Journal of Theoretical Biology ■ (■■■■) ■■■–■■■

Contents lists available at ScienceDirect

Journal of Theoretical Biology

journal homepage: www.elsevier.com/locate/yjtbi

Bayesian inference of whole-organ deformation dynamics from limited space-time point data

Q1 Yoshihiro Morishita [a,b,*,1], Takayuki Suzuki [b,c,1]

[a] Laboratory for Developmental Morphogeometry, RIKEN Center for Developmental Biology, Kobe 650-0047, Japan
[b] PRESTO, Japan Science and Technology Agency, 4-1-8 Honcho Kawaguchi, Saitama, Japan
[c] Division of Biological Science, Graduate School of Science, Nagoya University Furo-cho, Chikusa-ku, Nagoya 464-8602, Japan

HIGHLIGHTS

- To quantify tissue deformation map is important for understanding morphogenesis.
- Detailed cell behaviors during vertebrate development are often difficult to measure.
- We develop a novel method to estimate deformation map from limited landmark data.
- The method is validated using artificially-generated data sets.
- In vivo validation is done by applying it to the data for chick limb development.

ARTICLE INFO

Article history:
Received 16 December 2013
Received in revised form
17 April 2014
Accepted 18 April 2014

Keywords:
Morphogenesis
Development
Deformation map
Q4 Chick limb
Estimation

ABSTRACT

To understand the morphogenetic mechanisms of organ development and regeneration, it is essential to clarify the inter-hierarchical relationship between microscopic, molecular/cellular activities and organ-level tissue deformation dynamics. While the former have been studied for several decades, the latter – macroscopic geometrical information about physical tissue deformation – is often missing, especially for many vertebrates. This is mainly because live recording of detailed cell behaviors in whole tissues during vertebrate organogenesis is technically difficult. In this study, we have developed a novel method that combines snapshot lineage tracing with Bayesian statistical estimation to construct whole-organ deformation maps from landmark data on limited numbers of space-time points. Following the validation of the method using artificially generated data sets, we applied it to the analysis of tissue deformation dynamics in chick limb development. A quantitative tissue deformation map for St.23–St.24 has been constructed, and its precision has been proven by evaluating its predictive performance. Geometrical analyses of the map have revealed a spatially heterogeneous volume growth pattern that is consistent with the expression pattern of a major morphogen and anisotropic tissue deformation along an axis. Thus, our method enables deformation dynamics analysis in organogenesis using practical lineage marking techniques.

1. Introduction

One of the main goals in the study of organ morphogenesis is to understand how dynamic changes in organ morphology are realized as outcomes of coordinated molecular and cellular phenomena. To achieve this goal, quantification of tissue-level deformation dynamics with high accuracy is critical; construction of tissue deformation maps and their geometrical analyses enable us to determine when and where distinctive deformation patterns occur, such as spatially-biased tissue expansion and globally-aligned local tissue stretching. Such analyses will act as guideposts in molecular and cellular studies aimed at understanding the inter-hierarchical relationships among molecular, cellular, and tissue-level events.

Over the past several years, quantitative deformation analysis has become an active field of research, especially in studies using monolayer epithelial tissues of drosophila, zebrafish, and chicken embryos (Butler et al., 2009; Blanchard et al., 2009; Taniguchi et al., 2011; Voiculescu et al., 2007; Graner et al., 2008). Epithelial monolayers are particularly suitable for cellular-level time-lapse imaging by conventional confocal microscopes due to their relative thinness, transparency, and small number of target cells (1–10^3).

Q3 * Corresponding author at: Laboratory for Developmental Morphogeometry, RIKEN Center for Developmental Biology, Kobe 650-0047, Japan.
Tel.: +81 78 306 3147.
E-mail address: morishita@cdb.riken.jp (Y. Morishita).
[1] Both authors contributed equally to this manuscript.

http://dx.doi.org/10.1016/j.jtbi.2014.04.027

Please cite this article as: Morishita, Y., Suzuki, T., Bayesian inference of whole-organ deformation dynamics from limited space-time point data. J. Theor. Biol. (2014), http://dx.doi.org/10.1016/j.jtbi.2014.04.027

Deformation analyses based on velocity fields, such as Particle Image Velocimetry (PIV), have succeeded in capturing deformation characteristics from imaging data (Supatto et al., 2005; Raffel et al., 1998). In many vertebrate organs, however, "in toto imaging" or live recording of detailed cell behaviors in whole tissues with high resolution is difficult; it is highly labor intensive and often not applicable to large tissues (e.g., sometimes consisting of millions of cells) or to experimental systems that are not suitable for genetic labeling. One can often obtain landmark data only at limited space-time points and with only low resolution, from which velocimetric analyses are not suitable for estimating tissue deformation maps and deformation characteristics, especially in the case of large deformation processes.

There are only a few reports on the quantification of tissue deformation dynamics for understanding vertebrate organ shape based on limited landmark data. Filas et al. (2008) proposed a method in which a portion of the landmark data for a 2D surface is locally fitted by quadratic polynomials, and tissue strain is estimated. The method was applied to chick brain and heart development. Although this method is suitable for calculating the local strain of tissues at each position in an organ, it is difficult in a statistical sense to precisely estimate a whole-organ deformation map that reflects the information on the positional changes of all landmarks at once. Marcon et al. (2010) proposed a method to estimate the spatio-temporal pattern of deformation characteristics of mouse limb development based on the spatial distribution of clonal cells at different developmental stages and an assumption about tissue mechanical properties (in particular, the elasticity of the mesenchyme). The resulting estimated deformation pattern was almost symmetric about the anterior–posterior (A–P) axis; however, the result was not consistent with that of another lineage analysis in the experimental study by Harfe et al. (2004), in which it was suggested that the deformation dynamics are asymmetric along the A–P axis. Although the reason for this inconsistency is not clear, since the initial distribution of cells in the clonal analysis was unknown, the validity of the estimated deformation pattern cannot be addressed in statistical terms.

