Natural and controlled symmetry breaking analyses in biological systems

Lalit Prakash Saxena

Symmetry breaking is present in every biological system, at microscopic and macroscopic levels, present in nature. It can be divided into two types, natural symmetry breaking and controlled symmetry breaking, described by organismal adaptation in natural environment and forced perturbations in human-controlled situations respectively. Natural symmetry breaking adheres biological systems complexities, organismal adaptations, and mechanisms at cellular levels. Controlled symmetry breaking of cells focus on cell migration, morphogenesis, self-organization, and soluble and insoluble cues.

Keywords: Symmetry breaking, biological systems, natural, controlled, human perturbations.

SYMMETRY breaking occurs as a transition state with a prognosis that defines the variability of a system, at both inter- and intra-dependent consistent developmental stages. Scientifically, it is the process that breaks this consistent growth by moving the system to a more mature, patterned and unpredictable state[1]. Symmetry breaking is evident in almost every biological system – whether at microscopic and macroscopic levels or both – transition state is more likely to be persistent in an organism of a genus for existence. There are examples in nature that share this hypothesis, which include natural camouflage of animals, adaptation of carnivorous plants, and precisely mentioning, cellular differentiation in embryonic development.

The detailed studies and a closer look at a cell-culture population reveal that symmetry breaking produces predetermined arrangements of cells within the population, naturally. These arrangements can be visualized in terms of cell migration (uni-, bi- or multi-directional, singly, paired or groups), cell growth (increase in size, shape or number), self-organization (patterned division) along with morphogenesis. This led to the foundation of symmetry breaking in controlled circumstances, which means it is controllable under human perturbations and observations. However, the complexities present in biological systems restrict human perturbations and control in analysing the details of symmetry breaking. Thus, it is significant to distinguish symmetry breaking in both natural and human-controlled environments; this simplifies the study of biological systems with discrete perspectives. Symmetry breaking in biological systems consists of two types, namely natural symmetry breaking and controlled symmetry breaking, described by organismal adaptation in natural environment and forced perturbations in human-controlled situations respectively.

Natural symmetry breaking of cells is a hoary concept, influencing since the beginning of the study of biological system complexities that employed cells. These studies describe the aspects of polarization states of a cell, which is vital for its smooth functioning and energy transfer, enhancing the properties like self-organization, cell motility and morphogenesis. However, the physical studies consider polarization states and energy transfer as parallel terms that describe the stability of a system, more precisely, the symmetrical state of a system[2].

Before moving forward towards symmetry breaking in biological systems, it is useful to recall the concepts of symmetry in mathematics and physics, as well. In mathematics, symmetry is one of the geometrical concepts that deals in line and rotational symmetries of a geometric object. The number of possible symmetries of an object, distinctly depends on the geometric transformations set and properties taken into consideration that remain unchanged. For example, a circle has a rotational symmetry, since its shape and size remain unchanged after rotation, in either clockwise or counterclockwise directions. Accordingly, a square is said to have a rotational symmetry of order 4. Figure 1 shows a circle and a square with an axis of rotation revealing rotational symmetry.

The study of symmetry is important because of its frequent use in day-to-day life and more because of the beautiful designs it can provide us. Furthermore, bilateral symmetry is a form of symmetry in which an object or figure consists of two equal halves on either side of a midline (line of symmetry). For example, the patterns on the wings of butterflies.

In physical sciences, an invariance of an object or system to a transformation profoundly reveals the concept of symmetry. For example, the three states (phases or forms)

Lalit Prakash Saxena is in the Department of Computer Science, University of Mumbai, Vidyanagari, Santacruz (E) Mumbai 400 098, India.
e-mail: lasaxmail@aol.com

of water – solid (ice), liquid (water) and gas (vapours or steam). The change of water from one state to the other is known as phase change or transformation. Figure 2 shows the three states of water and points from where the phase change takes place depending on the temperature fluctuations. Recalling physical systems, any perturbed fluctuation crossing a critical point is responsible for the phase change from solid to liquid, or liquid to gas and breaks the symmetrical state of the water. This acknowledges the occurrence of symmetry breaking, more precisely, transitions that transform a system from a symmetrical state into one or more predetermined patterned states. The chemical sciences too has much on theoretical aspects of symmetry analysis[3].

