Quantitative comparative analysis of limb morphogenesis between chick and Xenopus embryo

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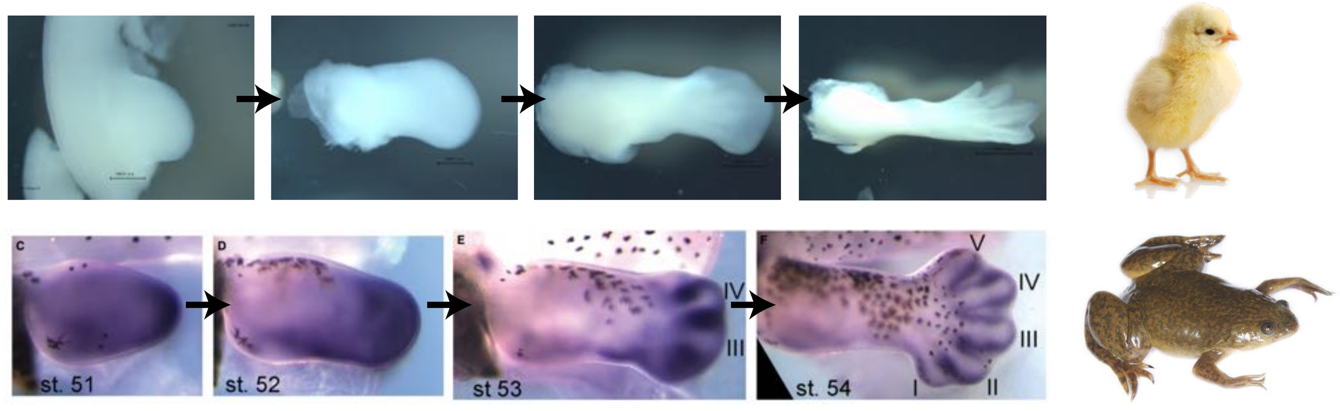
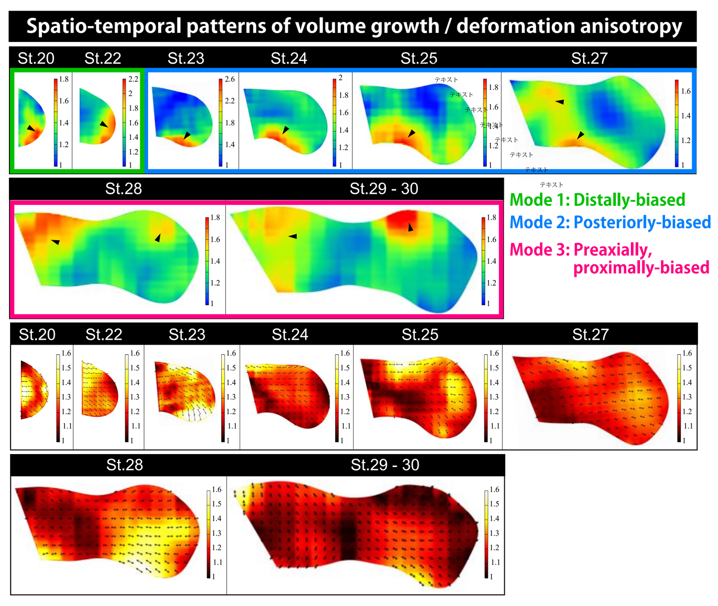
How similar/different are tissue deformation dynamics during development of homologous organs?

