# Chapter 10
# The Living Cell

The living cell is the unit of life. Therefore, without knowing how the cell works on the molecular level, it would be difficult to understand how embryos develop or how species evolve (Waddington 1957; Gerhart and Kirschner 1997; West-Eberhard 2003). Most experimental data on the living cell have been obtained from "dead" cells, since living cells must be destroyed in order to isolate their components for purification and analysis (Sect. 3.1.5). To determine how living cells (*dissipatons*) work based on the experimental data measured from "dead" cells (*equilibrons*), however complete, is not an easy task, just as reconstructing musical melodies from sheet music would not be easy if one does not know the rules of mapping sheet music to audio music or does not have the ability to sing from sheet music. It is probably fair to say that, despite the massive amount of experimental data on the cell that has accumulated in the literature and on the World Wide Web as of the first decade of the twenty-first century, we still do not understand how the myriad structural components of the cell interact in space and time to exhibit the dynamic phenomena we recognize as life on the cellular level. The major goal of this book is to propose, in the form of a model of the living cell called the Bhopalator (Fig. 2.11), the theoretical concepts, molecular mechanisms, and physicochemical laws and principles that may facilitate uncovering the rules that map cell structures to cell functions.

## 10.1 The Bhopalator: A Molecular Model of the Living Cell

Although it had been known since the mid-nineteenth century that the cell is the smallest unit of the structure and function of all living systems (Swanson 1964), it was apparently not until 1983 that the first comprehensive theoretical model of the cell was proposed (Ji 1985a, b, 2002b). In that year, a theoretical model of the living cell called the *Bhopalato*r (Fig. 2.11) appeared in which both the *energetic* and *informational* aspects of life were integrated on an equal footing, based on the

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supposition that life is driven by *gnergy*, the complementary union of *information* and *energy* (Sect. 2.3.2). The name Bhopalator reflects the fact that the cell model was born as a result of the two lectures that I presented at the international conference entitled *The Seminar on the Living State*, held in Bhopal, India in 1983. The suffix, "-ator" indicates that the model is based on the postulate that the cell is a *self-organizing chemical reaction-diffusion systems* (i.e., a dissipative structure or a dissipaton) (Sects. 3.1 and 9.1).

The Bhopalator model of the cell consists of a set of *arrows* (i.e., *directed edges*) and *nodes* enclosed within a three-dimensional volume delimited by the cell membrane (Fig. 2.11). The system is thermodynamically open so that it can exchange matter and energy with its environment (see Arrows 19 and 20) (Sect. 2.1.1). The arrows indicate the directional *flows of information* driven by free energy dissipation. The solid arrows indicate the flow of information from DNA to the final form of gene expression postulated to be the *dissipative structures* theoretically investigated by Prigogine and his schools (Babloyantz 1986; Kondepudi and Prigogine 1998; Kondepudi 2008). These dissipative structures are in turn assumed to exert feedback controls over all the solid arrows, as indicated by the dotted arrows (Fig. 2.11).

One of the most distinct features of the Bhopalator is the role assigned to *dissipative structures* of Prigogine. Thus, IDSs (intracellular dissipative structures) (Sect. 3.1.2) are assumed to be both the *final form* of gene expression and the *immediate or proximal causes* for cell functions. Another novel feature of the Bhopalator model of the cell is the assertion that all nonrandom (or goal-directed) motions of biopolymers and associated small molecules in the cell are driven by *conformons*, the packets of mechanical energy and control information embedded in biopolymers (Chap. 8). Although there was no direct empirical evidence for IDSs or conformons when the Bhopalator was first proposed in 1983, the experimental data supporting these molecular entities emerged in the mid-1980s and throughout the 1990s, as reviewed in Sects. 8.3 and 9.1.

An updated version of the Bhopalator is presented in Fig. 10.1 using the formalism of a bionetwork (Sect. 2.4). All of the 12 edges or steps shown in this figure are present in the original version of the Bhopalator (Fig. 2.11), except Steps 8, 9, 10, and 11. The unidirectional arrows indicate the direction of information flow driven by appropriate conformons (i.e., packets of gnergy), which are not shown explicitly. The symbol, A → B, can be interpreted to mean that A *affects*, *influences*, *causes,* or *gives rise to* B. IDSs are any structures inside the cell that require the dissipation of free energy into heat to be maintained and hence disappear upon the cessation of free energy supply to the cell (e.g., membrane potential, RNA levels, ATP levels).

In Fig. 10.1, Steps 1, 2, and 3 represent the familiar processes – *transcription*, *translation,* and *catalysis*, respectively. Steps 4, 5, and 6 indicate the feedback controls exerted by IDSs on DNA, RNA, and proteins. Step 12 implies that the cell affects its environment through IDSs; that is, IDSs are the immediate causes of cell functions (Sect. 10.2), although cell functions do implicate, in addition, DNA, RNA, proteins, as symbolized by the large square bracket. Steps 7, 8, 9, 10, and 11,

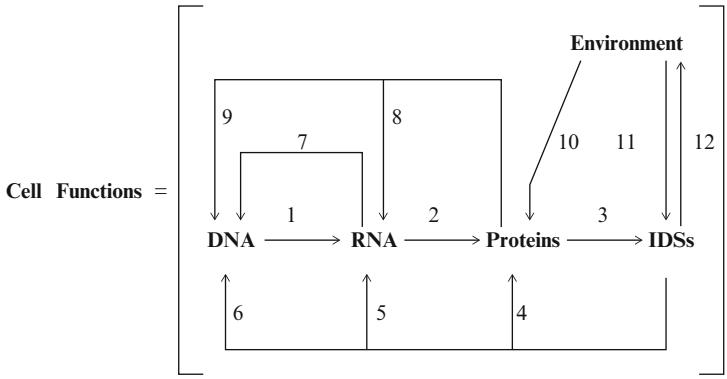


**Fig. 10.1** The Bhopalator 2011: a bionetwork version of the Bhopalator model of the living cell (Sect. 2.11). Not shown in the figure are the *biochemicals* that serve as the free energy source for generating the mechanical energy packets called *conformons* (Sect. 8.4), which drive all goal-directed motions of biopolymers, the most fundamental characteristics of life at the cellular level

not included in the original version of the Bhopalator, represent the following unidirectional interactions:

7 = RNA control over DNA (e.g., siRNA, microRNA),
8 = protein control over DNA (e.g., transcription factors),
9 = protein control over RNA (e.g., RNA-binding proteins),
10 = receptor-mediated input of environmental information (e.g., hormones, cytokines, morphogens), and
11 = nonreceptor-mediated interactions with environment (e.g., mechanical pressure, osmotic pressure, radiative damages)

Figure 10.1 provides a convenient *visual* summary of the complex molecular interactions and their properties that underlie life on the cellular level. The *text* version of these interactions and properties is given below:

1. The ultimate form of expression of genes is not proteins (i.e., *equilibrons*) as is widely assumed but IDSs (*dissipatons*) (Sect. 3.1). To emphasize this point, IDSs are *prescinded* (Sect. 6.2.12) to formulate what I call the *IDS-cell function identity hypothesis* in Sect. 10.2.
2. IDSs exert feedback controls over DNA (Step 6), RNA (Step 5), and proteins (Step 4).
3. IDSs are postulated to be the sole agent through which the cell affects its environment as indicated by the unidirectional arrow 12 in Fig. 10.1. This postulate is an alternative expression of the *IDS-cell function identity hypothesis*.
4. Environment can affect DNA in two ways – through (1) receptor-mediated mechanisms (see Steps 10 and 9), and (2) nonreceptor-mediated mechanism (see Steps 11 and 6).

