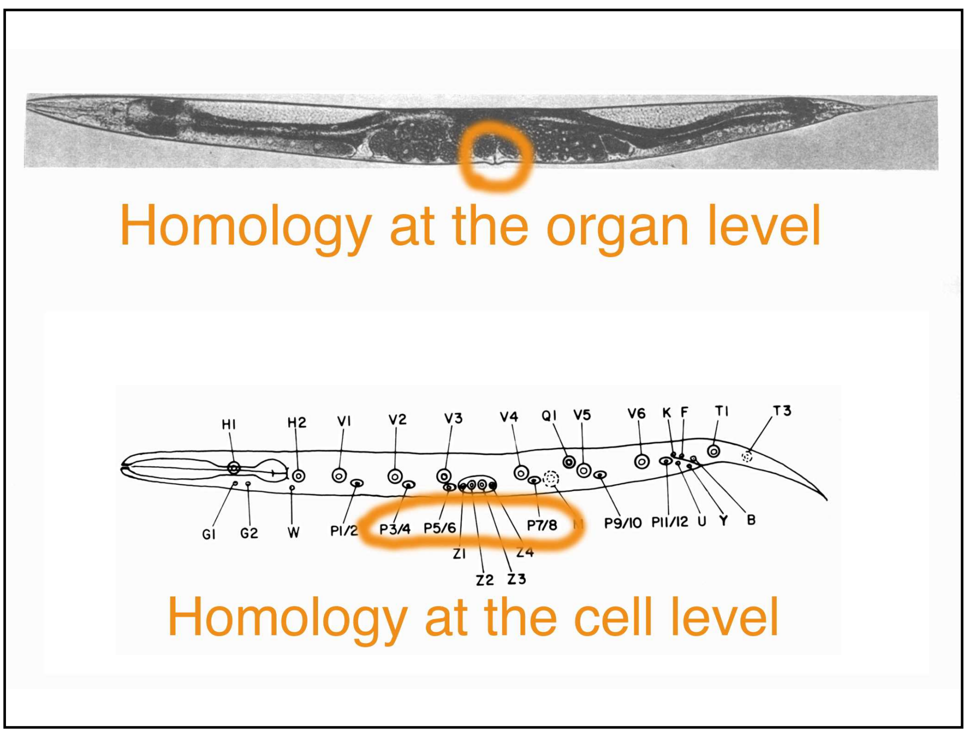
Drosophila melanogaster
eye photoreceptor induction
EGF-Ras-MAP kinase

Molecular conservation

Reuse in non-homologous contexts

➡ Evolution of development of homologous structures


The nematode zoo
Teratorhabditis
Panagrolaimus
Mesorhabditis
Pristionchus
Panagrellus
Diploscapter
Cephalobus
Caenorhabditis
Acrobeloides
Rhabditoides
1 mm


Homology at the organ level
H1
H2
V1
V2
V3
V4
Q1
V5
V6
K
F
T1
T3
G1
G2
W
P1/2
P3/4
P5/6
P7/8
P9/10
P11/12
U
Y
B
Z1
Z2
Z3
Z4
Homology at the cell level