Chick/Xenopus limb development

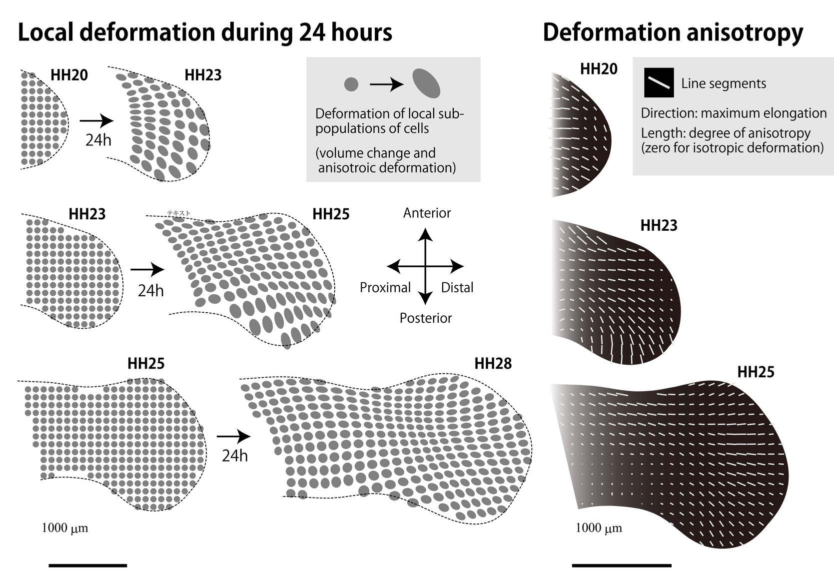


Size and shape of limb buds are different between species, while the gene set for each organ development and gene expression patterns are basically common.
Then, **how about physical tissue deformation ?**

Previous works: quantitative tissue deformation analysis for chick limb development showed that **globally-aligned local deformation anisotropy, not local growth, has the greatest impact on limb shaping.**

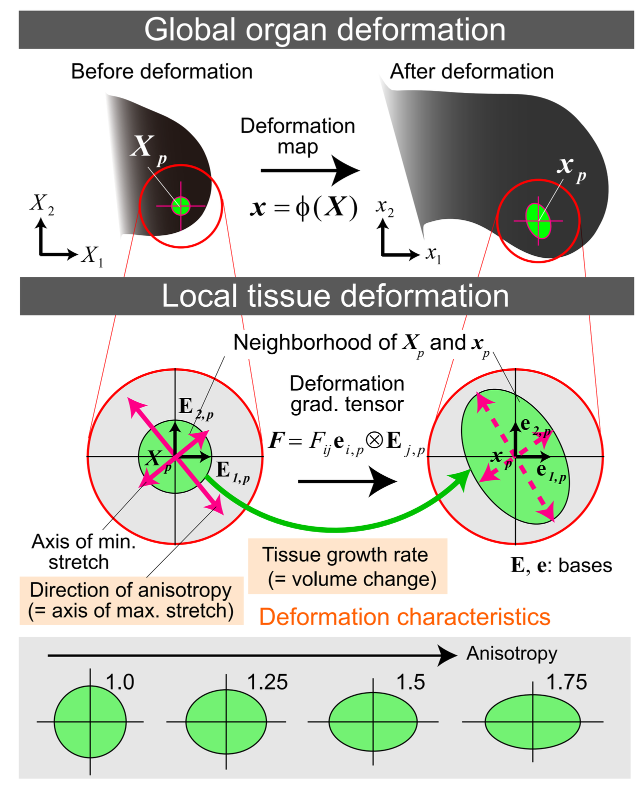


[Morishita, Kuroiwa, Suzuki, **Development** 2015]



[Suzuki and Morishita, **Curr. Opin. Gen. Dev.** 2017]

Math. description of deformation

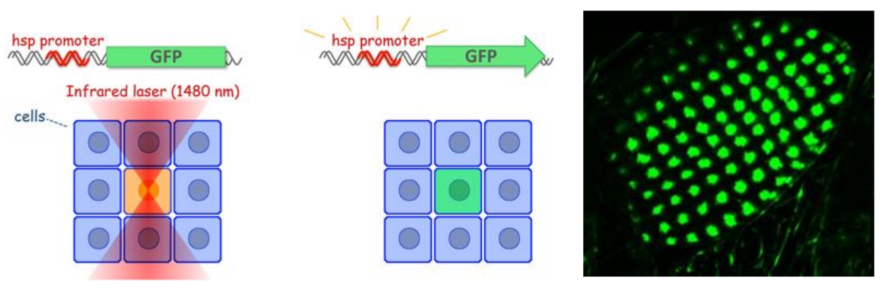


Quantifying tissue deformation dynamics of Xenopus limb (methods and results)