5. Through the two mechanisms described in (**4**), the environment of the cell can cause the two types of changes in DNA – (1) changes in nucleotide sequences (*genetics*), and (2) changes in the three-dimensional structure of DNA including covalent modification of bases and DNA-binding proteins without changing its nucleotide sequence (*epigenetics*; Riddihough and Zahn 2010; Bonasio et al. 2010).
6. There are two types of environment-induced genetic and epigenetic changes described in (5) – (1) *heritable* from one cell generation to the next, and (2) *nonheritable*. Heritable genetic changes are well known in biomedical sciences (Mundios and Olsen 1997; Chu and Tsuda 2004). Environment-induced heritable epigenetic changes (EIHEC), well established experimentally, is known as Lamarckism or lamarckian (Ji 1991, p. 178, Jablonka 2006, 2009) and may play a fundamental role in both *phenotypic plasticity* and *evolution* itself (West-Eberhard 2003).
7. There are two types of environment-induced heritable epigenetic changes (EIHEC) – (1) *rapid* with the time constant $\tau$, comparable to or less than the life span of organisms, and (2) *slow* with the time constant $\tau$', comparable to the lifespan of species (say, $10^2 \times \tau$ or greater) and to geological times. The study of rapid EIHEC constitutes a major part of developmental biology and phenotypic plasticity, whereas the study of slow EIHEC is a newly emerging aspect of biological evolution (West-Eberhard 2003).
8. The causes of cell functions, that is, the factors that affect cell functions directly or indirectly, can be identified with the directed arrows in Fig. 10.1, either singly or as groups of two or more arrows.
9. The causes of cell functions divide into two types – (1) *external causes* or environment (e.g., temperature, humidity, salinity, pressure, radiation, environmental chemicals including nutrients), and (2) *internal causes*, namely, DNA, RNA, proteins, and/or IDSs.
10. The internal causes of cell functions may be divided into at least three groups – (1) the proximal (IDSs in Fig. 10.1), (2) the intermediate (proteins and RNA), and (3) the distal causes (DNA). The external causes of cell functions may be similarly divided. Thus, the living cell, as modeled in the Bhopalator 2011, embodies a complex web of both internal and external causes that interact with one another. Such complex systems of interactions may be difficult to analyze and discuss without the aid of the visual diagram provided by the Bhopalator 2011, that is, Fig. 10.1.
11. The system of the unidirectional arrows constituting the Bhopalator model of the living cell symbolizes orderly, nonrandom motions/movements of biopolymers and their associated small molecules inside the living cell (e.g., active transport of ions across cell membrane mediated by membrane ion pumps, RNA polymerse movement along DNA, myosin movement along actin filament, kinesin and dynein movement along microtubules, and chromosome remodeling). According to the Second Law of Thermodynamics (Sect. 2.1.4), no orderly motions such as these are possible without dissipating requisite free energy, and this free energy dissipation is postulated to be

mediated by conformons, which provide the molecular mechanism for the chemical-to-mechanical energy conversion based on the generalized Franck–Condon principle (Chap. 8).

12. Cell functions entail transmitting *genetic information* in space (e.g., from the nucleus to the cytosol; from the cytosol to the extracellular space) and time (e.g., from an embryo to its adult form; from one cell generation to the next) through what has been referred to as the Prigoginian and the Watson-Crick forms of genetic information, respectively (Ji 1988). The Bhopaltor model of the living cell identifies the Prigoginian form of genetic information with IDSs and the Watson-Crick form with DNA.

To recapitulate, the updated version of the Bhopalator shown in Fig. 10.1 embodies the following key principles, theories, and concepts discussed in this book:

1. The *principle of self-organization* and dissipative structures (Sect. 3.1).
2. The *gnergy principle* that all self-organizing physicochemical processes in the Universe are driven by gnergy (Fig. 4.8), the complementary union of information (gn-) and energy (-ergy), the discrete units of which being referred to as gnergons which include *conformons* and *IDSs* (Sect. 2.3.2).
3. The living cell is a *renomalizable bionetwork* of *SOWAWN machines* (Sect. 2.4.2).
4. The cell function is an *irreducible triad* of *equilibrons*, *dissipatons*, and *mechanisms* (Sect. 6.2.11).
5. *The IDS-cell function identity hypothesis* (see Sect. 10.2) results from *prescinding* (Sect. 6.2.12) IDS from other more distal causal factors of cell functions.
6. The Bhopalator can provide a common theoretical framework for effectuating both *development* (Sect. 15.8) and *evolution* (Sect. 14.7) through genetic and epigenetic mechanisms obeying the Principle of Slow and Fast Processes, also known as the *generalized Franck–Condon principle* (Sect. 2.2.3).
7. Because of (6), the Bhopalator provides a sound theoretical basis for unifying *genetics* and *epigenetics* on the one hand and *evolutionary developmental biology* (EvoDevo) (Carroll 2006) and *developmental evolutionary biology* (West-Eberhard 2003) on the other.

## 10.2 The IDS-Cell Function Identity Hypothesis

As already pointed out in Sect. 10.1, IDSs in Fig. 10.1 are the only node among the four nodes that is connected to cell's environment via a unidirectional arrow, implying that IDSs are the *most proximate causes* of cell functions (also called cell behaviors, phenotypes, or phenons). Thus, IDSs are unique among the possible causes of cell functions that are at different distances from the effects or cell functions, DNA being most distant. The idea that IDSs are the immediate causes

of cell functions will be referred to as the *IDS-cell function identity hypothesis* (ICFIH). It is clear that asserting ICFIH does not entail denying the causal roles for other cell constituents, namely, proteins, RNA, and DNA but emphasizes the immediacy of IDSs among the four possible causes of cell functions (see Sect. 12.5 for further details).

## 10.3 The Triadic Structure of the Living Cell

*Dissipative structures* are distinct from *covalent* and *conformational* (also called *noncovalent*) structures in that they are "far-reaching" or "global" in contrast to covalent and noncovalent structures whose effects are localized within one (in the case of covalent structures) or a set of contiguous molecules in physical contact (in the case of noncovalent structures). The "far-reaching" (or "global") effects of dissipative structures inside the cell can be mediated by electric field (in the case of action potentials) or mechanical tensions (in the case of the cytoskeletons, the dynamics of interconnected microfilaments, intermediate filaments, and microtubules, supported by ATP or GTP hydrolysis). Ingber (1998) and his colleagues have obtained direct experimental evidence showing that local perturbations of a living cell under mechanical tensions can propagate throughout the cell, which phenomenon these authors referred to as "tensegrity," or *tensional integrity*. Thus, Ingber's *tensegrity* belongs to the class of intracellular dissipative structures (IDSs).

It is suggested here that dissipative structures are essential (along with covalent and noncovalent ones) for cell *reasoning* and *computing* because their "far-reaching" effects provide mechanisms to coordinate many physicochemical processes occurring at different loci inside the cell, just as the "far-reaching" axons allow the physicochemical processes occurring within individual neurons to get coordinated and organized in the brain to effectuate human reasoning (Table 10.1).

If these assignments are correct, the following conclusions may be drawn:

1. In agreement with Hartwell et al. (1999) and Norris et al. (1999, 2007a, b), it is suggested here that a new category of structures (i.e., dissipative structures or dissipatons) must be invoked before biologists can understand the workings of the *living cell* (e.g., metabolic regulations, signal transduction, mitosis, morphogenesis, etc.), just as physicists had to invoke the notion of *strong force* (in addition to *electromagnetic force*) before they could explain the stability of atomic nuclei or quantum dots (see Sect. 4.15) to explain size-dependent optical properties of nanoparticles (http://en.wikipedia.org/wiki/Quantum.dot).
2. Reasoning process is not unique to the human brain but can be manifested by cellular and abiotic systems meeting certain structural requirements in agreement with the ideas of Wolfram (2002) and Lloyd (2006) in the field of computer science. This conclusion seems in line with Wolfram's *Principle of Computational Equivalence,* according to which all natural and artifactual processes

**Table 10.1** Three categories of structures in the cell and the brain. The third structure, which is built on the first two structures, is thought to be essential for reasoning/computing, or the ability of a physical system to respond to input stimuli according to a set of rules or programs

| | Peircean categories[a] | | |
|---|---|---|---|
| Level | Firstness | Secondness | Thirdness |
| Cell | *Chemical reactions* (covalent interactions) | Biopolymer–biopolymer interactions (noncovalent interactions) | *Dissipative structures* (space- and time-dependent gradients) |
| Brain | *Gradient structures* (e.g., membrane potentials) | *Information transmission* (from one neuron to another) | *Neural networks* (connected via action potentials and neuro-transmitters; space- and time-dependent) |

[a]See Sect. 6.2.2

obeying a set of rules are equivalent to computation (Wolfram 2002, pp. 715–846). Also the postulated ability of the cell to reason seems consistent with the isomorphism thesis between cell and human languages (Ji 1997a, b, 1999b, 2002b), since, without being 'rational', neither humans nor cells would be able to use a language for the purpose of communication.

3. Humans can reason (i.e., the *Thirdness* phenomenon exists in the human brain), only because cells and abiotic systems in nature in general behave rationally (and not randomly); i.e., the *Thirdness* phenomenon exists in Nature, independent of human mind. The universality of *Thirdness* asserted here may be closely related to what Rosen called *Natural Law* that guarantees the ability of the human mind to model nature (Rosen 1991).

## 10.4 A Topological Model of the Living Cell

There is now an abundance of experimental evidence suggesting that cells, both normal and diseased, are affected by *five distinct classes* of factors or determinants as indicated in Table 10.2.

It is clear that the Bhopalator 2011 shown in Fig. 10.1 is consistent with the content of Table 10.2, although biochemicals are not explicitly indicated in the cell model. To graphically represent the equal importance (to be referred to as the "equipotency hypotheses") of all of these five factors in determining the properties and behaviors of the cell, the *body-centered tetrahedron* may be utilized as shown in Fig. 10.2.