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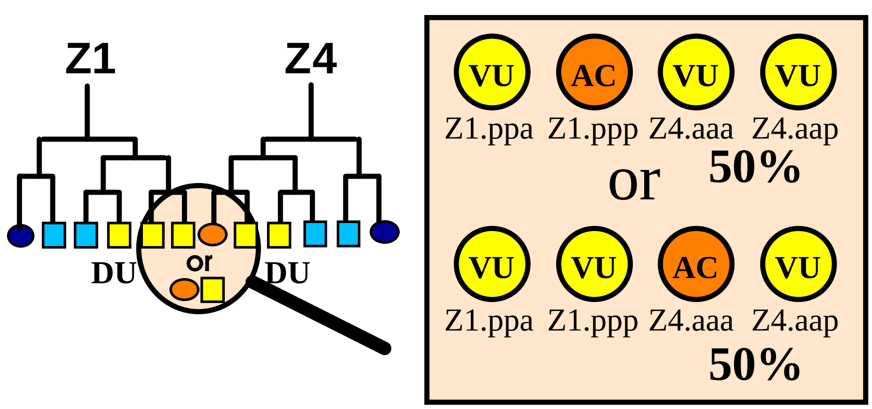
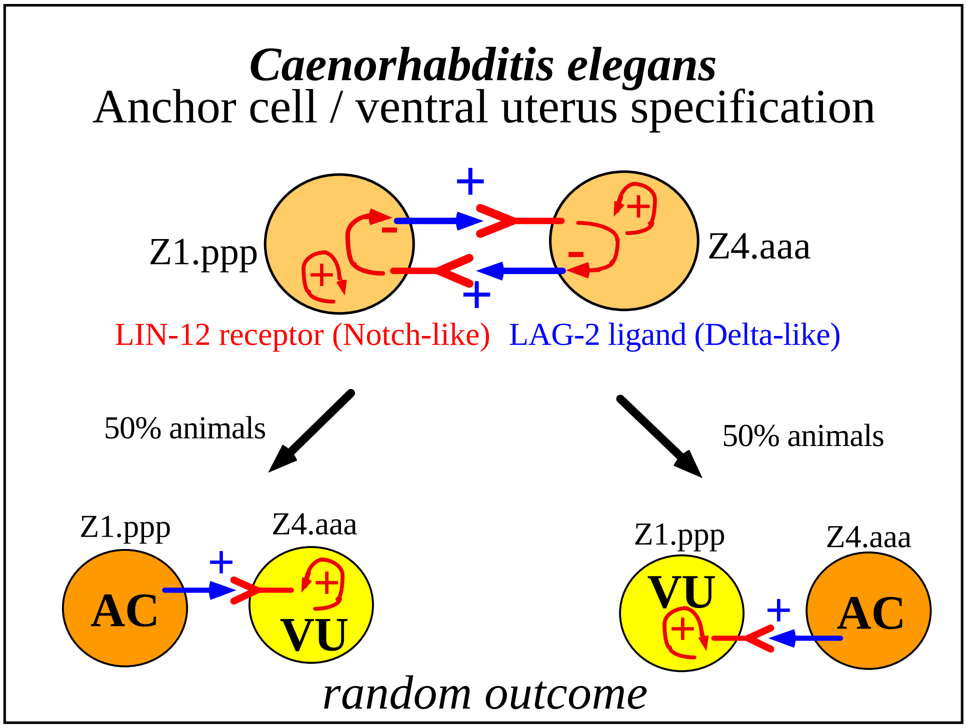
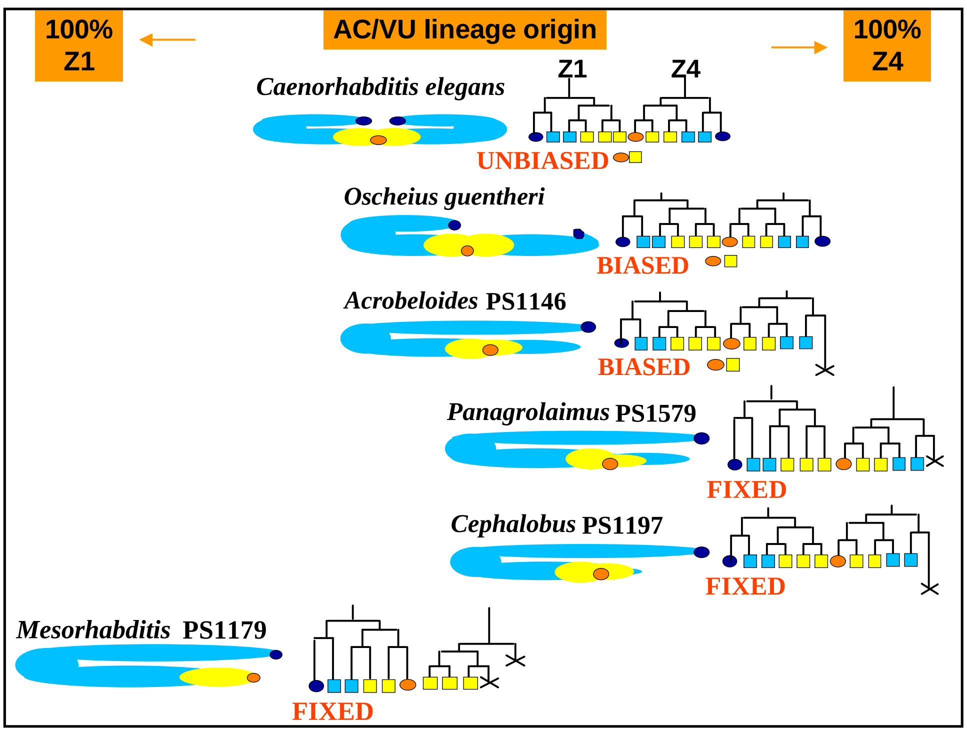
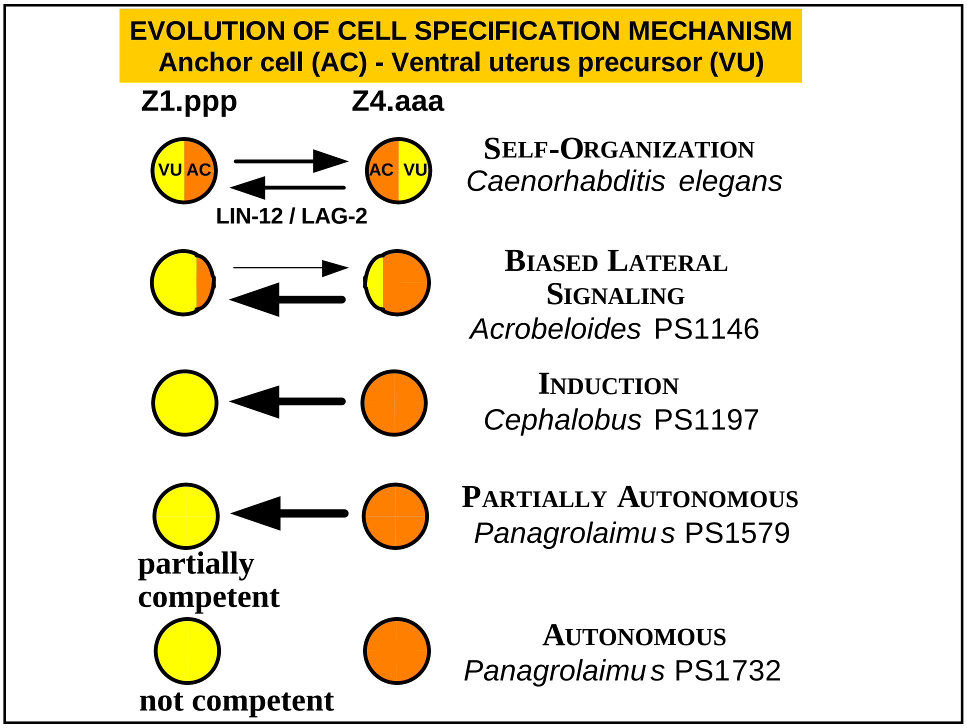
Caenorhabditis elegans

The ventral uterus group



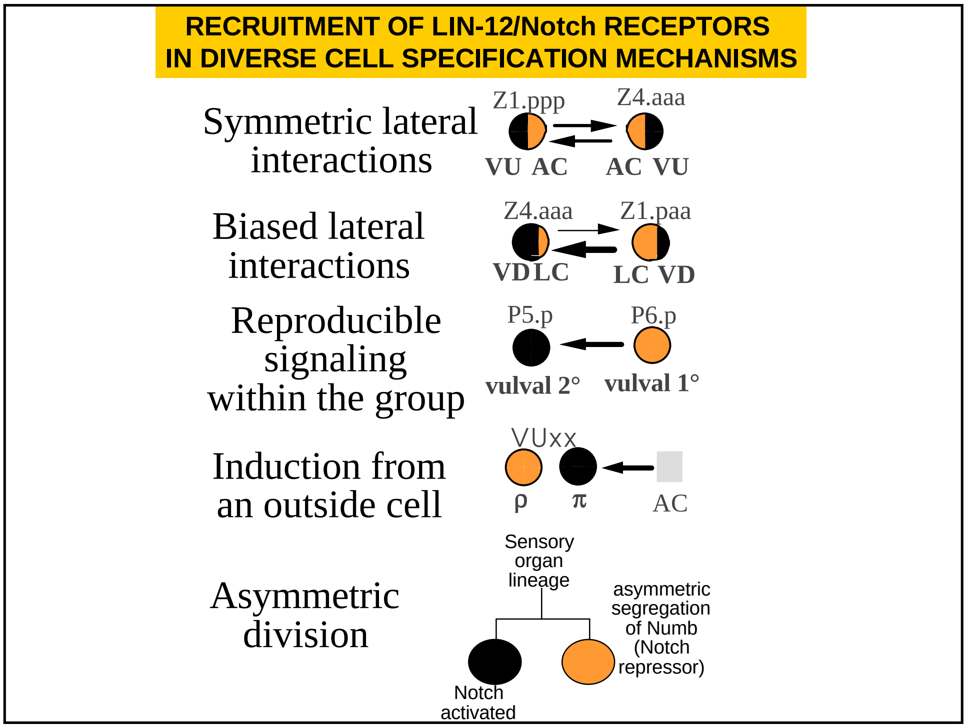

Caenorhabditis elegans
Anchor cell / ventral uterus specification
Z1.ppp
Z4.aaa
LIN-12 receptor (Notch-like)
LAG-2 ligand (Delta-like)
50% animals
50% animals
Z1.ppp
Z4.aaa
AC
VU
Z1.ppp
Z4.aaa
VU
AC
random outcome