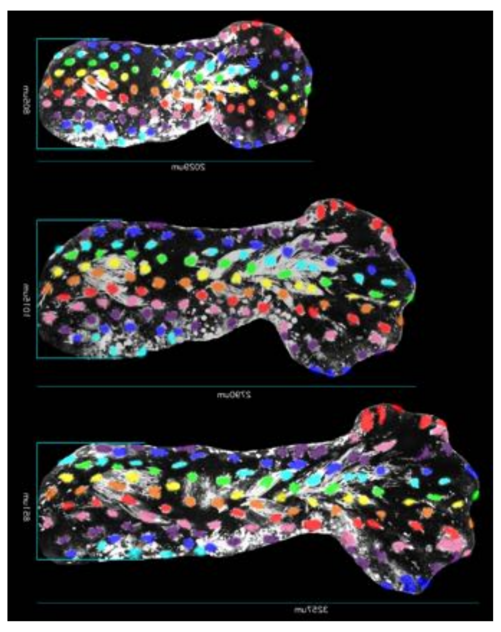
Cell lineage tracing by heat shock labeling

Heat shock promoter system enables "conditional" gene expression
Heat shock response is one of the major stress responses and is widely conserved in all organisms. Heat stress initiates transcription of heat shock proteins (HSP) downstream of a promoter. As hsp promoters can be easily induced, they have often been used for gene induction at discretionary timing in transgenic organisms.

Single-cell heating will be achieved by IR irradiation under a microscope
Recently, systems for tissue- or cell-level gene induction using heat shock promoters and laser irradiation have been reported in teleost fishes. Among them, the infrared laser-evoked gene operator (IR-LEGO) system using an IR laser (wavelength of 1480 nm) can achieve highly efficient and reproducible gene induction even in a single cell with minimized cellular damage. This system has also been shown to be applicable to various organisms.



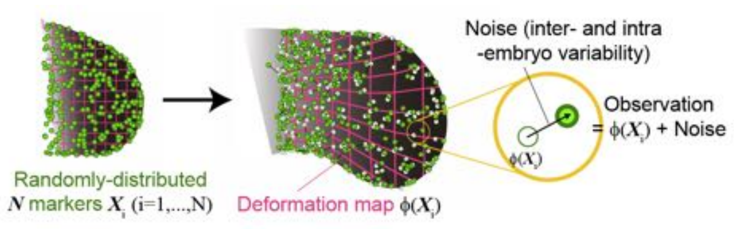
[Kamei et al., **Nat Methods**, 2009]
[Kawasumi et al., **Dev. Growth Differ.**, 2015]



Reconstructing tissue deformation maps from limited landmark data

We recently developed a statistical method that combines snapshot lineage tracing with Bayesian statistical estimation to construct whole-organ deformation maps from limited space-time point data. We applied the method to the cell lineage tracing data obtained by heat shock labeling and obtained spatio-temporal patterns of deformation characteristics for Xenopus hindlimb development.