One difference between the cell models depicted in Figs. 10.1 and 10.2 is that, in Fig. 10.1, the five possible causes for cell functions are organized in the order of their distance from their ultimate effects, namely, cell functions, whereas Fig. 10.2 does not contain such hierarchical information.

**Table 10.2** The five classes of factors affecting the behavior of living cells

| Determinants | Examples | Explanations |
|---|---|---|
| 1. DNA | Mutations in certain genes (e.g., p53 gene [Levine et al. 2004]) lead to cancer and other pathological consequences | Mutated genes lead to alterations in protein amino acid sequences which often lead to altered protein conformations and functions |
| 2. RNA | Colon cancer cells show statistically significantly different patterns of changes in mRNA levels compared to those of normal cells (Stengel 2005) | RNA molecules not only mediate (through mRNA) but also regulate (through snRNA, and microRNA, etc.) the coupling between genotypes (DNA) and phenotypes (proteins) |
| 3. Proteins | A diarylquinoline drug, known as R207910, binds to the membrane component of the ATP synthase in *Mycobacterium tuberculosis*, thereby killing the organism (Andries et al. 2005) | Proteins are the only macromolecules in the cell (except ribozymes) that can harvest free energy from chemical reactions by catalyzing them. This means that, without proteins, no energy-requiring processes (without which no life can exist) can be carried out by the cell. Proteins are molecular engines/motors/rotors/machines out of which the cell is constructed (Alberts 1998) (Chap. 10) |
| 4. Biochemicals | Depriving oxygen kills all aerobic cells | Without biochemicals, no chemical reactions can occur inside the cell, depriving the cell of all free energy sources and hence of life |
| 5. Environment | Most cells can survive only within narrow ranges of environmental conditions to which they have adapted through long evolutionary history, including temperature, pressure, humidity, neighboring cells, radiation, and nutrient chemicals, etc. | Most cells have evolved to survive and perform their specialized functions only under stringently defined environmental conditions. For example, although all the cells in the human body have about 25,000 genes, different subsets of them are expressed in different parts of our body, depending on their *micro-environmental conditions*, leading to the liver, the kidneys, the heart, or the brain, etc. |

Several testable predictions in the field of DNA microarray technology (Alon et al. 1999) may be formulated based on the model of the cell shown in Fig. 10.2:

1. When the level of a mRNA molecule changes in a cell due to some perturbations, it is impossible to attribute such changes solely to DNA changes (e.g., changes in transcription rates), because proteins (e.g., transcription factors, RNA polymerase, histones, DNA topoisomerases, etc.), biochemicals (e.g., ions, pH, ATP, etc.), and environmental conditions (e.g., tissue specificity, microcirculatory situations, neighboring cells, etc.) may be responsible for a part or all of the changes in mRNA levels being measured (cf. the "equipotency hypothesis" above).

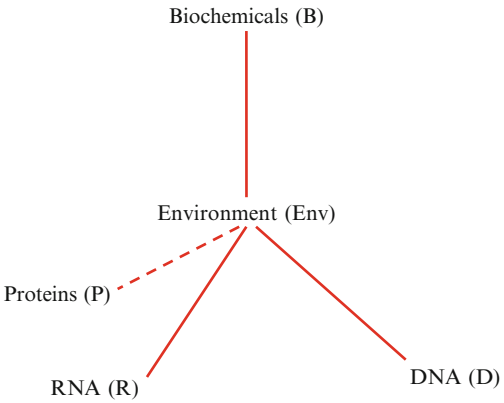


**Fig. 10.2** A simple topological model of the living cell viewed as a *body-centered tetrahedron (BCT)*. The tetrahedron is the simplex of the three-dimensional space, an *n-dimensional simplex* being defined as the simplest polyhedron in an n dimensional space (Aleksandrov et al. 1984). The six edges connecting the four vertices (B, D, R, and P) are not shown for brevity. One unique feature of BCT is that all the nodes (including the center) are in simultaneous contact with one another, a topological property suggestive of the physical situation where changing one node affects all the others

2. We may distinguish two kinds of causalities – the *direct* and the *indirect* causalities. For example, if a perturbation causes mRNA levels to change, it may be due to *direct* effects on any one or more of the apexes (i.e., biochemicals, DNA, RNA and proteins), or indirect effects mediated by environment which are affected by the perturbation, or due to indirect effects on DNA, proteins, or biochemicals which affect mRNA levels through their actions on the environment.
3. Mutations in DNA may affect mRNA levels measured with DNA microarrays in some but not all mutated cells, depending on the environmental conditions (e.g., tissue specificity, or microcirculatory variations within a given tissue).

The model of the cell depicted in Figure 10.2 reveals the material components of the cell that determine the structure and function of the cell under a given environmental condition. A similar *topological structure* of the cell can be constructed (see Figure 10.2a) wherein the nodes are occupied by *theoretical* (rather than *physical*) components that have been proposed to account for the structure and function of the living cell over a period of two and a half decades (1972-1997). It is interesting to point out that the experimental evidence for the cell force concept was not recognized until toward end of writing this book as discussed in Section 12.13. The theoretical components of the Bhopalator are collected in Table 10.2A in the order of their publication and with the experimental evidence supporting them.

The four theoretical components of the Bhopalator are all essential to account for the phenomenon of life on the cellular level in molecular terms and inseparably linked to one another mechanistically. The intimate relations among these components can be diagrammatically represented as a *body-centered tetrahedron* (BCT) (Figure 10.2a) wherein every node is in direct contact with all the other

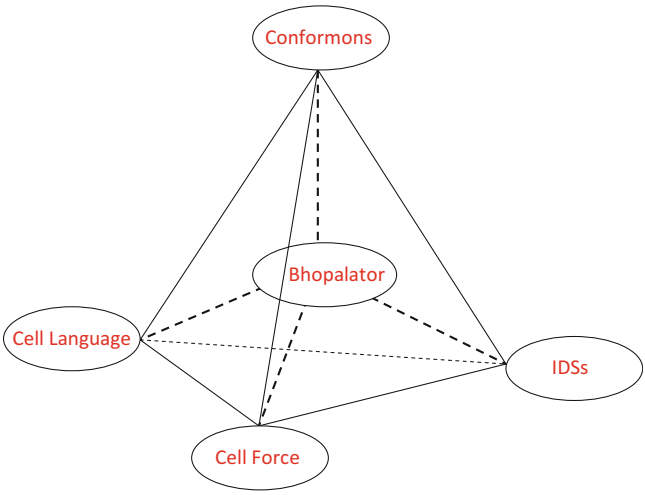


**Figure 10.2a** The body-centered tetrahedron representation (BCT) of the Bhopalator model of the living cell. The four major theoretical elements of the Bhopalator have been proposed between 1972 and 1997 (see Table 10.2A). The inseparable connections among the four theoretical components are symbolized by the BCT whose vertices/nodes are in direct contact with one another without any mediation

**Table 10.2A** The theoretical components of the Bhopalator (Ji 1985a,b). IDSs = intracellular dissipative structures. BRE = blackbody radiation-like equation

| Theoretical Components | | Reference | Experimental Evidence | Discussed in |
|---|---|---|---|---|
| 1 | Conformons | Green and Ji 1972a,b; Ji 2000 | Single-molecule mechanics of the myosin head | Chapter 8 and Section 11.4.1 |
| 2 | IDSs | Ji 1985a,b | Intracellular $Ca^{++}$ gradients | Chapter 3 |
| 3 | Cell force | Ji 1991 | Whole-cell RNA metabolic data fitting BRE | Sections 12.12 and 12.13 & Appendix L |
| 4 | Cell language | Ji 1997a,b | Quasi-determinism in genotype-phenotype coupling | Sections 6.1.2 and 12.10 |

nodes without any mediation. The Bhopalator model of the living cell has both a *physical structure* (see Figures 2.11 and 10.2) and a *theoretical structure*. The theoretical structure of the Bhopalator is the *inseparable connectedness among the four theoretical elements* listed in Table 10.2A that can be geometrically represented by BCT. What the BCT representation of the Bhopalator implies is that

> "*It is impossible to account for the workings of the living cell without simultaneously taking into account all of the four theoretical elements, i.e., the conformon, IDS, the cell force, and the cell language, and that no single theory is therefore sufficient to provide a complete understanding of the living cell.*" (10.1a)

We may refer to Statement (10.1a) as the *four-fold theoretical requirement* of the living cell.

The BCT is a 3-dimensional network with 5 nodes and 10 edges. The meanings of the nodes are evident in their names, but those of the 10 edges are not so obvious and require explanations. For example, the edge connecting nodes 3 (cell force) and 4 (cell language) embodies the following explanations:

a) Cell language is a form of organization.
b) Organization is a form of work.
c) Work is the product of a *force* and a *displacement*.
d) Therefore, cell language requires the existence of a *force* acting inside the cell (whichwas named the *cell force* in 1991).