The concept of symmetry is not limited only to the geometry in mathematics, physical and chemical sciences; however, it has extended conceptual applications to biological sciences too. Now considering the cases in the evolutionary history of life on the Earth, the prokaryotic cells existed approximately 3.6 billion years ago. The existence of prokaryotic cells is in the form of symmetry that inspires predetermined forms of life on earth seen today. For a class of thinkers, symmetry in organisms

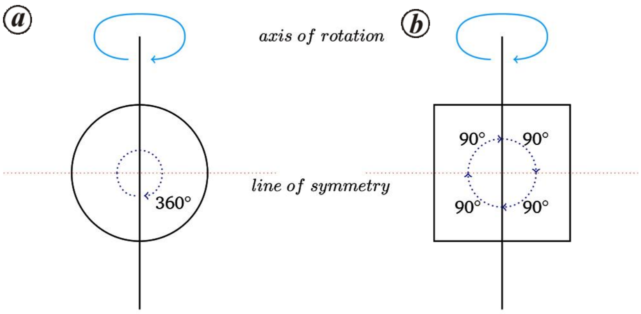

Figure 1. ***a***, Circle with perfect symmetry. ***b***, Square with rotational symmetry of order 4.

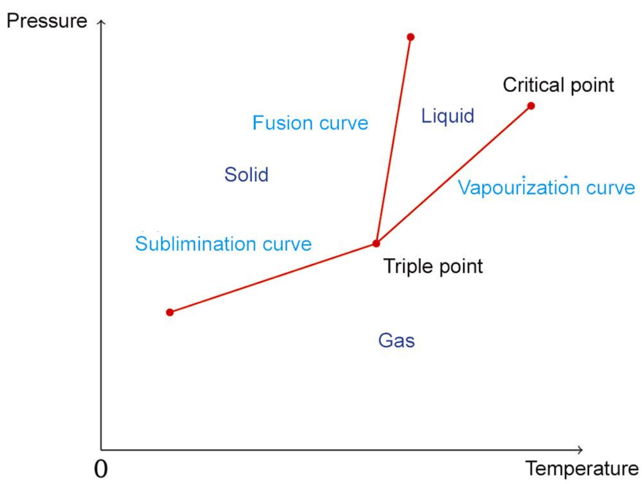

Figure 2. Three states of matter, namely solid, liquid and gas, showing sublimination, fusion and vapourization curves.

is the branch of biology that deals with the rational arrangement of body parts equating on either side of the line of symmetry. This line of symmetry equally separates and resembles the shapes, sizes and locations of both the body parts, familiarizing and validating the existence of symmetry[4]. The symmetry in biology has three forms, namely spherical, bilateral, and radial; that is, an organism definitely exhibits any one of the types. With an exception to this validation, however approximate, the *Porifera phylum* (sponges) is the only group within animals that shows no symmetry. In addition, bilateral symmetry is the most common form of symmetry existing in nature – more than 500 million years ago – inspiring the humans to study and explore more about symmetry and its existence.

When it comes to human sciences, the early development phase is zygote – a simple fertilized egg produced by the joining of two gamete cells by means of sexual reproduction – which develops into a more complex individual following a series of symmetrical transformations. These transformations encompass the processes of fertilization, mitosis, cellular differentiation and other multiplicative methods, however complicate, breaking the symmetry to engender predetermined patterned organismal forms. This is a bit confusing in exploring the initial developmental stages, as we do not know what exactly controls these developments. In the embryonic development, the successive cleavages (division of cells) from single-celled zygote to 2–4 cells embryo, and to 16–32 cells form the morula[5]. For mammalian developmental stages, these cleavages are in a symmetrical pattern and will follow exactly the same for other mammals too. Thus, the initial morula stage of development from a zygote is an instance of perfect symmetry. The cleavages occur at the predetermined instances, unless the external cues interferes; however, no clues are known that can explain this phenomenon.