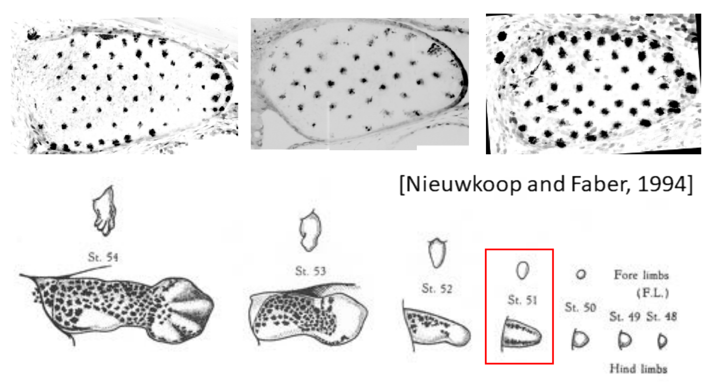
[Morishita and Suzuki, **J. Theor. Biol.**, 2014]
[Morishita et al., **Nature Commun.**, 2017]



Construction of Bayeian statistical model
Marginal likelihood

$$L = \iint P_D(\boldsymbol{x} \mid \boldsymbol{\theta}, \sigma^2)\pi_1(\boldsymbol{\theta} \mid w_1^2, f_1)\pi_2(f_1 \mid w_2^2, f_2)d\boldsymbol{\theta}df_1$$

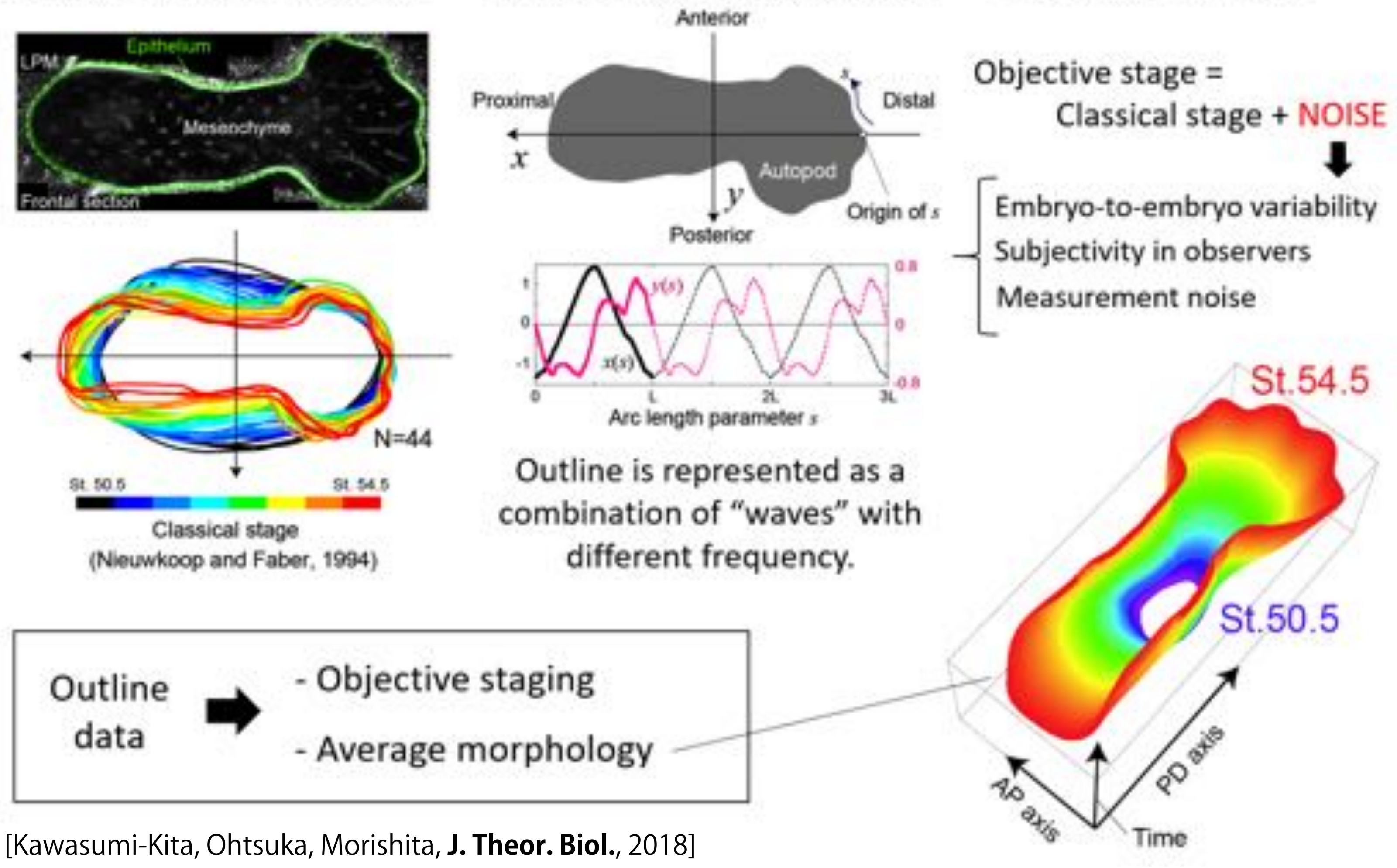
■ **A problem**: **embryo-to-embryo variability in size/shape and staging ambiguity** are not negligible in performing quantification and integration of deformation dynamics for different embryos
The right three limb buds looks like the buds at St.51.