Similar sets of explanations may be constructed for most, if not all, of the remaining edges.The *cell force* was postulated in 1991 to be a new force in nature (after gravitational, electromagnetic, weak, and strong forces) that is responsible for the *functional stability* of the biochemical processes going on inside the living cell, just as the strong force is responsible for the *structural stability* of atomic nuclei despite electrostatic repulsion. The cell force concept was formulated in analogy to the strong force and is supported by a qualitative application of the Yang-Mills gauge field theory to cell biology (Section 12.13; see also Appendix L). In Section 12.13, the first experimental evidence is discussed that is provided by the whole-cell RNA metabolic kinetic data measured with DNA microarrays and interpreted using the concepts derived from the *renormalization group theory* (Huang 2007).

## 10.5 The Atom-Cell Isomorphism Postulate

There may exist a set of principles and properties commonly manifest in both the atom and the living cell. For convenience, we will refer to this notion as the *atom-cell isomorphism postulate* (ACIP), and the set of the principles and the features common to the atom and the cell as the ACIP set. If ACIP is true, we can anticipate that our current knowledge on the atom will provide us with a useful theoretical guide for modeling the living cell. Whether ACIP is true or not will depend solely on whether or not the cell model constructed on the basis of it leads to results useful in (1) explaining and organizing existing experimental data on the cell, (2) generating testable hypotheses in basic as well as applied researches in cell biology (e.g., drug design, predictive toxicology, stem cell research, etc.), and (3) resolving cell-related controversies such as the definition of genes (Sapp 1987), the evolution-creation debate (Ruse 2005), stem cell wars (Herold 2007), and science-religion discourses (Ji 1993; Barbour 1997; Polkinghorne 2002, 2010; Kurtz 2003).

One of the elements of the ACIP set is the notion that the atom and the cell can be viewed as networks constructed out of two types of nodes emanating from a common root, as shown in Fig. 10.3 and explained in Table 10.3. Just as the atom is composed of hadrons (i.e., heavy particles, including protons and neutrons) and leptons (i.e., light particles, including electrons and muons) interacting through

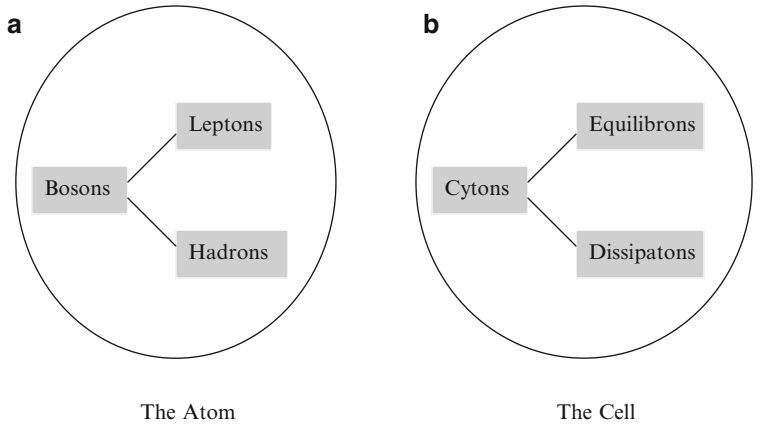


**Fig. 10.3** Two types of particles constituting the atom and the cell. Hadrons are heavy particles such as protons and neutrons, and leptons are light particles including electrons and muons (Han 1999). *Cytons*, first invoked in (Ji 1991) are the hypothetical physical entity operating inside the cell and analogous to bosons in physics that mediate the interactions between equilibrons and dissipatons

**Table 10.3** The atom and the living cell as two different types of networks consisting of two different types of nodes and edges

| | Atom | Cell |
|---|---|---|
| 1. Node type 1 | Hadrons | Equilibrons |
| 2. Edge type 1 | Strong force (mediated by gluons) | Covalent bonds (mediated by electrons) |
| 3. Node type 2 | Leptons | Dissipatons |
| 4. Edge type 2 | Electromagnetic force (mediated by photons) | Noncovalent bonds |
| 5. Interaction mechanisms | Exchange of bosons (e.g., photons, gluons) | Exchange of *cytons* (e.g., conformons, IDSs) |
| 6. Common principle | Franck–Condon principle | Generalized Franck–Condon principle |
| 7. Diameter, m | $10^{-10}$ | $10^{-5}$ |
| 8. Relative volume | 1 | $10^{15}$ |
| 9. Relative complexity[a] | 1 | $10^{15}$ |
| 10. Thermodynamic systems | Closed | Open |
| 11. Networks | Passive | Active (and renormalizable) (Sect. 2.4) |

[a] It is assumed that the complexity of a physical system as measured by its algorithmic information content (Sect. 4.3) is approximately proportional to its volume

bosons (e.g., photons; see Glossary for definitions of these terms), so the cell can be thought of as composed of two types of particles, equilibrium and dissipative structures that interact through the mediation of *cytons*, the cellular analog of bosons (Ji 1991, pp. 94–96) (see Rows 1, 3 and 5 in Table 10.3).

As indicated earlier, the terms e*quilibrons* and *dissipatons* have been coined to represent the concepts of the *equilibrium* and *dissipative structures,* respectively, that were formulated by I. Prigogine in the 1970s (Babloyantz 1986; Prigogine 1977, 1980; Kondepudi and Prigogine 1998; Kondepudi 2008). *Equilibrons* include DNA nucleotide sequences, and three-dimensional protein structures that can exist without any dissipation of free energy, while *dissipatons* include dynamic structures such as action potentials, intracellular gradients of all kinds, including $Ca^{++}$ (Sawyer et al. 1985) and RNA gradients in space (Lécuyer et al. 2007) and time (Garcia-Martinez et al. 2004), whose maintenance requires continuous dissipation of free energy (Sect. 3.1). In addition, each network contains two types of edges as indicated in Rows 2 and 4 in Table 10.3. The internal structure of the atom is held together by the forces acting on subatomic particles through the mechanisms of exchanging gluons and photons, two of the members of the family of bosons in quantum field theory (Han 1999; Oerter 2006). The cellular analogs of these interactions in the atom are not yet known but two possibilities have been suggested – *conformons*, mechanical strains of biopolymers driving goal-directed molecular motions (Sect. 8) (Ji 1985a, 2000), and *IDSs*, cytoplasmic chemical concentration and mechanical stress gradients that integrate molecular processes inside the cell (Sect. 9) (Ji 1991, 2002b). Conformons and *IDSs* may be considered to be reifications of the *cyton* (also called the *cell force*) (Ji 1991, pp. 95–118), just as photons and gluons can be viewed as reifications of bosons (more on this in Fig. 10.4). The electronic transitions in atoms obey the Franck–Condon principle (see Fig. 2.4). In (Ji 1974b, 1991), this principle was generalized and applied to enzymic catalysis (see Row 6 in Table 10.3) (Sects. 2.2.3, 7.1.3, and 8.2).

The last three rows in Table 10.3 exemplify those features and principles that are distinct between the atom and the cell and hence do not belong to the ACIP set. For example, under physiological conditions of temperature and pressure, the atom acts as a closed thermodynamic system (being able to exchange energy but not matter with its environment, except under very harsh conditions such as in a nuclear reactor), while the cell acts as an open system (able to exchange not only energy but also matter with its environment) (Sect. 2.1). In part because of this thermodynamic difference, the edges in the atomic network are fixed and unable to change, while those of the cell are dynamic and able to form or dissolve wherever (space) and whenever (time) needed by the cell, driven by the free energy of chemical reactions catalyzed by intracellular enzymes. For this reason, we can refer to the atomic network as *passive* and the network constituting the cell as *active* (see Row 9 in Table 10.3). The time- and space-dependent intracellular network conceptualized here can also be viewed as a *renormalizable* network in the sense that the cell is capable of reorganizing or regrouping its nodes to realize different functions in response to environmental inputs (Sect. 2.4) and cells themselves can become nodes of multicellular systems such as the brain.