It is obvious that the discussion to this point might have created some uncertainty in understanding the relationship between the terms symmetry and symmetry breaking, and self-propounding terms like uniformity, randomness and order. The following discussion will provide an idea about these terms and their relationships. An object or a figure is said to possess a symmetry if it remains invariable after a transformation, like rotation, shift or reflection around an axis[6]. Thus, symmetry suggests an order and uniformity, while asymmetry suggests disorder and randomness. Further, it can also be concluded that higher the order lower the randomness, or lower the order higher the randomness and increase symmetry decreases in randomness, or decrease in symmetry increases randomness. There is randomness in symmetry breaking; interestingly, it follows a predetermined order in the formation of structured patterns. This reveals that order dominates randomness. Symmetry breaking is the process that breaks the symmetry, or uniformity, or disrupts the order, proliferating randomness.

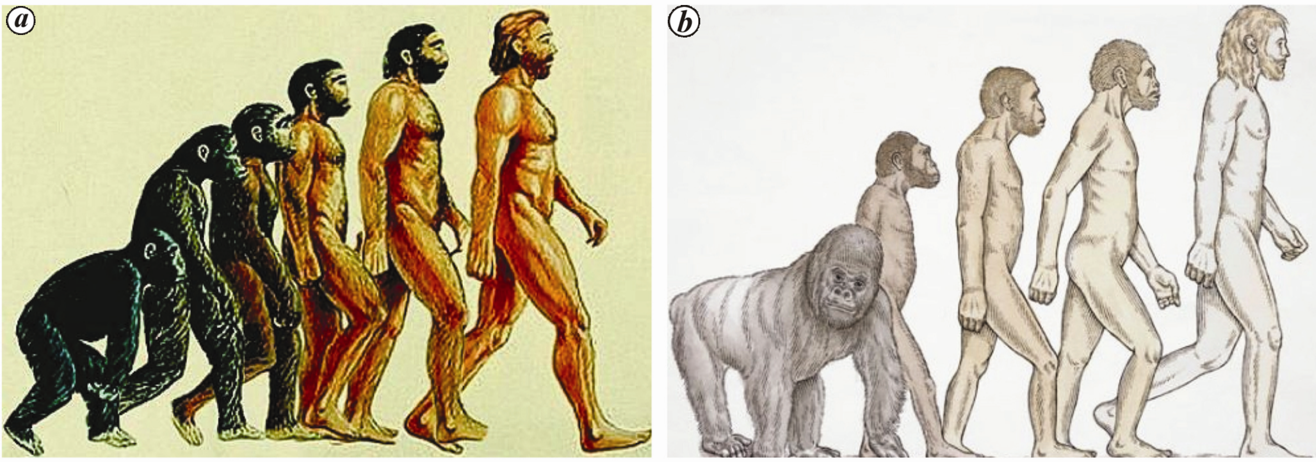

Figure 3. Natural symmetry breaking describing organismal adaptation in natural environment. ***a***, Example 1, questionable human evolution from chimpanzees (Image courtesy: http://www.solarnavigator.net/animal_kingdom/humans/humans.htm). ***b***, Example 2, questionable human evolution from gorillas (Image courtesy: http://alainamabaso.com/tag/gorillas/).

Any external (unpatterned) change in the shape of either circle or square would break its rotational symmetry, when considering the shape of the geometrical objects only. This is considered as a transition state, where a circle or a square loses its previous shape and state of symmetry under controlled perturbations. Transition is known as a change in the state; for example, a circle to a non-circle or a square to a non-square shape. Hence, this introduces the concept of symmetry breaking in geometrical objects in particular and in mathematics as whole. A prevalent change either in the state of an object or shape of a figure from its original state is called a transformation. For example, in geometry, a square has four transformational shapes, where these four shapes resemble the original square. Moreover, a symmetric changeover state for an object or a figure accurately resembling its original state is called a symmetric transformation state; that is, the state is too symmetric to be called asymmetric.