[Nieuwkoop and Faber, 1994]

Objective and morphometric staging

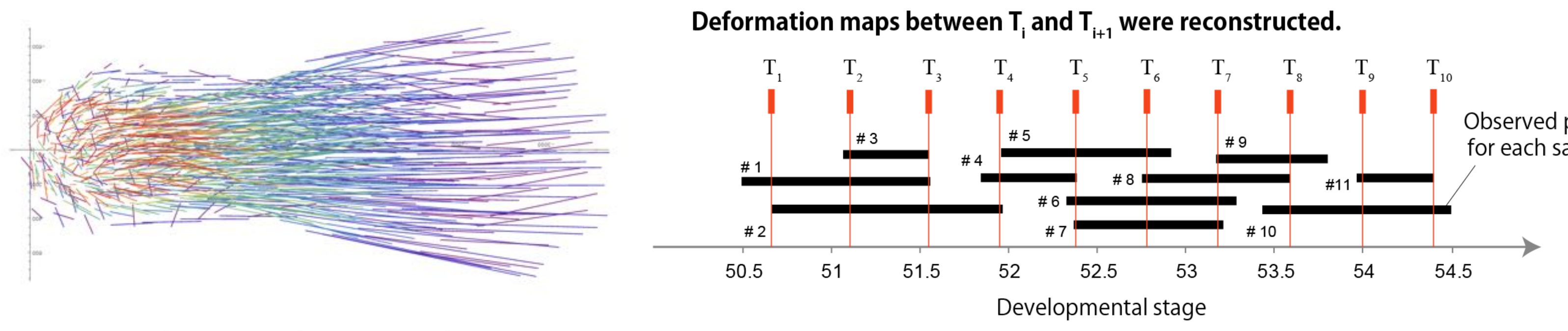
We propose a novel method for objective and continuous staging of developing organs, based on cross sectional images whose contours are represented as 2D closed curves. In our method, morphology is quantified by an elliptic Fourier descriptor (EFD) commonly used in the morphometrics field. The corresponding Fourier coefficients generally change over time with changing organ morphology, and thus coefficients that are highly correlated with classically-defined stages are candidates for the explanatory variables in our newly proposed staging. As a natural extension of classical staging, we define an objective stage by the weighted linear sum of the candidate variables and perform multilinear regression analysis with the assumption that ambiguity in classical staging due to such subjectivity and developmental asynchrony is modeled as a discrete probability distribution around a given morphometric stage.