It is truly amazing to find that there apparently exists a set of common principles and features that are operative in two material systems whose linear dimensions

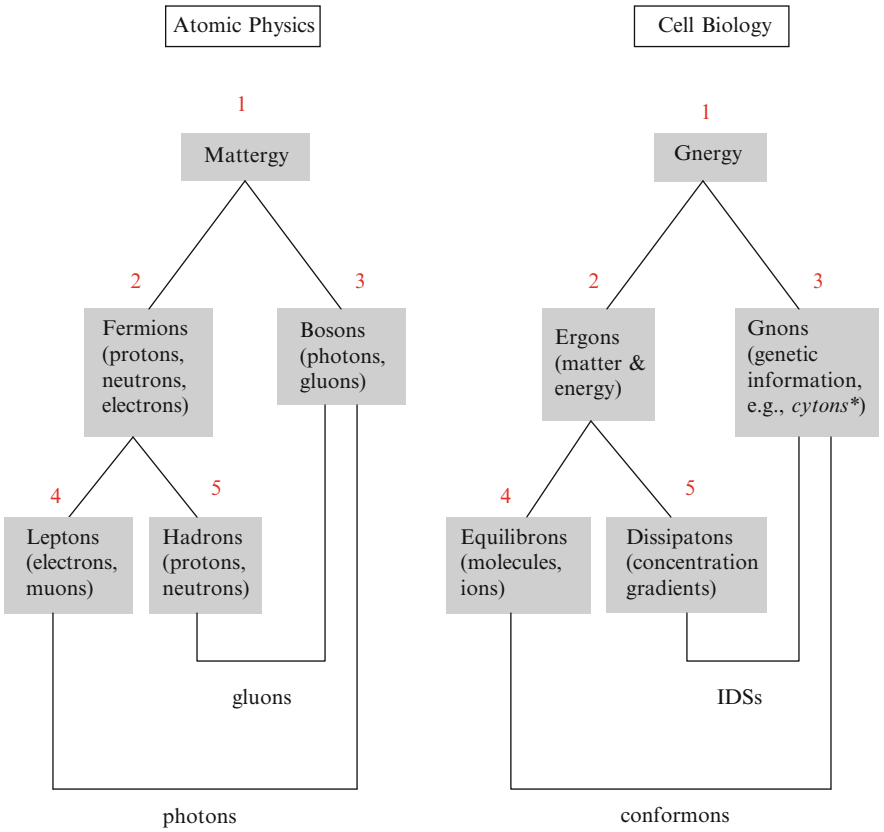


**Fig. 10.4** A more detailed network representation of the atom-cell isomorphism postulate (ACIP). The claim of ACIP that the structures and functions of the atom and the cell share a common set of principles and features thought to be reflected in the symmetry between the topologies of the two networks: Although the labels of the nodes and edges are different, the two networks are topologically identical. It is interesting to note that, since mattergy and ergons are synonymous, the mattergy tree (i.e., atomic physics) is enfolded in the gnergy tree (i.e., cell biology), which makes the topology self-similar or recursive (Sect. 5.2.4). For the unusual terms indicated by italics, see the text. *The term *cyton* was coined in (Ji 1991, pp. 110–114) to indicate the physical mediator of the cell force. The cell force is postulated to be the fifth force of Nature (after the strong, weak, electromagnetic and gravitational forces) that is responsible for the life-preserving dissipative structures of the living cell, in analogy to the gluon that mediates the equilibrium structure-preserving strong force acting inside the nucleus of the atom despite the electrostatic repulsion between protons (Han 1999). The non-Abelian gauge theory of Yang and Mills (Huang 2007) provides a qualitative support for the concept of the cell force as detailed in my January 19, 1990 letter to Prof. C. N. Yang (see Appendix K), and it is hoped that this letter will be of some interest to those mathematical physicists who may be interested in *mathematicizing* the cell force concept only qualitatively connected to the Yang-Mills gauge theory in Table 10.1 in the latter

differ by a factor of $10^5$ and volumes by a factor of $10^{15}$. The natural question that arises is whether this is just a coincidence or a reflection of some deeper connection that exists between the atom and the cell. The latter possibility appears to gain some credibility when we expand the comparison between the atom and the cell even further as detailed in Fig. 10.4.

*Equilibrons* are stable under normal conditions, while *dissipatons* are unstable, requiring continuous dissipation of free energy to be maintained.

The three types of particles shown in Fig. 10.3 that constitute the atom are actually embedded in a more complex network rooted in matter/energy (or mattergy) as shown on the left-hand side of Fig. 10.4. The *atomic network* shown here consists of five nodes (labeled 1 through 5) and six edges, two of which are identified as gluons (see Edge 3–5) and photons (Edge 3–4). If ACIP is valid, it should be possible to construct a similar network for the cell, and this anticipation appears largely realized by the cell network topology shown on the right-hand side of Fig. 10.4. To populate the nodes and edges of the cell network in accordance with ACIP, it was necessary to introduce five new terms (in addition to *equilibrons*, *dissipatons*, and *cytons*), namely, *gnergy*, *ergons, gnons, conformons,* and *IDSs* that had all been previously invoked in connection with the model of the universe (known as the Shillongator) based on the gnergy principle that originated in cell biology (Sect. 2.3.2) (Ji 1991, pp. 156–163, 230–237). It should be pointed out (1) that all the terms appearing in the cell network are written in italics to indicate the fact they are new to science, and (2) that the names of these terms are arbitrary and can be replaced by other terms as long as they serve equivalent roles in the cell network consistent with ACIP. It is clear that the topology of the atomic network (i.e., the left-hand side of Fig. 10.4) provides a useful theoretical framework to organize the set of the eight new concepts and terms, that is, *gnergy, ergons, gnons, cytons, equilibrons, dissipatons, conformons,* and *IDSs,* that I have introduced into cell and molecular biology during the past four decades (Green and Ji 1972a, b; Ji 1974a, b, 1991, 2000, 2002b, 2004a, b), which may be interpreted as indirectly supporting the ACIP.

A quantitative support for the ACIP was provided by the surprising findings that the mathematical equations similar in form to the blackbody radiation equation discovered by M. Planck in 1900 accounted for single-molecule enzyme kinetics of cholesterol oxidase (Ji 2008b) and the genome-wide RNA metabolism of budding yeast undergoing glucose-galactose shift (Ji and So 2009d) (see Sects. 11.3.3 and 12.12). The first systematic characterization of the ACIP was presented in Table 1.15 in (Ji 1991) where the term 'the cyton' appears for the first time and the force mediated by the cyton was given the name 'cell force', in analogy to the 'strong force' mediated by gluons. Therefore, if the ACIP is true, there must exist a new force, the cell force, which may be viewed as constituting the fifth force of nature after the strong, weak, electromagnetic, and gravitational forces (Han 1999, Huang 2007). Thus the ACIP may be alternatively referred to as the *cell force hypothesis* (CFH), and it may be asserted that the CFH formulated in 1991 was in part quantitatively validated in 2008–2009 (Ji 2008b, Ji and So 2009d).

## 10.6 A Historical Analogy Between Atomic Physics and Cell Biology

When I first saw a picture similar to the one shown in Fig. 10.5a in an international conference on DNA microarray data analysis held at Rutgers around 2003, I was struck by the superficial similarity between this picture and the atomic absorption spectra such as shown in Fig. 10.5b. The former displays the concentration of RNA molecules in cells encoded by various genes displayed on the left-hand side of the

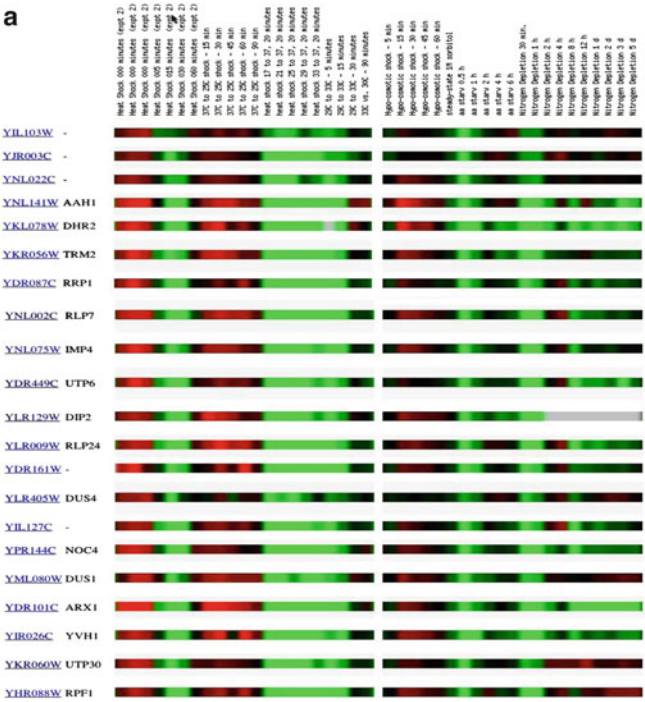


**Fig. 10.5** (**a**) *The microarray expression profiles*: The changes in the RNA levels of a group of yeast genes induced by environmental manipulations; *red* = increase; *black* = no change; *green* = decrease; *gray* = data missing or not measured. (**b**) The atomic spectra of the hydrogen atom: (*1*) The hydrogen atom absorption lines detected in the light from *Zeta Tauri*. (*2*) The same absorption lines observed in the light from another star, 11 *Camelopaadlis* (Moore 1963, p. 472)

figure that are induced to increase (red/yellow) or decrease (blue) under different experimental conditions (listed in the top row), whereas the latter shows the wave numbers (i.e., the number of waves per cm) of light *absorbed* when the electron in the hydrogen atom undergoes transitions from one energy level to another upon illumination (Moore 1963; Corney 1977). Figure 10.5a is about the cell and Fig. 10.5b is about the atom, but they both reflect the probabilities of some events occurring along appropriate structural coordinates in each system. The two columns of colored horizontal bars in (**A**) represent the RNA level profiles of two different mice subject to different experimental perturbations, and the tw rows in (**B**) represent the absorption or emission bands of hydrogen atoms in two different stars.