100% Z1
AC/VU lineage origin
100% Z4
Caenorhabditis elegans
Z1
Z4
UNBIASED
Oscheius guentheri
BIASED
Acrobeloides PS1146
BIASED
Panagrolaimus PS1579
FIXED
Cephalobus PS1197
FIXED
Mesorhabditis PS1179
FIXED



The developmental module AC/VU is useful to describe development in *C. elegans*, but it is broken in evolution

'Intermediates' are found



CONSERVATION of MOLECULES

(e.g. gene expression pattern, pathway involvement) does not imply conservation of

SPECIFICATION MECHANISM

importance of details in the molecular interaction network

ex: HOM-C genes!!!

MODULAR ORGANIZATION OF DEVELOPMENT

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MODULAR ORGANIZATION IN EVOLUTION

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(5) Morphological evolution and the body plan

Problem:

Since distinct developmental modules use the same molecular modules, how can evolution occur in one developmental module without affecting the rest of the organism (pleiotropy)?

Note: Modularity in the dynamics of developmental modules is not sufficient for evolutionary independence between modules

Modularity in Gene Evolution

GENE DUPLICATION

Redundancy and subfunctionalization

EVOLUTION OF CODING REGIONS

Protein domains - shuffling,
phosphorylation sites in different tissues, etc.

EVOLUTION OF GENE EXPRESSION

Modularity in cis-regulatory regions

Modularity of gene organization
(promoter, coding region)
might allow for
quasi-independent
evolution
of developmental modules.

What are the relative roles of
coding vs. regulatory sequence evolution?
In ubiquitous vs. regulatory molecules?

MODULAR ORGANIZATION OF DEVELOPMENT

(1) Supracellular modules

(2) Modules of interacting molecules

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MORPHOLOGICAL EVOLUTION BY DEVELOPMENTAL 'INNOVATION'

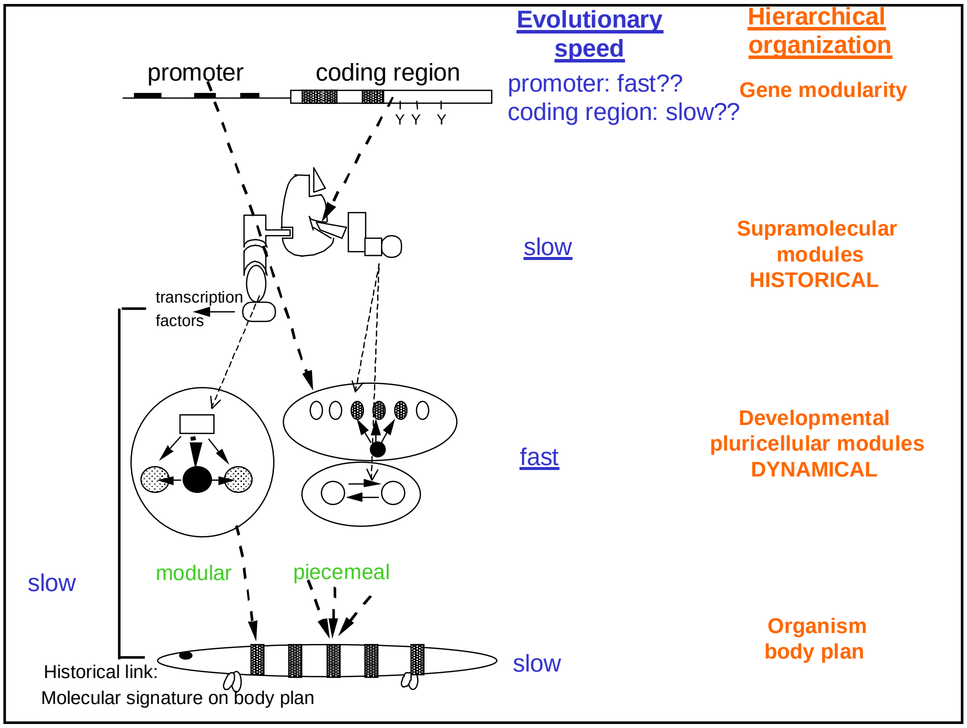
linkage/ breakage of (sub)modules
facilitated . by the evolutionary flexibility in the dynamics of molecular modules
. by redundancy

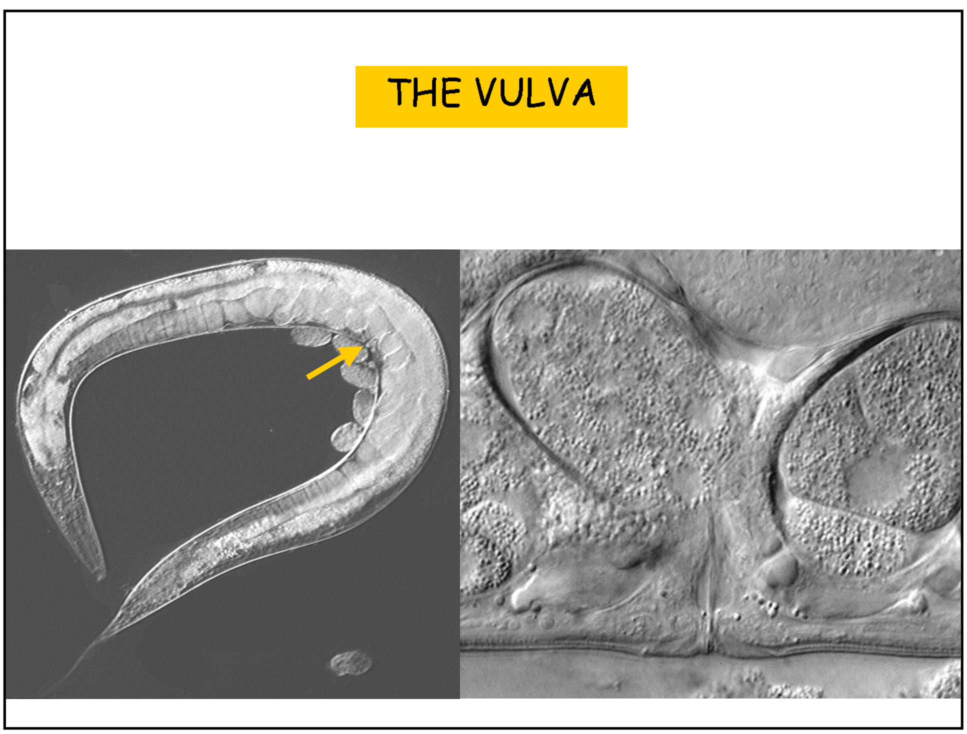
nesting
reuse of the same molecular pathways