Under plausible prebiotic conditions, macromolecules polymerize spontaneously favouring the formation of polypeptides, further resulting in the formation of prokaryotic cells[7]. This formation is a series of intermediate transition states that favoured the evolution of life forms, however ploddingly, exceptionally breaking the symmetry to dominate the transition states. Here, it can be understood or considered that the effect of the external cues in these developments favoured the existence of symmetry and its breaking. Some scientists believe in the endosymbiotic theory, supporting the evolution of eukaryotic cells from prokaryotic cells, however, empirically there are rejections to this theory as well. A review paper by Lane and Martin[8] states, 'All complex life is composed of eukaryotic (nucleated) cells. The eukaryotic cell arose from prokaryotes just once in four billion years, and otherwise prokaryotes show no tendency to evolve greater complexity'.

An alteration – whether natural or a controlled modification – to this stability leads to the concept of symmetry breaking of the system, raising a need of controlling factors to achieve the transition state. In the case of mammalian cells or a cell-culture population, a transition state is a naturally controlled environment, which least influences the cell growth and motility. Natural symmetry breaking adheres to biological systems complexities, mainly the organismal adaptations and mechanisms involved at cellular levels. The human evolution is a long debated topic, whether chimpanzees or gorillas were our ancestors. A recent communication, however, opposes, both these and confines this prediction to a new evolutionary origin of humans[9]. According to Mauk, '... Humans did not evolve from apes, gorillas or chimps. We are all modern species that have followed different evolutionary paths, though humans share a common ancestor with some primates, such as the African ape....'

Figure 3 shows the evolutionary predictions of humans based on symmetry breaking under organismal adaptations in the natural environment. Considering each of the evolutionary phases, there are transition states in between each phase. It is this phase where the symmetry breaking took place, proposed to induce the transition state according to the natural environment. However, each evolutionary phase took more than hundreds of thousands of years to adapt in accordance with the then present natural environment. This massive time gap is because of the complexities of biological systems prevailing at the cellular levels in an organism. Organismal adaptations according to the cellular differentiation and environmental control took a long time in achieving the transition state that transferred one evolutionary phase to the other.

The occurrence of natural symmetry breaking opened the doors to explore controlled symmetry breaking under predetermined livelihood conditions. The study of controlling factors, however, suggests more and more perturbations, mainly the structural cues in the cellular cytoplasm responsible for cellular differentiation. The controlled symmetry breaking of cells in controlled environments focuses on migration of cells, morphogenesis, self-organization, and other soluble and insoluble molecular inhabitants or structural cues. The researches tend to find evitable effects of cues, matrix proteins (mainly collagen and elastin), on migration and growth of cell(s) in a controlled environment[10]. A unit of two or four cells for experimentation in the development of a mammalian tissue confines an even arrangement in symmetry breaking, with deliverables on random mobility in the same or different direction and morphological self-organization. The cellular morphology and growth patterns tend to adapt its environment, according to the soluble and insoluble molecular inhabitants or structural cues.

Figure 4 shows an example of human-controlled perturbations in understanding the organismal-level symmetry analysis. At first glance, it might appear as a simple crossing over between a horse and a donkey, and the offspring combinations. However, the controlled symmetry breaking is the cause for this genetic symmetry and combinations that a mule and other organisms, as a whole, are produced from these controlled perturbations. This analysis works for the human-controlled environment at organisms level. In addition, scientists are involved in molecular, cellular, and systems level analyses. Once the cellular differentiation, cell growth and morphogenesis

