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Topological singularities and symmetry breaking in development

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ABSTRACT

The review presents a topological interpretation of some morphogenetic events through the use of well-known mathematical concepts and theorems. Spatial organization of the biological fields is analyzable in topological terms. Topological singularities inevitably emerging in biological morphogenesis are retained and transformed during pattern formation. It is the topological language that can provide strict and adequate description of various phenomena in developmental and evolutionary transformations. The relationship between local and global orders in metazoan development, *i.e.*, between local morphogenetic processes and integral developmental patterns, is established. A topological inevitability of some developmental events through the use of classical topological concepts is discussed. This methodology reveals a topological imperative as a certain set of topological rules that constrains and directs embryogenesis. A breaking of spatial symmetry of preexisting pattern plays a critical role in biological morphogenesis in development and evolution.

1. Introduction

1.1. Topological constraints and directionality in biological morphogenesis

The living organisms inhabit and develop in the real physical space and are organized according to the properties of this space. The complexity of the world is constrained by the simplicity of the basic laws of physics (Goldenfeld and Kadanoff, 1999). The course and outcome of biological evolution is strongly influenced by constraints, which play an important role and have both positive and negative values; evolutionary development can result in discontinuities and directionality of morphological transformations (Sará, 1999). In developmental morphogenesis, an important constraint lies in mechanodependence (Harris et al., 1981; Oster et al., 1983; Beloussov, 1998; Ingber, 2005; Beloussov, 2012).

The topological structure of phenotypic space gives the topological explanation of developmental and evolutionary transitions as “the topology of the possible” (Stadler et al., 2001). The topological properties of space are involving in topological dynamics of forms during ontogenesis, so we can discuss the topological determination of individual development.

Since topology operates with the most general properties of spaces as mathematical subjects, an adequate description of biological morphology can be obtained through the use of topological terminology (Listing, 1847; Thompson d’Arcy, 1942; Needham, 1936; Waddington, 1940, 1968). René Thom (1923–2002), a brilliant mathematician, who devised catastrophe theory, put forward a topological description and modeling of embryogenesis (Thom, 1969, 1997). Thom argued that the discrete character of biological morphogenesis involves qualitative topological discontinuities (Thom, 1996). Thereby, the topological models would be the adequate models of real biological objects and processes. Elsdale pioneered in applying a topological theorem (the theorem on the sum of the indices of the singularities in a vector field) to experimental biology and revealing singularities in fibroblast confluent layer *in vitro* (Elsdale, 1972, 1973; Elsdale and Wasoff, 1976).

Following Thom (1969, 1996, 1997), we applied topological concepts and theorems to describe and explain form dynamics during development and evolution, since developmental and evolutionary modifications of topological patterns are discrete, qualitative steps in biological morphogenesis involving symmetry breaking (Maresin and Presnov, 1985; Presnov et al., 1988, 2010; Presnov and Isaeva, 1990, 1991, 1996; Isaeva et al., 2006a, 2008). This methodology reveals a topological dependence and topological constraints of biological morphogenesis. The topological approach to description of biological forms and morphogenetic processes has become a more common practice (Chin-Sang and Chisholm, 2000; Jockush and Dress, 2003; Cherdantsev, 2006; Pivar, 2007).

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Interrelations between local and global aspects are well established in mathematics (Milnor, 1963; Petersen, 1999; Atiyah, 2002), and topology enables us to analyze a transition from local parameters to global ones. This view is connected to an old idea of embryologists concerning the integration of parts and local parameters in embryos (Driesch, 1894; Gurwitsch, 1922; Child, 1941; Wolpert, 1969, 1989; see Section 2). So, the topological theory of biological morphogenesis relates the concepts of positional information, morphogenetic field, local and global (integral) orders of morphogenesis, and symmetry breaking. The theory presents a topological interpretation of some developmental events through the use of well-known concepts and theorems and puts forward the problem concerning the morphogenetic role of topological singularities of morphogenetic fields and spherical surgeries of the surface of metazoan organism changing the topological genus of the surface in development and evolution.

The topological approach makes it possible to consider as a whole the succession of shape transformations during embryonic development and evolution. The present review includes the topological description of morphogenetic patterns in onto- and phylogenesis, *in vivo* and *in vitro*, relationship between local and global (integral) orders, topological dependence and topological constraints of biological morphogenesis.

Symmetry propagation and symmetry breaking are essential processes in physical and in biological morphogenesis (see Bouligand, 1996), in development and evolution of animals and plants (Palmer, 2004; Li and Bowerman, 2010). Because an animal body is formed from a spherically symmetrical egg, symmetry breakdown is one of the fundamental processes of development (Hirokawa et al., 2009).