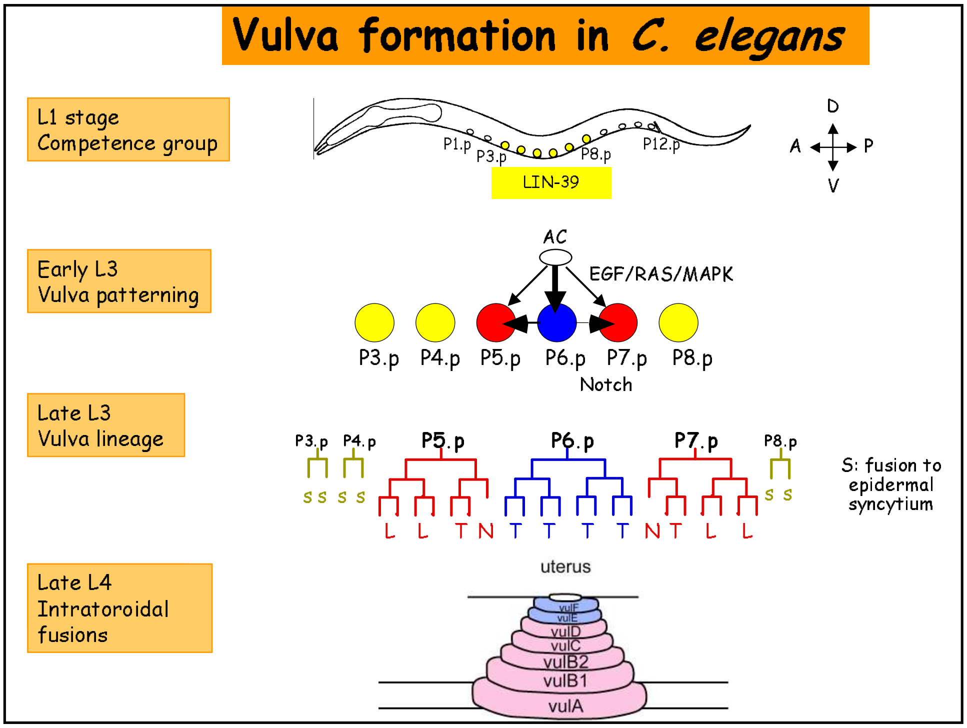
diversification by symmetry breakage
facilitated by small asymmetries

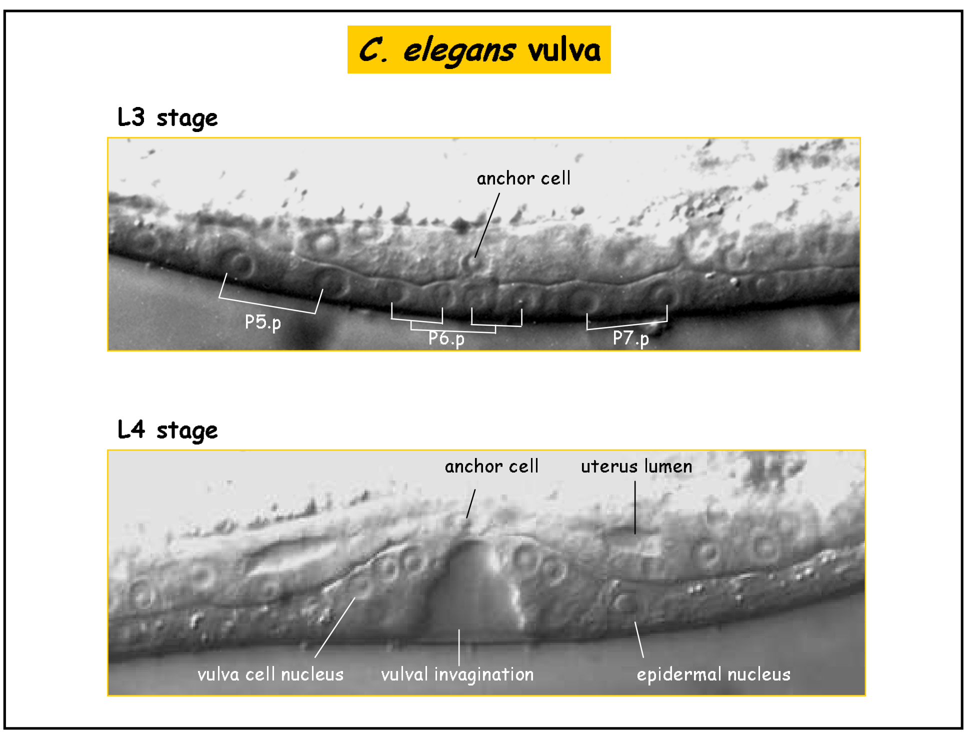
CONSTRAINTS ON BODY PLAN?

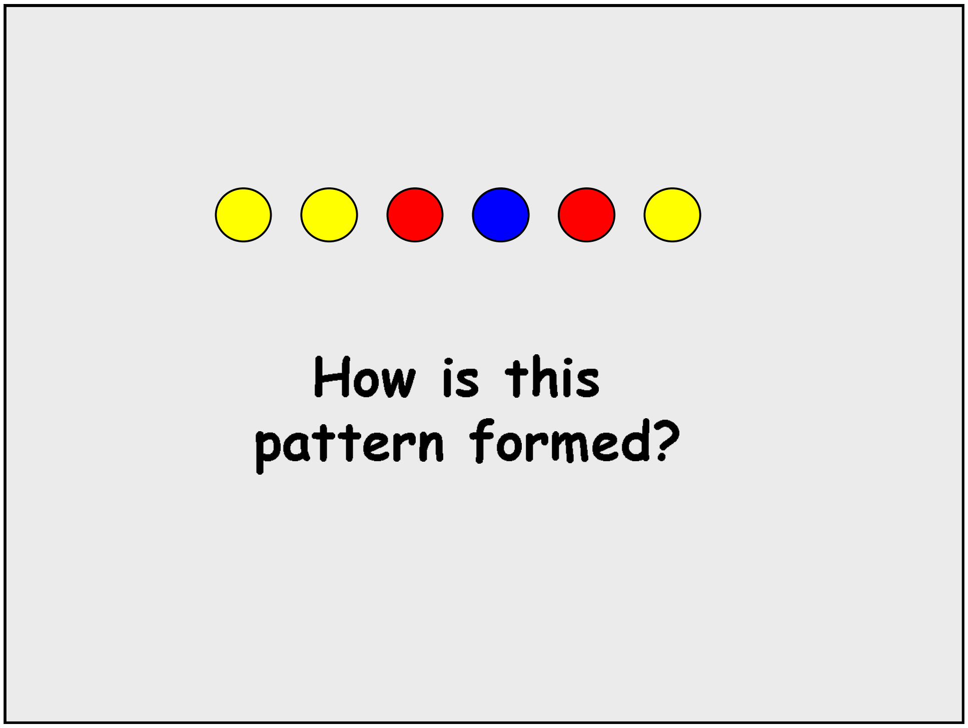
- not because early development is constrained
- not as much constrained in plants