If this qualitative similarity between *the cell* and *the atom* is not limited to the surface appearance but reflects a deeper connection as suggested in Table 10.4, cell biologists might derive some useful lessons from the history of atomic physics. For example, around 1890, Johannes Lydberg found that the absorption or the emission lines of the hydrogen atom obeyed a simple formula,

$$\acute{\upsilon} = \mathrm{R}\,(1/\mathrm{m}^2 - 1/\mathrm{n}^2) \tag{10.1}$$

where $\acute{\upsilon}$ is the wave number (or the number of waves per cm) of the light absorbed, m and n are positive integers where $\mathrm{n} = \mathrm{m} + 1, \mathrm{m} + 2, \ldots$, for different series of absorption lines such as the Balmer series, Lyman series, Paschen series, etc., and R is the Rydberg constant (109,677 $\mathrm{cm}^{-1}$) (Atkins 1998). N. Bohr later showed that m and n are associated with the ground and excited states, respectively, of the electron in the hydrogen atom (Moore 1963; Corney 1977) (see Fig. 10.6). This formula remained a mystery until 1913, when Bohr proposed a theoretical model of the hydrogen atom based on the combination of the experimental data on atoms obtained by Rutherford and the theoretical concept of the *quantum of action* discovered by M. Planck in 1900 from his analysis of blackbody radiation data. The Bohr's atomic model led to the correct interpretations of the meanings of m and n as indicated above and to the calculation of the Rydberg constant from the fundamental constants of physics.

The superficial similarities between the microarray data shown in Fig. 10.5a and the line spectra shown in Fig. 10.5b led me to entertain the following analogy:

> The cDNA array technology may be to cell biology of the twenty-first century what the line spectroscopy was to the atomic physics of the twentieth century. (10.2)

This and other related analogies and comparisons are summarized in Table 10.4. This table is not meant to be exhaustively complete but lists only those items related to the theoretical cell biological research that I have been engaged in during the past four decades and, thus, may omit many related contributions made by other researchers, for example, the work of Craig Benham on SIDSs (stress-induced duplex destabilizations) which is directly related to the concept of conformons (Benham 1996a, b).

The term "ribonoscopy" appearing in Row 2 is defined as the experimental technique for studying genome-wide (i.e., over the whole set of genes in a cell) changes in the levels of the RNA (ribonucleic acid) molecules inside the cell

**Table 10.4** An analogy between atomic physics and cell biology based on the similarity between *line spectra* and *microarray gene expression profiles* shown in Fig. 10.5

| Parameter | Atomic physics | Cell biology |
|---|---|---|
| 1. Time | Nineteenth to twentieth century | Twentieth to twenty-first century |
| 2. Experimental technique | Atomic absorption/ emission Spectroscopy (nineteenth century) | cDNA array technology (1995) (*ribonoscopy*; Sect. 12.8.2) |
| 3. Changes measured | Electronic energy levels | RNA concentration levels (ascending, descending, or staying steady) associated with specific metabolic functions |
| 4. Perturbed by | Photons | Environmental chemicals/factors including hormones, cytokines, and neurotransmitters |
| 5. Experimental data | Atomic line spectra | Patterns of RNA level changes in the cell (*ribons*, RNA trajectories or RNA waves) |
| 6. Data determined by | Atomic structure | Cell structure |
| 7. Regularities | Lyman series Balmer series Pfund series, etc. | Patterns of RNA level changes (or ribonic spectra) obeying the blackbody radiation-like equation (BRE) (Sect. 12.12) |
| 8. Theoretical model | Bohr's atom (1913) | The Bhopalator (Ji 1985a, b, 2002b) |
| 9. Basic concepts | Quantum of action (1900) | The conformon as the *quantum of biological communication* (Green and Ji 1972a, b; Ji 1991, 2000) IDSs (Ji 1985a, b) Modular biology (Hartwell et al. 1999) Hyperstructures (Norris et al. 1999, 2007a, b) SOWAWN machines (Ji 2006b) |
| 10. Theory and principles | Quantum theory (1925) Franck–Condon principle (Reynolds and Lumry 1966) | The conformon theory of molecular machines (Ji 1974a, b, 2000) Cell language theory (Ji 1997a, b) Molecular information theory (Ji 2004a) Generalized Franck–Codnon principle (Ji 1974a, 1991) |
| 11. Philosophy | Complementarity (1915) | Complementarism (Ji 1995) (Sect. 2.3.4) |
| 12. A unified theory of physics, biology, and Philosophy | *The Tarragonator* (Appendix A; Ji 2004b) | |

measured by cDNA arrays (Sect. 12.1) and other methods as functions of environmental perturbations. So defined, ribonoscopy is an experimental technique for ribonomics, a term recently coined by Keene (2006) to denote the genome-wide study of RNA changes in cells. In other words, it may be suggested that

Ribonoscopy is to ribonomics what spectroscopy is to atomic physics. (10.3)

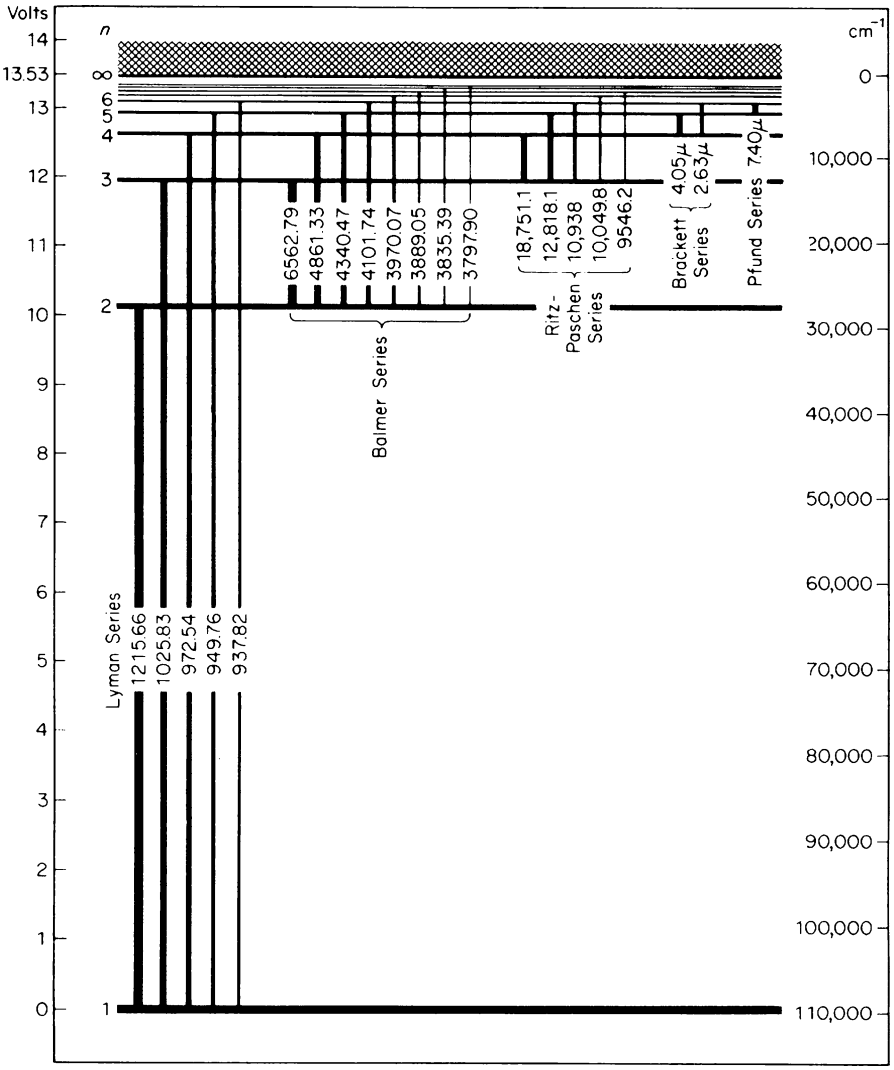


**Fig. 10.6** Energy levels of the hydrogen atom (Moore 1963, p. 475)

The term "ribon" is derived from "rib-" meaning *ribonucleic acid* and "-on" meaning discrete entity or trajectory and defined as the *patterns* of time-dependent variations of RNA levels measured with DNA arrays *inside the cell* (such as exemplified by the RNA trajectories shown in Fig. 9.1 in Sect. 9.2). Ribonics is then the study of *ribons*. When convenient, *ribons* can also be referred to as *RNA dissipatons, r-dissipatons, RNA trajectories, or RNA waves*, since all these terms refer to different aspects of the same reality. Since the mRNA levels are determined by both transcription rates and degradation rates (Ji et al. 2009a), *ribons* are

evidently species of IDSs (intracellular dissipative structures; see Sect. 3.1.2). The advantage and the utility of the term "ribons" derive from the fact that it is directly connected to the rich results of the theories of *dissipative structures* formulated by Prigogine and others in the 1980s (Babloyantz 1986; Kondepudi and Prigogine 1998; Kondepudi 2008).

