3. *Infectious disease*:
   - Transient or chronic stimulation of immune system during infection influences cell dynamics: lymphocyte clonal expansion, triggered by the infection, can induce competition with nonspecific lymphocytes; lymphocytes may be activated upon release of inflammatory cytokines.

As a whole, lymphocyte dynamics depends on genetic and environmental influences, and also evolve according to pathologies, infection, gestation, and treatments. When cells evolved in "full" peripheral compartments, homeostatic regulations and competition may put forth and interfere with the intrinsic cell population dynamics. In contrast, when cells evolved in "empty" compartments, cell dynamics may be considerably enhanced to support the cell repopulation.

Organ

The presence or absence of a lymphoid organ (e.g., surgical/chemical thymectomy, thymus graft, splenectomy, bone marrow irradiation. . .) can dramatically perturb lymphocyte dynamics, migration, and turnover.

Lymphoid Populations

Cell populations can be defined according to their phenotype, function, repertoire of antigen-specific receptors, or naïve, effector, memory state of differentiation, etc. At the cell population level, several parameters can be investigated such as cell production, flux, residence time, division (number of cell cycles, rate of proliferation), death rate, migration, recirculation, etc. The interpretation of this wealth of data then consists to define input, output, self-renewal and transition rates in the defined cell populations by estimating relative percentages and numbers of lymphocytes.

Single Lymphocytes

Investigations can help to define further the numbers, phenotype, function, repertoire of single cells.

Molecular Levels

- Gene or protein expression, cell surface expression (TCR, BCR expression, repertoire, cell pathways/ signal transduction. . .) can be addressed at the levels of cell populations or individual cells.
- Telomere length: The erosion of telomeres is a sign of cell senescence and aging of the lymphocytes (Rufer et al. 1998), see ► Lymphocyte Dynamics and Repertoires, Biological Methods, Fig. 1.
- Nucleus fragmentation is a process involved during induced cell death that can be measured at the single cell or cell population levels.

Time

The time scale has also to be considered to assess Lymphocyte Kinetics.

Cross-References

► Lymphocyte Dynamics and Repertoires, Biological Methods

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Organism-Specific Metabolic Databases

► Specialized Metabolic Component Databases

Organization

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Definition

The *organization* of an entity refers to the arrangement of its component parts and their operations (or functions), and to how it results in the capacities of the whole or the phenomena of interest. Often, organized entities are complex and hierarchical: their parts are themselves organized entities.

Characteristics

A large part of the biological tradition maintains that the main characteristic of living beings is their organization, as the very term "organism" denotes. Even so, it is not evident that this concept pertains to the theoretical vocabulary of mainstream contemporary biology (i.e., the theory of evolution of the Modern Synthesis and Molecular Biology) or to the philosophy of biology inspired by it. Yet, although the notion of organization, as well as that of organism, may have been neglected by those, its elucidation has remained an important goal for other approaches operating in the life sciences of the twentieth century, such as Systems Theory, Cybernetics or Artificial Life, as well as for Embryology and developmental biology. Besides, the concept played an important role in the history of biology and its significance might be reinvented and rearticulated with the advance of contemporary Systems Biology.

Some historians think that the notion of organization was the key concept that constituted biology as a science around the beginning of the nineteenth century, as Foucault explained in his "The order of things" (Foucault 1966). However, even then and increasingly later, there has been a unsolved conflict between the view that tries to account for the material and generative properties of organized beings and the evolutionary one, for which an organized being inherits its organization from another organized being via reproduction. Thus, for Jacob (1970) the problem of organization was resolved with the elucidation of the structure of DNA in the 50s and the development of the notion of program in molecular biology to explain heredity and evolution. However, this path of research became increasingly reductionist in the sense that it tried to define all biological problems in terms of the properties of molecules. That is why organicist ideas are invoked again by those trying to challenge reductionist conceptions and emphasize that, being unlike the inert, life cannot be found at the level of components, such as molecules, but critically depends on how these components interact among them (Gilbert and Sarkar 2000). This aim appears in vindications of Systems Biology such as this one in a Nature editorial (2005): "What is the difference between a live cat and a dead one? One scientific answer is 'systems biology.' A dead cat is a collection of its component parts. A live cat is the emergent behavior of the system incorporating those parts." Thus, part of Systems Biology – specially what O'Malley and Dupré (2005) call "systems theoretic biologists" – considers that the difference that accounts for the "systemhood" has to do with organization.

Nevertheless, the philosophical and scientific characterization of organization remains to be done, as there is no "paradigmatic" or consensual account. Even among those who appeal for the centrality and non-dispensability of the notion for biology we can distinguish different understandings responding to different intuitions:

Abstract organization. Some authors look for a logical abstract conception of organization. For example, Maturana and Varela (1980) explain the autonomy of the living organism as a definition of life (see ▶ Systems, Autopoietic), substantiated by the difference between being self produced and being produced by others (that is why they feel that evolutionary accounts treat living systems as non autonomous). In living systems the organization of relations generates an identity: "the relations that define a system as a unity, and determine the dynamics of interaction and transformations which it may undergo as such a unity, constitute the organization of the system" (Maturana and Varela 1980, p. 137). They do not understand the notion of organization in the mechanistic language of parts and wholes, but in terms of abstract machines that, instead of computing problems set by external programmers (as the Turing machine does), realize a self defined identity in a space of interactions. The research program on autopoiesis seeks to study living organization at a logical formal level, considering that the material (or structural properties) of the components that realize the autopoietic organization play no role in its explanation. Rosen's work on M,R systems is similar in that it stresses the notion of closure: organisms are different from machines because they are closed to efficient causation.