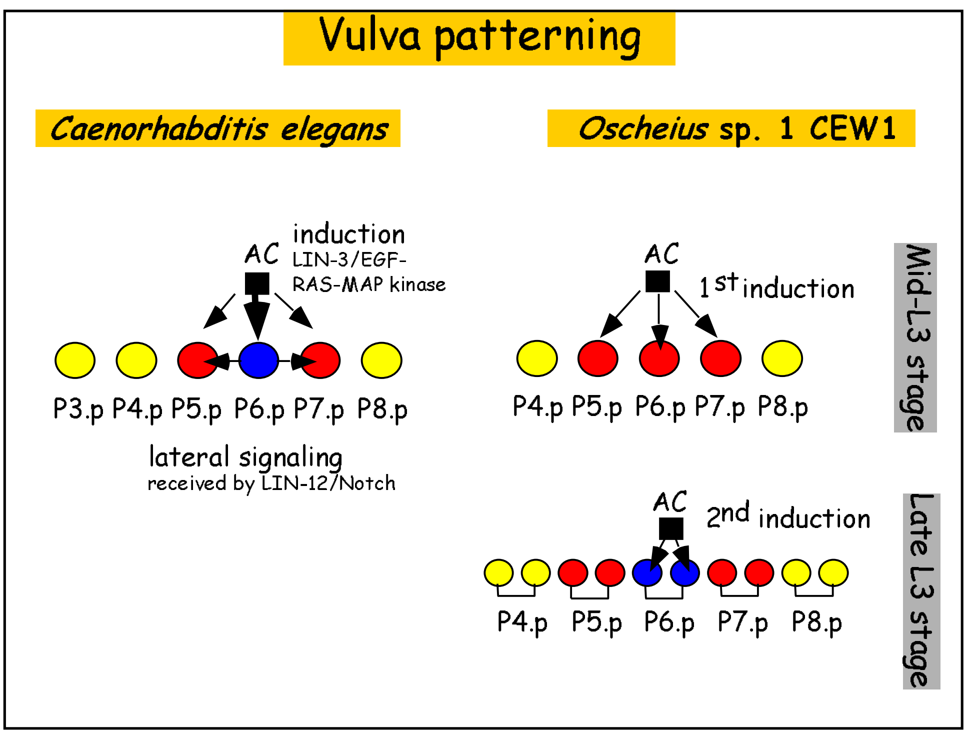

Evolutionary speed
Hierarchical organization
promoter
coding region
promoter: fast??
coding region: slow??
Gene modularity
slow
Supramolecular modules
HISTORICAL
transcription factors
fast
Developmental pluricellular modules
DYNAMICAL
slow
modular
piecemeal
Organism body plan
Historical link:
Molecular signature on body plan
slow