Just as the atomic spectroscopic technique measures the electronic energy levels in the atom, so *ribonoscopy* measures the RNA concentration levels (ascending, descending, or staying steady) in the cell that appear to be quantized (see Sect. 12.13) and are associated with target metabolic functions (Row 3). The former is affected by the absorption of photons by the atom and the latter by the binding of environmental signaling molecules by the cell (Row 4). The results of measurements are *atomic line spectra* for the atom and the *time-dependent patterns* of the changes in RNA concentrations in the cell, namely, *ribons* or *r-dissipatons, RNA trajectories, or RNA waves* (Row 5). An important lesson to be learned from the atom-cell analogy is that, just as the atomic spectra are determined by (or reflect) the internal structure of the whole atom including electrons, protons, and neutrons, so the patterns of the RNA concentration profiles measured with DNA arrays are determined by (or reflect) the functional state of the whole cell, including the sate of enzymes, the cytoskeletons, and biochemical concentrations (Rows 6 and 7). Another lesson to be learned from the atom-cell analogy may be this: Just as the atomic line spectra of the hydrogen atom were impossible to interpret quantitatively before Bohr's model of the atom was formulated in 1913, so it may be that the patterns of RNA levels measured with DNA arrays may be impossible to interpret without a theoretical model of the living cell such as the Bhopalator proposed in 1985 (Row 8). The basic theoretical concept embodied in the model of the atom proposed was that of the quantum of action discovered by Planck in 1900. The basic concepts underlying the Bhopalator model of the cell include the conformon viewed as the quantum of biological communication (Ji 1991, p. 122), IDSs, and SOWAWN machines (also called modules and hyperstructures) (Row 9). Quantum mechanical principles such as the Franck–Condon principle are necessary and sufficient to account for all atomic phenomena. Similarly, it is suggested here that the conformon theory of molecular machines (which includes or enfolds the generalized Franck–Condon principle), the cell language theory, and the molecular information theory are necessary and sufficient to account for the observable properties of the living cell (Row 10). It is of particular interest to note that the same principle known as the *Principle of Slow and Fast Processes* (Ji 1991, pp. 52–56) is postulated to operate at both the atomic and cellular levels in the form of the Franck–Condon principle and the generalized Franck–Condon principle, respectively (Row 10). Bohr developed the philosophy of complementarity beginning in 1915 based on the principles of quantum mechanics (Murdoch 1987; Pais 1991; Plotnitsky 2006; Herbert 1987). The realization in the 1970s and 1980s that Bohr's complementarity concept can be extended into enzymology in the form of the information-energy complementarity, which in turn could be extended back to physics in the form of the principle of *gnergy*, the ultimate driving force for all self-organizing processes in the Universe (see Fig. 4.8), led to the formulation of a

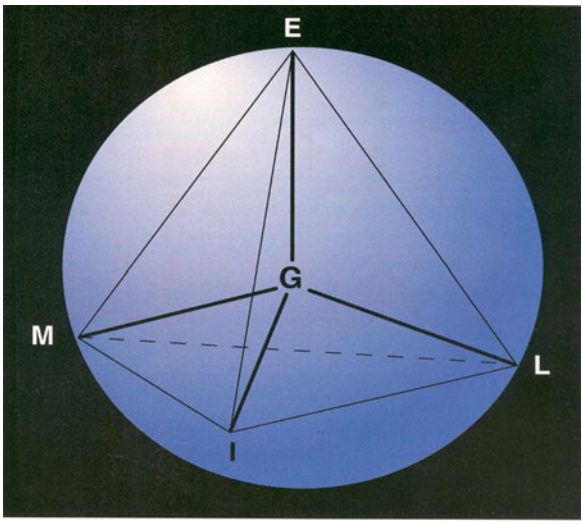


**Fig. 10.7** The gnergy principle of the Universe depicted as a body-centered tetrahedron. There are five nodes: (1) Gnergy (**G**), (2) Energy (**E**), (3) Matter (**M**), (4) Information (**I**), and (5) Life (**L**). There are two supplementary pairs in this Figure: (1) the (E + M) pair constituting *mattergy*, and (2) the (I + L) pair constituting *liformation*. *Mattergy* and *liformation* are complementary aspects of *gnergy* (see Table 2.6). The model of the Universe based on the gnergy principle is known as the Shillongator (Ji 1991) (Reproduced from Ji 2004b)

**Table 10.5** The body-centered tetrahedron as an iconic sign (Sect. 6.2.1) of the Universe and its constituents. The five nodes are numbered as in Fig. 10.7 (Reproduced from Ji 2004b)

| | The five nodes of the body-centered tetrahedron | | | | |
|---|---|---|---|---|---|
| Systems | 1 | 2 | 3 | 4 | 5 |
| 1. Universe (Ji 1991) | Gnergy (G) | Energy (E) | Matter (M) | Information (I) | Life (L) |
| 2. Cell (Fig. 10.2) | Environment | Biochemicals | Proteins | RNA | DNA |
| 3. Body (Ji 1991) | Motion system | Nervous system | Circulatory system | Endocrine system | Immune system |
| 4. Mind (Ji 2004b) | Biochemicals | DNA | Cells | Brain | Mind |
| 5. Signs (Ji 2004b) | Gnergy | Sign processor | Representamen (*Firstness*) | Object (Secondness) | Interpretant (*Thirdness*) |

new philosophical framework called complementarism (Ji 1991, 1993, 1995) (Row 11), according to which the ultimate reality is the complementary union of irreconcilable opposites.

Finally, as evident in Table 2.6, complementarity enfolds supplementarity in that the two nodes of gnergy are occupied with two supplementary pairs called *mattergy* or matter and energy on the one hand and *liformation* or life and information

on the other. Hence, Gnergy can be geometrically represented as the center of a body-centered tetrahedron with four vertices occupied by energy (E), matter (M), information (I), and life (L) as shown in Fig. 10.7. The model of *computation*, *mind,* and *signs* constructed on the basis of BCT (body-centered tetrahedron) has been referred to as the *Tarragonator* (Row 12) (Ji 2003a, b; Appendix A).

The *body-centered tetrahedron* (BCT) was found to provide a useful topological template to organize the various sets of related ideas in many fields of inquiries, as summarized in Table 10.5, which has led me to suggest that BCT may represent a universal code (Ji 2004b).

## 10.7 Evolving Models of the Living Cell

It appears that one of the first theoretical models of the living cell was proposed by J. Watson when he described a model of protein synthesis in cells diagrammatically (see Fig. 10.8a) in a letter to Crick in 1954, 1 year after the publication of their historic paper announcing the double-helical structure of DNA (Judson 1979, pp. 262–270). Watson's model of protein synthesis consists of three nodes (DNA, RNA, and proteins) and four edges. The main point of the model was the idea that protein synthesis occurs not on the DNA double-helix as suggested earlier by Gamow (Judson 1979) but on RNA molecules (see the vertical line in Fig. 10.8a), which idea was later superseded by the Crick's notion of the adaptor molecule subsequently identified as transfer RNA. The Watson mechanism of protein synthesis contained a deficiency – namely, the idea of chemically transforming one of the two strands of DNA double helix into an RNA molecule in the nucleus, which was then exported to the cytosol for protein synthesis (see the horizontal edge connecting DNA and RNA in Fig. 10.8a). Despite this shortcoming in mechanistic details, the Watson model of protein synthesis may be accorded a great historical significance because it is one of the first theoretical models of the cell ever proposed on the molecular level based on then available experimental data.

In contrast to the Watson model of 1954, which contained three types of objects (i.e., DNA, RNA, and proteins), the Bhopalator model of the cell proposed in 1982 at a conference held in Bhopal, India (and published 3 years later in [Ji 1985a, b]) contains two additional types of biological objects, i.e., *dissipative structures* of Prigogine, also called Intracellular Dissipative Structures (IDSs) in Ji (1985a, b) or *dissipatons* in Sect. 3.1) and *conformons*, conformational strains of biopolymers carrying mechanical energy to drive goal-directed molecular motions (Chap. 8). IDSs (a species or token of *dissipations*) are dynamic structures (also called "attractors" in nonlinear dynamics [Scott 2005]) consisting of chemical concentration and mechanical stress gradients within the cell, whereas conformons are dynamic mechanical deformations that are postulated to be localized to sequence-specific sites within biopolymers (Ji 1974b, 2000).