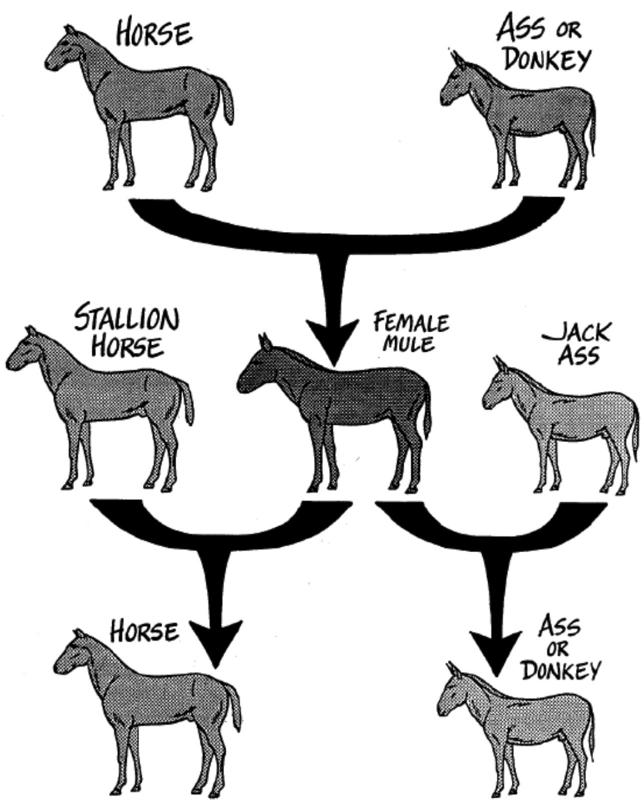

Figure 4. Controlled symmetry breaking describing forced perturbations in human-controlled situations (Image courtesy: http://evolution-facts.com/Ev-V2/2evlch15.htm).

come under human control, the symmetry breaking in biological systems would no longer be a hidden mystery.

In order to achieve more predictability as a result of application of symmetry breaking, sensitivity of external cues and prevalent environmental conditions have to be kept in control. Thus, controlled symmetry breaking will have more resultant predictability than that of natural symmetry breaking. This supports to have a clear distinction between natural and controlled symmetry breaking analyses in biological systems. For example, internal and external cues are responsible in biochemical signalling pathways; however symmetry breaking occurs in the absence of any directional cues[11]. In mammalian developmental stages, the transformations occur at each stage, resulting in symmetry breaking. Cell division in frog, holoblastic cleavage forms asymmetrical (disproportionate) concentrations of the cytoplasm and or of the nucleus.

To have greater predictability in the evolutionary transitions, a practical understanding of endosymbiosis (primary endosymbiosis – free living organism engulfs a bacterium, secondary endosymbiosis when an eukaryote engulfs an organism which already engulfed bacterium), membrane infolding (membrane surrounding the engulfed prokaryote cells), genome analysis, and protein synthesis is essential. Controlling the mechanism underlying prokaryotic cell division would tend to explore more predictabilities, however progressively, chromosomal replication is of utmost importance in prokaryotic development. Chromosomal replication is followed by segregation, organelles development and cell division. Evolutionary transitions can occur, such as amino acids formation, protein analysis, genetic code sequencing and initializing prebiotic processes.

There are doubts whether cellular differentiation is carried in the cells or not. Most researchers, believe, cells do not carry and possess any information about cellular differentiation and symmetry breaking respectively. This makes it difficult to understand the exact trend of symmetry breaking in organisms. Some researchers claim to have explored asymmetry and its patterns in organisms. Thus, this would provide a way to understand, if not a breakthrough, and to discover the unclear path of symmetry breaking. With cellular – migration, growth and division – differentiation, being known, detailed information regarding its functionality is still a mystery while several analyses involved fruit flies[12,13], mouse[14,15], and other organisms[16,17] to solve this puzzle.

Cell morphology and migration analysis using material surface topography are new concepts in this line, which attempt to unearth cellular complexities responsible for morphogenesis. Material surface topography explores detailed properties of a material surpassing surface electron movement visible through microscopic measurements. The recent developments in surface topographic analysis and control through image analysis influence cell morphology. The study of mammalian cell behaviour, which is critical in medical implants and tissue engineering, imaged by fluorescent microscopy, time-lapse microscopy, and scanning electron microscopy (SEM) analyse hepatic cell behaviour by inducing nano-porous and micro-grooved surface structures[18]. The study reveals completely different changes compared to the well-spread cells on the flat surface plate. Spheroidal morphology of the cells with no elongation and alignment is visible on the nano-porous surfaces, while enhanced cell growth with elongation and aligned morphology is seen on microgrooved substrates. This work highlights insights and encompasses benefits of this study on hepatocellular carcinoma metastasis, tissue engineering, and medical implant design. Cell morphology and migration stratum study using artificial nano-porous or micro-grooved substrates is an interesting option in material surface topography, which explores cell morphological features and migratory behaviour.