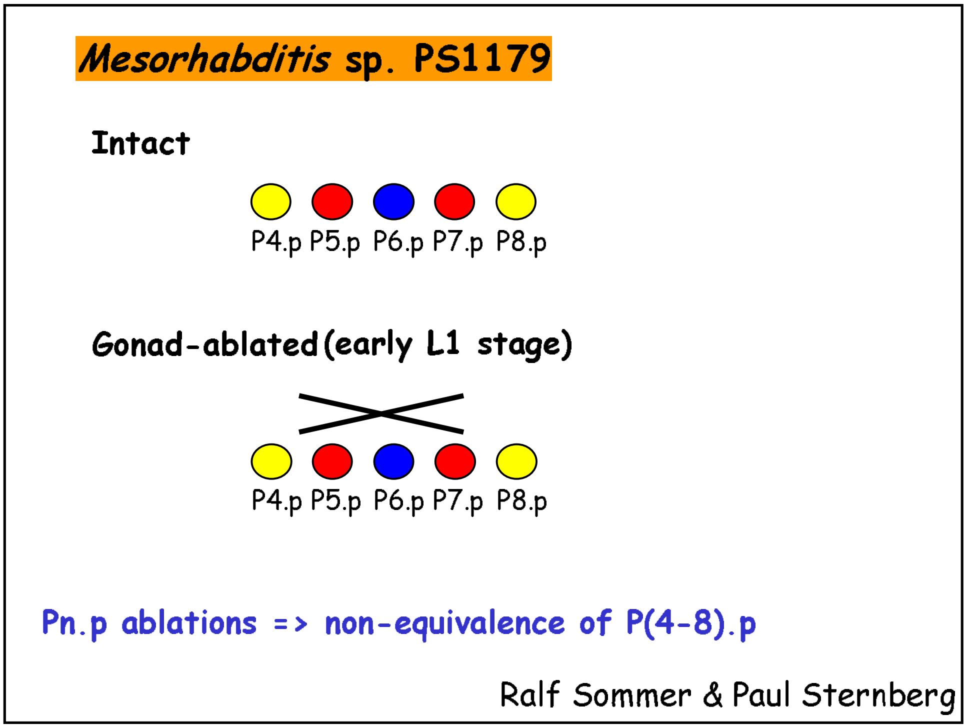

THE VULVA

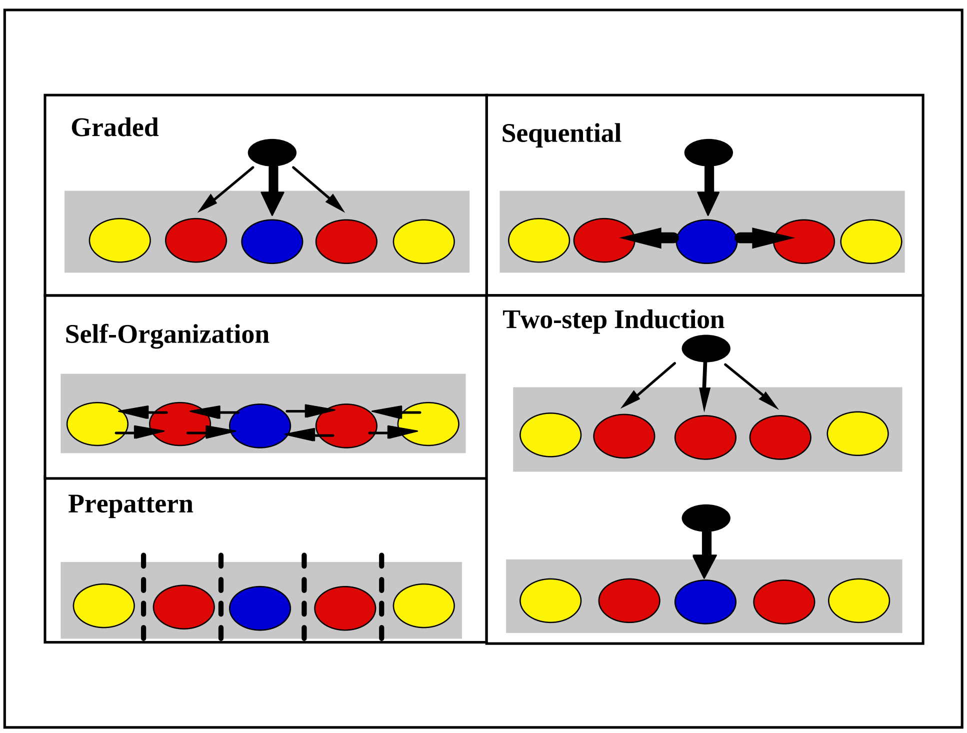

Vulva formation in C. elegans
L1 stage
Competence group
P1.p
P3.p
P8.p
P12.p
LIN-39
D
A
P
V
Early L3
Vulva patterning
AC
EGF/RAS/MAPK
P3.p P4.p P5.p P6.p P7.p P8.p
Notch
Late L3
Vulva lineage
P3.p P4.p P5.p P6.p P7.p P8.p
S S S S
L L T N T T T T N T L L
S S
S: fusion to epidermal syncytium
Late L4
Intratoroidal fusions
uterus
vulF
vulE
vulD
vulC
vulB2
vulB1
vulA


C. elegans vulva
L3 stage
anchor cell
P5.p
P6.p
P7.p
L4 stage
anchor cell
uterus lumen
vulva cell nucleus
vulval invagination
epidermal nucleus


How is this
pattern formed?


Vulva patterning
Caenorhabditis elegans
Oscheius sp. 1 CEW1
AC
induction
LIN-3/EGF-
RAS-MAP kinase
P3.p P4.p P5.p P6.p P7.p P8.p
lateral signaling
received by LIN-12/Notch
AC
1st induction
P4.p P5.p P6.p P7.p P8.p
Mid-L3 stage
AC
2nd induction
P4.p P5.p P6.p P7.p P8.p
Late L3 stage


Mesorhabditis sp. PS1179
Intact
P4.p P5.p P6.p P7.p P8.p
Gonad-ablated (early L1 stage)
P4.p P5.p P6.p P7.p P8.p
Pn.p ablations => non-equivalence of P(4-8).p
Ralf Sommer & Paul Sternberg


Graded
Sequential
Self-Organization
Two-step Induction
Prepattern

The mechanisms patterning the vulva precursor cells vary extensively among these nematodes

(whereas the pattern does not in most cases).

Redundancy between developmental mechanisms ensures precision in a given species

and might in turn favor rapid evolution of these mechanisms

(large changes in the weight of different mechanisms may be quasi-neutral).

Microevolutionary example:
Panagrolaimus sp.
Degree of requirement for the gonadal induction versus pre-patterning along the antero-posterior axis

Microevolutionary analysis

- Genetic dissection of phenotypic variation is possible

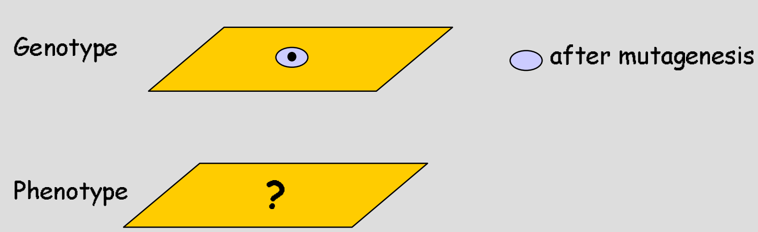
in hermaphroditic nematodes

- Genetically homogeneous populations
  - studies of developmental variants/noise
  - recombinant inbred lines are easily driven to homozygosity

Microevolution within *C. elegans* or *Oscheius* sp. 1
(and then comparison of their evolvability)

Mutagenesis effect vs. Observed microevolutionary change
=> imprint of selection

Mutagenesis



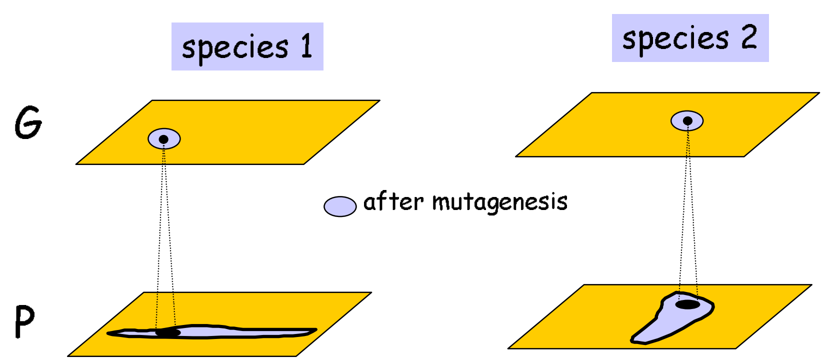
COMPARING THE VULVA SCREENS

The spectrum of vulva mutations isolated is very different in the two species:

C. elegans	*Oscheius* sp. 1 CEW1
Competence	Centering and competence
Vulvaless	Hypoinduction of both steps
Multivulva	Hyperinduction of 1st step
Lateral signaling	Too few divisions
	Too many divisions