Constrained organization. This abstract characterization of organization has been seen as problematic by other authors, who consider that even abstract whole systems need to fulfill some material or structural properties, such as thermodynamic or homeostatic conditions in order to be relevant to define life (see Moreno's paper in Boogerd et al. 2007; Etxeberria and Ruiz-Mirazo 2009). In this sense, although the organization cannot be reduced to the properties of parts, it needs to be constrained by some empirical parameters.

Mechanistic organization. The attempt to overcome the contradiction between "mechanism" and "organization" is the main feature of the view that considers that we need to take into account both the capacities of the whole and the structural properties of parts in order to explain organization (Bechtel and Richardson 2010; Wimsatt 2007). In it the structural properties of parts account for the organization of wholes, although the latter cannot be reduced to the former. It has been especially taken forward in studies of how forms of organization affect the complexity of the systems under study, and how they can be decomposed into parts. This approach is not opposed to evolutionary accounts, as it conceives that both the parts and the arrangements among them have evolved, so the organization is not only a theoretical or a priori hypothesis but it is under empirical enquiry. In fact, much of the research in evolutionary developmental biology (evo-devo) can be classified within this section. From this perspective it is possible to conceive, as Wimsatt does (2007), that research on living organization may be both reductionistic (in the sense that the material properties of parts are relevant) and holistic (in the sense that more than the knowledge of the parts is required to explain the whole), but this is a debated issue.

One philosophical issue underlying the difference among the three understandings of organization we have reviewed is the epistemological difference between the prevalence of theory (manifest in formal abstract approaches), and the requirement of starting from empirical data. In fact, concerning the functional characterization of a system or organization, especially with respect to computer aided scientific models (so important in systems biology), a newly defined dialectics of data versus theory is debated (see Krohs and Callebaut, in Boogerd et al. 2007).

Also prevalent is to question if a complex organization may be explained appealing solely to the physical and chemical characterization of the system, or if a distinctly biological one is required. Often a difference between order and organization is claimed. For Harold (2001), order is "a state in which the components are arranged in a regular, comprehensible, or predictable manner" (295), whereas organization is related to purpose, i.e., to the fact that each part has a function. Ordered states of a system have to do with regularity and predictability in the arrangement of components. However, although order can be found in the mineral world of rocks and geology, there is something more complex about organization than order thus understood. In this sense, living organization implies that organized entities have at least one purpose, and also that their parts are linked together to contribute to it. One way to avoid the problem of teleology arising here might be to say that living organization is self-organizing. But self-organization, the study of how system behaviors or patterns emerge from nonspecific interactions among lower-level components, cannot explain the emergence of function; it is closer to accounts for order than of purposeful organization. In this sense, Fox Keller (in Boogerd et al. 2007) has raised the problem that self-organizing systems can help understand the spontaneous generation of order in natural systems but not of function.

In sum, different kinds of worries have been raised concerning organizational approaches in the life sciences and different heuristics have been proposed to resolve the difficulties found. Some research strategies to study organizations stress the importance of some dialectics of decomposition and recomposition to study parts and wholes with the aid of computational modeling (Bechtel and Richardson 2010). The dialectics of analysis and synthesis is also very present in the discussion of approaches in Synthetic Biology (Etxeberria and Ruiz-Mirazo 2009). The problem of internalism has also been raised: Wimsatt drew attention to the fact that every investigation must divide a system from its environment and that methodological reductionism favors attributions of causal responsibility to "internal" parts of a system rather than those deemed external (see Brigandt and Love 2008). In addition, in evolutionary biology questions about organisms and organizations have been displaced by problems about individuals understood as units of evolution (genes, molecules, cells, organisms, groups, and species), but whose organization is not questioned or researched as such. In contemporary evolutionary biology the terms individual and organism are not co-extensive, thus the term organization cannot refer unambiguously to define individuals. Related to this is the question of how generic or universal are the characteristics of organizations. When organization is approached at an abstract level, the aim is to find important features that will apply to organizations across levels and realizations. This kind of research is now pursued by computational means such as the analysis of the behavior of very large networks.

Mechanist and reductionist accounts have been the preferred path taken by the main scientific practices of the twentieth century, assuming that progress towards better or more accurate explanations or predictions was more feasible that way. Now the combination of conceptual and methodological kinds of claims sustaining that trend might dissolve in view of the increased interest to find integrated explanations of living beings together with the new computational means developed to pursue them.

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Cross-References

▶ Autonomy
▶ Closure, Causal
▶ Complexity
▶ Constraint
▶ Mechanism
▶ Self-Organization
▶ Systems, Autopoietic

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Organization of Metabolic Networks

▶ Topology of Metabolic Reaction Networks

Orientation Histogram

▶ Extended Gaussian Image

Orientations Histogram

▶ Extended Gaussian Image for Pocket-Ligand Matching

Orthologs

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Definition

Orthologs are genes in two or more species that evolved from a common ancestral gene by speciation. Normally, orthologs retain the same function in the course of evolution. Ortholog identification is used for reliable prediction of gene function in newly sequenced genomes.