Symmetry breaking, in general, leads to more complex and patterned structures. However in biology, single-celled zygote cleavages to morula and finally develops into an organism – the most complex biological system. If at any instance – the transition state – researches in biological systems, whether through natural or manually controlled perturbations guide in the development of transformations from one stage to another, will lead in to control the development of an organism as whole. Controlling symmetry breaking at any level, molecular, cellular, tissue, system, or organism as a whole, would lead to predictable insights in developmental and evolutionary biology, and human sciences. Natural symmetry breaking follows a set of patterns of change (transitions). However, deep knowledge of these transitions is needed, facilitating more predetermined and predictable patterns regulating controlled symmetry breaking. An application of symmetry breaking leading to more insightful research in biology is the development of an artificial cell system – reconstituted actin cortices, exploring aspects of the structure and behaviour of actin network in the cortex[15].

Natural symmetry breaking seems to be essential, as it renders critical trials among researchers studying embryonic development, evolution sciences and organismal adaptations[19]. There are several questions that are still left unanswered to support the occurrence of symmetry breaking. Where does the symmetry breaking initiates in living organisms? Probably, symmetry breaking is evident at the following developmental levels, namely molecular, cellular, systems, and in the organism as a whole. What are the controlling factors responsible for the occurrence of symmetry breaking? It is mainly due to the effects of the environmental changes, and the cytoplasmic complexities also affect the cellular differentiation. What controls the symmetry breaking in achieving the transition state after a certain period of time or is it an ongoing continuous process? Some researchers believe that symmetry breaking is a peculiar form of morphogenesis. Symmetry breaking studies, however, presume, it is a naturally occurring unique process essential for the organisms to sustain in the natural environment.

Globally, the researchers are struggling to find the natural causes of symmetry breaking in biological systems at the cellular level. Moreover, the systems-level analyses at embryonic development need functionally detailed understanding of cellular differentiation. An immediate question that needs to be answered is: what are the physio-chemical processes responsible for guiding – during cell division, nourishment (morpho-, embryo-, and organo-) genesis, and cell motility or migration – the cells towards differentiation? In ref. 20, the analysis of cytoplasmic development in a controlled environment revealed the causes of symmetry breaking at cellular level. The developmental complexities in biological systems highly depend on the cellular differentiation. Thus, there has to be some hidden glocal processes that control the symmetry breaking and evolve to the transition states. However, fully controlled situations are still at their infancy and need rigorous perturbations and observations. Symmetry breaking is a confusing term, frequently there are chances of unpredictable patterns in the formation of structures. As stated earlier, the stages of embryonic development follow a pattern of division of cells (or cell differentiation) and can be an instance of symmetry breaking; but symmetry breaking is not limited to cell differentiation. There are various levels (molecular, cellular, tissue, systems, and organism) where symmetry breaking occurs. However, symmetry breaking is highly liberated, it is not confined to a certain level of differentiation or diversification.

The development and evolution studies reveal an interesting fact that symmetry breaking in organismal stratum in natural environment is a complicated phenomenon. The experiments based on genomic characteristics of several organisms confirmed the complex behaviours of biological systems. The occurrence of bilateral symmetries asserts and contradicts the present understanding about cellular differentiation and natural symmetry breaking in most of the organismal cells respectively. Thus, several studies now concentrate on the asymmetries in organisms at the molecular, cellular and systems level; however, insignificancies about complexities in biological systems still persist. Scientists are still struggling to answer the question regarding the causes of occurrence of symmetry breaking at various levels of development of asymmetrical patterns in bilaterally symmetrical organisms. In natural breaking of symmetry, the formation of organismal structures follows predetermined patterns. There are chances that unseen or unpredicted patterns are observed. For example, the existence of asymmetrical organisms. Thus, having a controlled phenomenon of breaking a symmetry (controlled symmetry breaking) would lead researchers in biology to discover more hidden treasures of nature. Probably, producing a new genus or species of an organism, if not, at least the known ones that are now extinct or on the verge of extinction.

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