⇨ different sensitivities of the systems to one-gene perturbation

Mutagenicity and evolvability

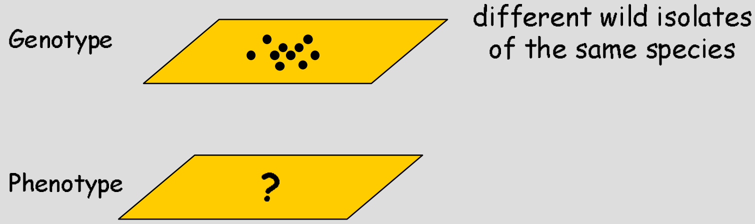


⇨ Assessment by mutagenesis of the "reachable" phenotypic states from a given genotype

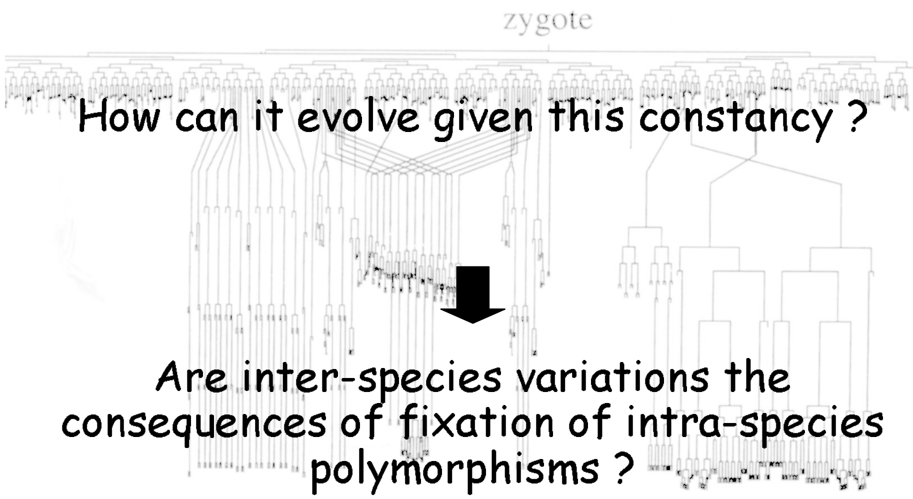
PHENOTYPIC NEIGHBOURHOOD

⇨ Correlation with wild variants ?

Microevolutionary variations



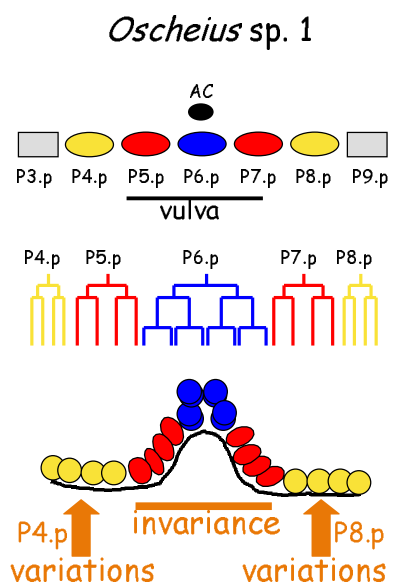
The cell lineage of a given species
of nematodes is globally invariant.



How can it evolve given this constancy ?

Are inter-species variations the
consequences of fixation of intra-species
polymorphisms ?

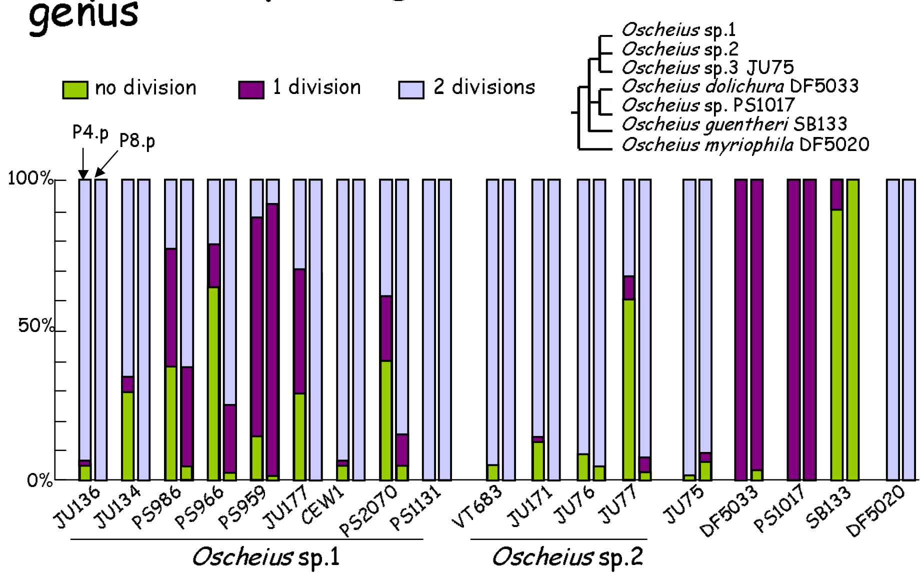
Microevolution of vulva precursor cell lineages within the *Oscheius* genus