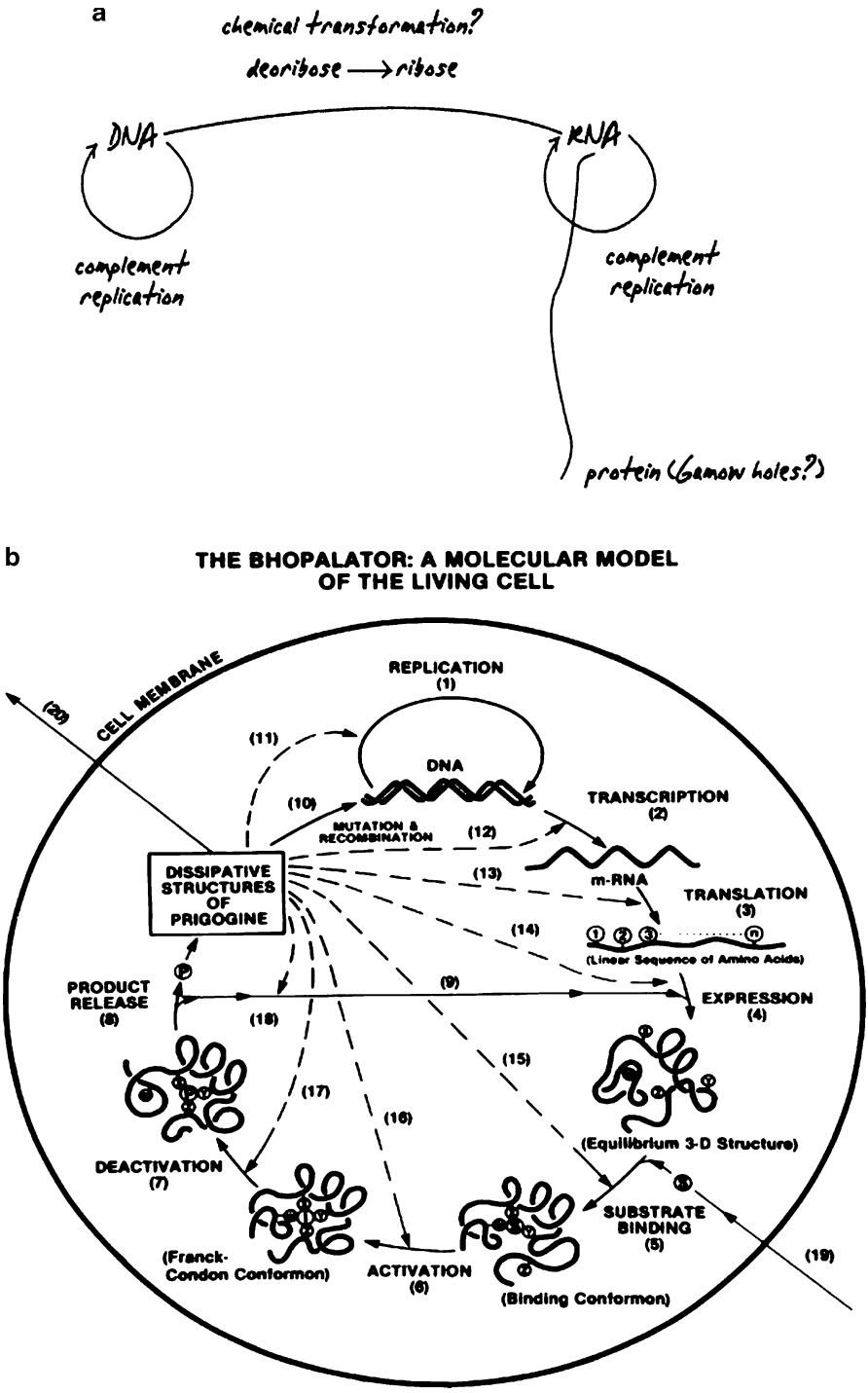


**Fig. 10.8** Evolving cell models. (**a**) The protein synthesis model of J.D. Watson (1954). (**b**) The Bhopalator model of the living cell (Ji 1985a, b). (**c**) A network model of the living cell (see Sect. 10.4)

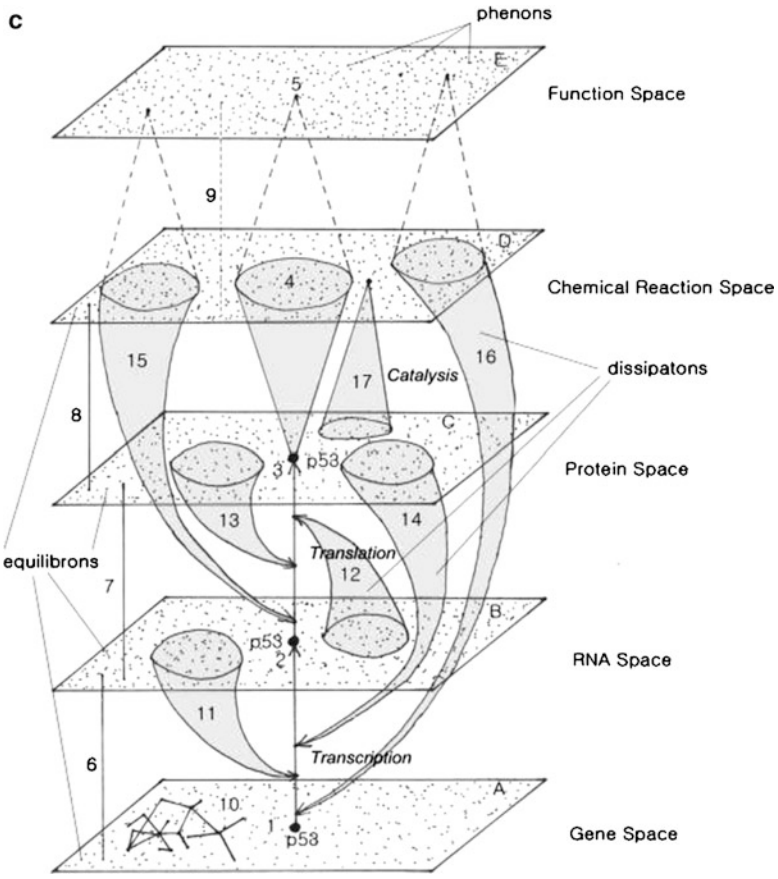


**Fig. 10.8** (continued)

The eight-dimensional *supernetwork* of Fig. 9.2 reproduced as Fig. 10.8c, is a *network* version of the Bhopalator model of the cell which is a *molecular* version. The most important new addition to the supernetwork model is the concept of "renormalization" (Sect. 2.4), namely, the cooperation among many entities of the cell to act as a transient unit of biological action. These so-called renormalization cones (also referred to as *dissipatons,* SOWAWN machines, or hyperstructures (Norris et al. 1999)) are symbolically represented as circular cones in Fig. 10.8c. The characteristic features of these three models of the cell are summarized in Table 10.6. The key theoretical concepts embodied in the models are listed in the second row of the table. The experimental findings that played key roles in the genesis of the models are given in the third row. The most pronounced differences among the models are their increasing complexities as evident in the increasing number of nodes and edges summarized in Rows 4 and 5. One surprising finding about Table 10.6 is the fact that, despite the enormous increase in the complexity of the models over the

**Table 10.6** The evolution of the theoretical model of the living cell, 1954–2011

| | Cell models | | |
|---|---|---|---|
| | Watson (1954) | Ji (1985a, b) | Ji (2012) |
| 1. Components | (1) DNA, (2) RNA, and (3) proteins | (1), (2), (3), (4) ion gradients, and (5) mechanical stress gradients | (1), (2), (3), (4), (5) and (6) Pathway-specific concentration waves as sounds of cell language (Sect. 12.8) |
| 2. New theoretical concepts | *DNA double-helix* (1) | *Conformons* (2) and *dissipative structures* (3) | *Renormalizable networks* (4) |
| 3. Experimental data | (1) Chargaff's rules of base pairing, (2) role of RNA in protein synthesis, and (3) X-ray structure of DNA | (1) Mechanically flexible proteins, (2) DNA supercoils, and (3) intracellular $Ca^{++}$ ion gradients | (1) Signal transduction pathways, (2) DNA microarray data, and (3) developmental biology |
| 4. Nodes | 3 | 8 | ? |
| 5. Edges | 4 | 20 | ? |

period of a half century, the number of new concepts underlying the models did not increase proportionately. It only increased from 1 to 3 to 4 (see Row 2). This may indicate that the eight-dimensional *supernetwork* model of the cell shown in Fig. 10.8c contains most, if not all, of the fundamental concepts needed to model the living cell.