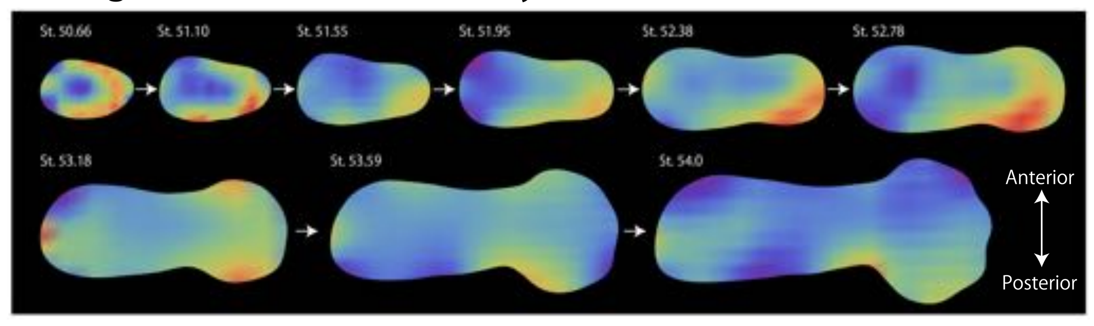
[Kawasumi-Kita, Ohtsuka, Morishita, **J. Theor. Biol.**, 2018]

Reconstructed deformation patterns

All data of cell trajectories from different 11 embryos after objective staging and size/shape normalization



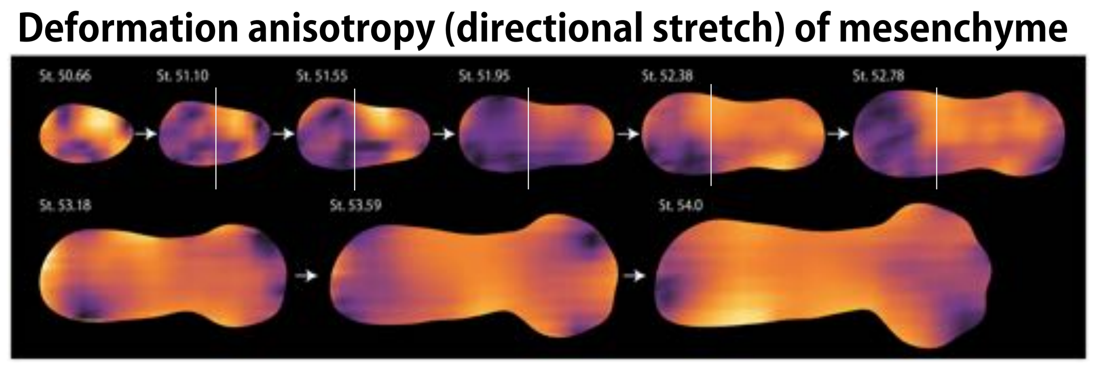
Area growth rate of mesenchyme



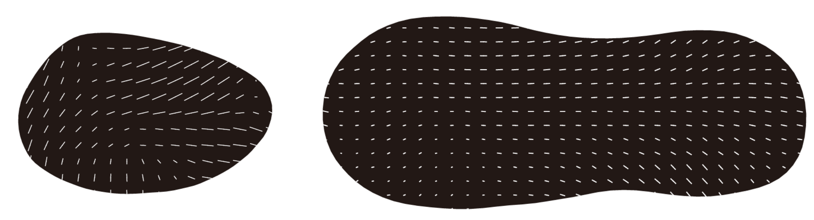
- Transition of spatial pattern of area growth rate

  Distally-biased growth
  -> distal/posterior growth
  -> uniform/unclear pattern

Deformation anisotropy (directional stretch) of mesenchyme



- Globally-aligned deformation anisotropy
- Larger anisotropy in a distal region (zeugopod+autopod) during early stages



Examples of distributions of deformation direction

[Kawasumi-Kita, Morishita et al., unpublished]

Chick and Xenopus deformation patterns show high similarity.

Ongoing works

How to quantify similarity/difference in dynamics between species?