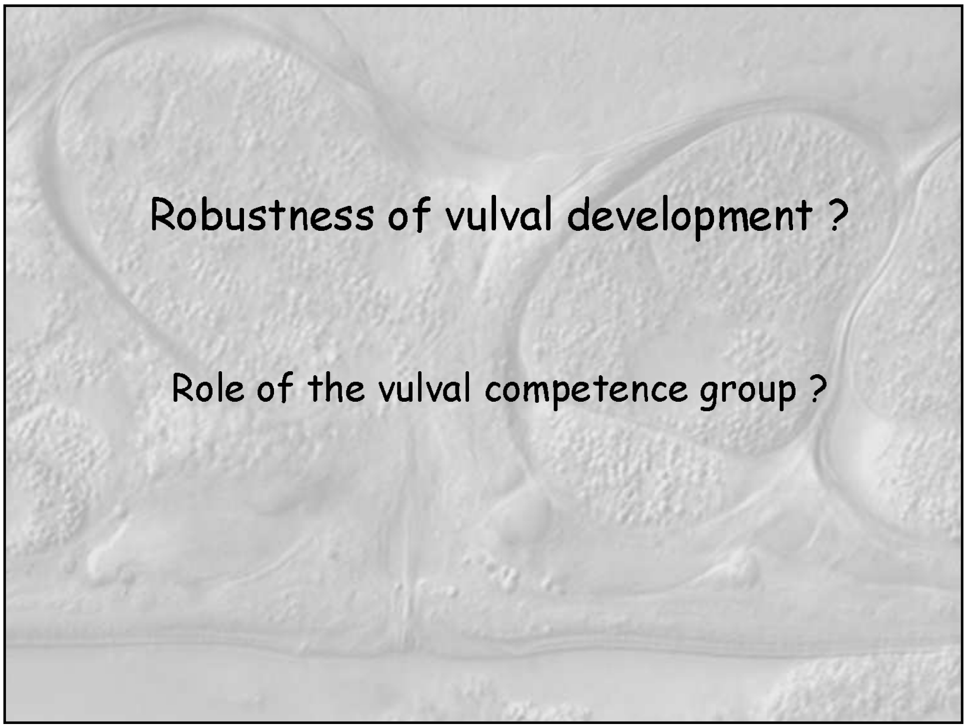
very common in the soil

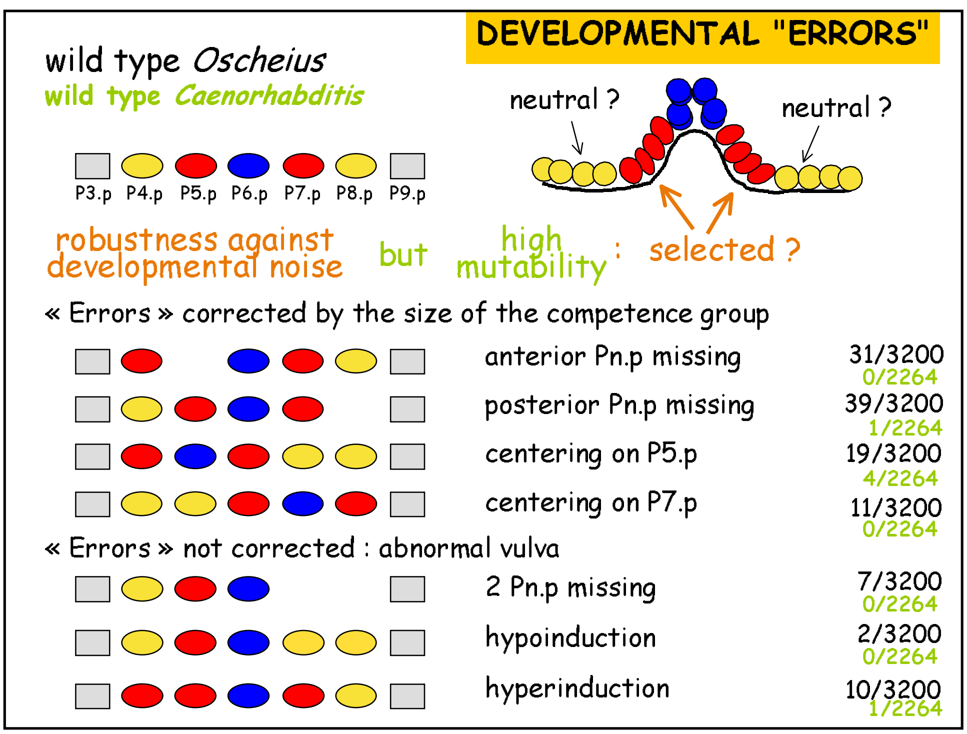
- Comparison between different strains of the same species
- Comparison between closely related species

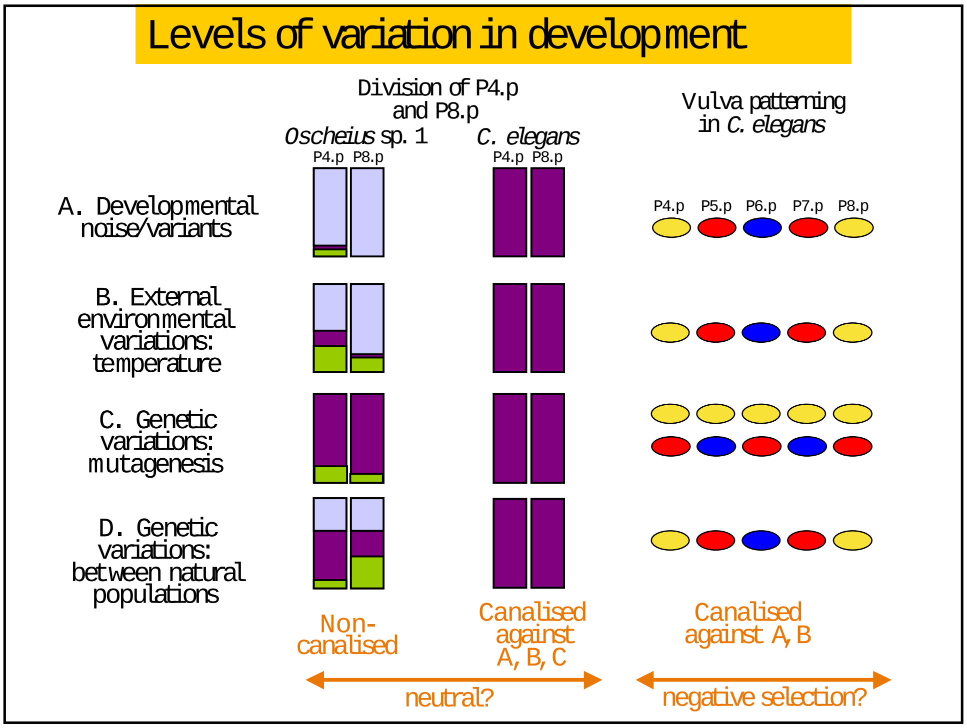
P4.p and P8.p lineages within the *Oscheius* genus



➡ variations between sister species affect those characters that are polymorphic within species


Robustness of vulval development ?
Role of the vulval competence group ?


DEVELOPMENTAL "ERRORS"
wild type Oscheius
wild type Caenorhabditis
P3.p P4.p P5.p P6.p P7.p P8.p P9.p
neutral ?
neutral ?
robustness against developmental noise
but
high mutability
:
selected ?
« Errors » corrected by the size of the competence group
anterior Pn.p missing 31/3200 0/2264
posterior Pn.p missing 39/3200 1/2264
centering on P5.p 19/3200 4/2264
centering on P7.p 11/3200 0/2264
« Errors » not corrected : abnormal vulva
2 Pn.p missing 7/3200 0/2264
hypoinduction 2/3200 0/2264
hyperinduction 10/3200 1/2264


Levels of variation in development
Division of P4.p and P8.p
Oscheius sp. 1
C. elegans
P4.p P8.p
Vulva patterning in C. elegans
P4.p P5.p P6.p P7.p P8.p
A. Developmental noise/variants
B. External environmental variations: temperature
C. Genetic variations: mutagenesis
D. Genetic variations: between natural populations
Non-canalised
Canalised against A, B, C
Canalised against A, B
neutral?
negative selection?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Marie-Laure DICHTEL
Sophie LOUVET-VALLEE
Mark VINEY & Paul STERNBERG
Caltech