Thus, spatial organization of living systems has a dynamical character, including discontinuities: topological catastrophes and symmetry breaking.

2. Morphogenetic fields and positional information

Many developmental biologists proposed holistic solutions of the problem of integrating factors in morphogenesis including concepts of morphogenetic fields (Gurwitsch, 1922; Weiss, 1968), organizers (Spemann, 1938), and gradients (Child, 1941). Diffusion of morphogens is the traditional assumption in most models of morphogenesis (Turing, 1952; Wolpert, 1969, 1989; Meinhardt, 1982; Murray, 2003). Wolpert (1969, 1989) introduced the term "positional information" provided by gradients of diffusible morphogens; positional information determines cell fate depending on the position in a developing system.

Various scalar and vector fields on subcellular, cellular, and supracellular levels of biological organization are manifested in heterogeneous distribution of structural components, in biochemical gradients, in vectorized subcellular transport and other functional activities, in ionic fluxes and accompanying electric fields, in fields of mechanical tensions, in directed cell movement *etc.* For example, transcellular ion currents in polarized cells generate electric fields as signals and as effectors of cell polarity at cellular and tissue levels (Nuccitelli, 1984). It was shown that spatial anisotropy in distribution of gene products in ooplasm determines the polarity of egg and embryo specifying polar axes of future organism (see Struhl et al., 1989; Nüsslein-Volhard, 1991). These results have provided evidence that the body pattern is organized by morphogen gradients emanating from localized sources at poles of the egg and cause a revitalization of the old idea of morphogenetic fields and diffusible morphogens (Slack, 1987; Gilbert, 2000; Palmer, 2004). In embryos, cell migration pathways during gastrulation and other morphogenetic processes (see Gilbert, 2000) visualize the morphogenetic vector fields.

The interdisciplinary challenge to discover the underlying mechanisms in the generation of biological patterns and forms is a central issue in developmental biology (Murray, 2000). Murray reasoned that two distinct theoretical approaches to biological pattern formation have had a significant effect on developmental biology: the Turing reaction–diffusion prepattern theory and the mechano-chemical theory of biological pattern formation (Murray et al., 1983; Oster et al., 1983; Harris et al., 1984; Murray, 2000, 2003).

2.1. Topological local and global order of morphogenetic fields

It is the topological language that can provide strict and adequate description of various phenomena in biological morphogenesis. Spatial organization of the biological fields is analyzable in topological terms; topological singularities inevitably emerge in biological morphogenesis retaining and transforming during pattern formation.

We understand morphogenetic fields as a distribution of physical values (*e.g.*, concentration) at each point of a certain domain of space-time. Scalar fields are characterized by a certain value in each point of the space. Vector fields are characterized in each point by a vector imaged as an arrow. Cell or molecular orientation is described also as field of directions – intervals with unit length without a vector value. The term "morphogenetic" is valid for biological fields only in the cases in which a causal relationship between a certain field pattern and a resulting morphogenetic pattern is found.

A spatial morphogenetic field is characterized by a relationship between local (short-range) and global (long-range) orders of the whole entity; the integral order of morphogenetic fields is defined by the local order, *i.e.* local forces manifest in large-scale form.

2.2. Topological positional information as symmetry of morphogenetic fields

We are using the term "topological positional information" to designate a relationship between local and global orders of a morphogenetic field (Presnov and Isaeva, 1991, 1996) understanding topological positional information as a kind of symmetry of morphogenetic fields (Presnov and Isaeva, 1990). Positional information determines the interrelation between local and global orders, transmitting from the local to the integral order within morphogenetic fields.

Using this concept of the topological positional information it is possible to establish the relation between the local morphogenetic factors and integral developmental patterns and to explain symmetry breakdown in development in terms of topological properties of spherical bodies.

The topological organization of the physical space, in which animal development takes place, or in other words topological positional information of corresponding morph genetic fields can explain some developmental events, particularly, symmetry transformations in development.

3. Egg cell singularities

3.1. Somatic cell polarization

Cytoskeletal systems transmit and integrate information across cellular dimensions; cytoskeleton rearrangements break cell symmetry (Mullins, 2009). A polarized cellular architecture is fundamental to cellular morphogenesis, cell fate differentiation, and formation of embryonic axes; physical and biochemical amplification systems can break cell symmetry by turning local signals (Li and Bowerman, 2010). For instance, symmetry breaking in