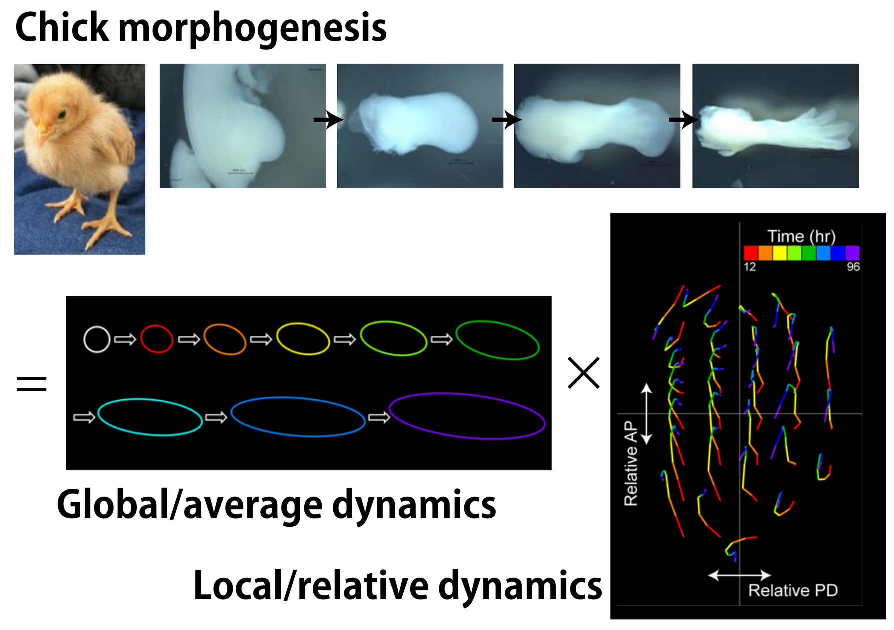
Decomposition of deformation dynamics into "species-specific global dynamics" and "species-independent local dynamics" ?

$$\boldsymbol{x}^C(t) = L^C(t) \times \boldsymbol{\xi}(t)$$

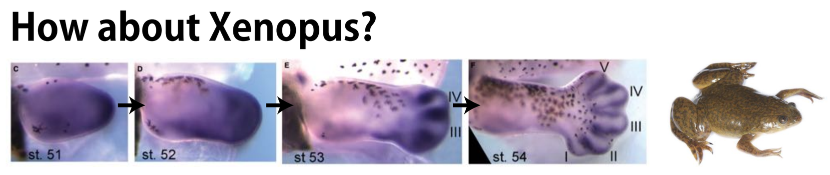
$$\boldsymbol{x}^X(t) = L^X(t) \times \boldsymbol{\xi}(t)$$

Absolute position — Species-specific global deformation (linear map) — Relative position

Chick morphogenesis

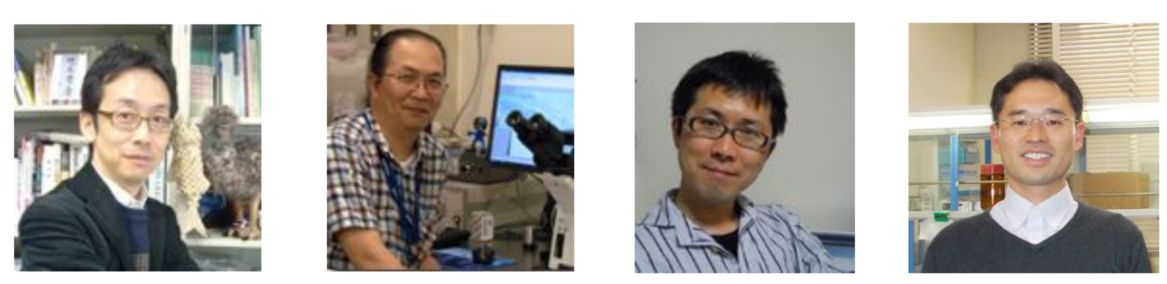


How about Xenopus?



Collaborators/acknowledgement

Xenopus limb development **Chick limb dev.**



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