In this study, we have developed a novel mathematical method that combines Bayesian statistical estimation and snapshot lineage marking to construct tissue deformation maps of whole organs from low resolution data. We have validated the method using various artificially generated maps that produce the same morphology but have different deformation dynamics in their internal tissues; estimated maps were precise enough to perform reliable tensor analysis of the deformation dynamics. Although the accuracy of estimation, of course, depends on parameters such as the quantity of landmark data and the intensity of noise originating from both measurement and intra/inter-embryo variability in tissue deformation processes, we have shown that the method works well for biologically plausible parameter ranges.

After validation of our method, we applied it to fluorescent-labeling data for chick limb development. While limb development has been a well-studied topic in vertebrate organogenesis for the past century, there is much less known about tissue-level deformation than there is about molecular and cellular events. Here we have constructed a quantitative tissue deformation map for the interval St.23–St.24 and validated the map by measuring its predictive performance. Geometrical analyses revealed a spatially heterogeneous volume growth pattern that is consistent with the expression pattern of a major morphogen and anisotropic tissue deformation along an axis.

Our approach broadens the range of target organs that can be analyzed, especially in vertebrates, whose deformation dynamics have been difficult to analyze, and will make it possible to bridge the gaps between inter-hierarchical phenomena.

2. Model and results

2.1. Characterization of tissue deformation dynamics: deformation map and deformation gradient tensor

Mathematically, the global deformation of organ morphology is described by a map (Bonet and Wood, 2008; Marsden and Hughes, 1983),

$$\boldsymbol{x} = \phi(\boldsymbol{X}), \tag{1}$$

where $\boldsymbol{X}$ and $\boldsymbol{x}$ are positional vectors for each cell or each piece of tissue before and after deformation, respectively (Fig. 1A). In the following, we use the upper case for the coordinates and bases (including their suffixes) before deformation, and the lower case for them after deformation. The deformation gradient tensor

$$\boldsymbol{F} = \sum F_{iK}\mathbf{e}_i \otimes \mathbf{E}_K \tag{2}$$

includes all information about local tissue deformation around a focal location, where $\mathbf{E}_K$ and $\mathbf{e}_i$ are orthonormal bases before and after deformation, respectively (Fig. 1B) (see Appendix A about tensors). Using map ϕ, the components of $\boldsymbol{F}$ are given as $F_{iK} = \partial\phi_i/\partial X_K$ (where X_K is the K-th component of $\boldsymbol{X}$). Intuitively, the tensor describes how a small circle (in a 2D scenario) or sphere (in a 3D scenario) surrounding the focal location deforms during a given time interval. Based on the right polar decomposition, $\boldsymbol{F}$ is

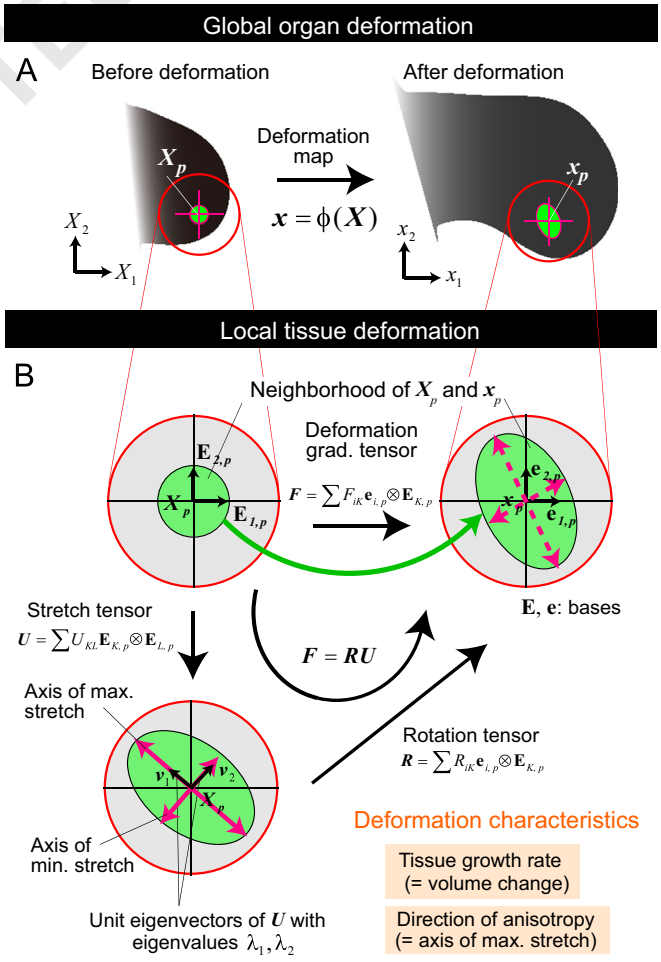

Fig. 1. Characterization of tissue deformation dynamics. (A) Global organ deformation is defined by map ϕ. (B) Local tissue deformation is defined by the deformation gradient tensor $\boldsymbol{F}$, whose components are calculated by using map ϕ. $\boldsymbol{F}$ is decomposed into $\boldsymbol{F} = \boldsymbol{RU}$, where $\boldsymbol{R}$ and $\boldsymbol{U}$ are the rotation tensor and the right stretch tensor, respectively. Tissue growth rate and deformation anisotropy are two key characteristics (see the main text for details).

Please cite this article as: Morishita, Y., Suzuki, T., Bayesian inference of whole-organ deformation dynamics from limited space-time point data. J. Theor. Biol. (2014), http://dx.doi.org/10.1016/j.jtbi.2014.04.027