Basic Biology for Born Engineers

Basic Biology for Born Engineers:

Living Mosaics

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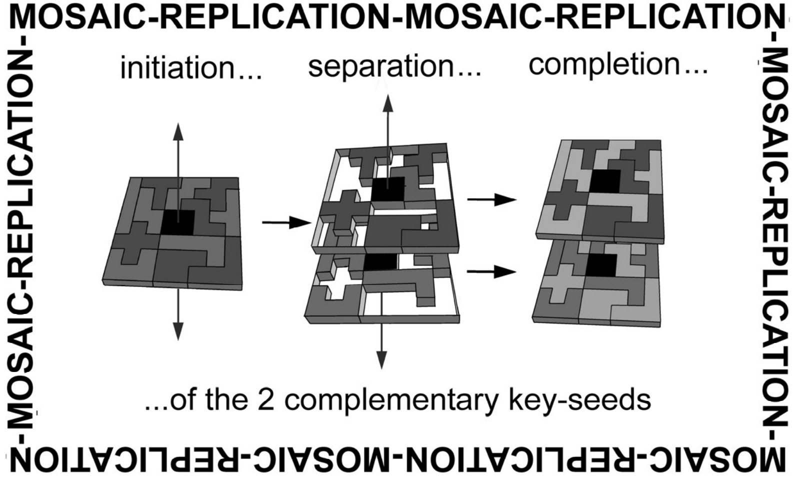
To my wife Veena,
whose encouragement and never less than loving criticism was invaluable.
To our children, Ananya and Ishan,
and with no less love
to my older children, Christine, Conrad, and Carl.

The opposite of a profound truth may very well be another profound truth.

(Niels Bohr, 1885 – 1962)



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SUMMARY

Like all technologies, terrestrial life must comply with fundamental engineering principles, lest it would fail. In particular, all life forms must consist of ***modules****, i.e. components that are*

(a) ***discrete*** *(there is no continuous transition between them), and*

(b) ***semi-autonomous*** *(most of their functions are completely independent, whereas a few need the cooperation of other components).*

Only then, an organism can assemble, service, repair, or replace parts and functions predictably without disrupting or disabling the rest.

The discreteness of the modules implies that all life forms are ***'mosaics'*** *of their specific, distinct modules (****'tiles'****) that operate under certain constraints (****'frame'****), which limits them, but also hold them together.*

The semi-autonomy of the modules implies that they cannot fit together automatically. On the contrary, their largely self-reliant actions tend to create conflicts between them. Hence, the modules of each living mosaic must find and maintain ways to ***fit together*** *with respect to their space, timing, forces and meaning.*

Mosaics may contain ***tangible*** *(material) modules or* ***symbolic*** *(mental) ones. The modules may interact and fit* ***physically*** *or* ***logically****.*

This book interprets living things as ***'living mosaics'****. Its perspective intends to provide a* ***novel, intuitive approach*** *for students of biology, medicine, engineering, and other disciplines, if they have a passion for the practical application of scientific insights. It intends to help* ***unify*** *the bewildering variety of biological phenomena, to* ***simplify*** *their classification, and to further their* ***understanding****. Most importantly, it offers a* ***unifying description of biological phenomena that is independent of*** *their sizes ranging from molecules to ecologies.*

The key concepts towards the understanding of living mosaics are ***'tasks', 'key-seeds', assembly-, replication-, and expression-mechanisms, cyclic behaviour, and their intriguing 'almost'-repeats.*** *Alas, like all real phenomena, they also give rise to a number of* ***paradoxes****.*

PREFACE

HOW EVOLUTION MUST CREATE SUPERB ENGINEERING

Today’s biologists understate all too frequently the logic, elegance, and boldness of the engineering of living things. I suppose, their reason is the fear that any emphasis on engineering would supply ammunition to the defenders of 'Intelligent Design' and ‘Creationism’.

This is unfortunate, because teaching how biological structures explain their functions helps the students’ retention and understanding. More importantly, recognizing intermediary stages and different levels of perfection of biological engineering provides convincing arguments *for* evolution, but not against it.

While proposing a unifying view of biological systems, the book tries to dispel the fear that permitting engineering principles into biology would invite religion into science. It does not. The existence of a supernatural engineer is neither provable nor disprovable by the finding that living systems comply with these engineering principles. They result from an evolution of their own, because the compliance with engineering principles creates quite large selective advantages for living systems.

Engineering principles also present important didactic advantages for science teachers by their remarkable power to unify our understanding of living things, regardless of their size and diversity. The present book will try to show this by presenting and analyzing in detail one specific engineering principle with which all living things must and do comply.

Based on my training as a physicist and many decades of experimental work in cell biology I decided to write about the engineering principle of ‘modularity’. It states that all life forms must be composed of **modules**, i.e. components that are

(a) **discrete** (there is no continuous transition between them), and

(b) **semi-autonomous** (most of their functions are completely independent, whereas a few need the cooperation of other components). Only then, can the organism or machine assemble, service, repair, or replace parts and functions predictably without disrupting or disabling the rest.

Since all living things obey this principle, it offers novel ways of classifying them, but also allows us to unify the explanations of their forms and actions.

I wrote this book for students of biology, medicine, and engineering. Besides logical thinking and an open mind, I expect the students to have at least high school knowledge of biology, histology, physiology, and arithmetic.

In return, biologists can rightfully expect from me certain documentations of scholarship, such as a complete reference list, and a thorough collection of accompanying notes. With my apologies to the experts, I risked the criticism of naiveté and of stating the obvious by forgoing those.

Instead, for the benefit of simplicity and clarity, I spent the lion's share of my efforts on designing didactic models and writing the computer programs needed for the 120 illustrations to support my lines of reasoning. I hope the results will be able to persuade experts and students alike to give it a chance. After all, today's easy access of students to powerful search engines renders the completeness of scholarly documentations rather obsolete. More importantly, in my experience of some forty years of teaching students of biology and medicine, the impact of eruditeness could intimidate them while they are still trying to slash their personal – and initially crude - trail through the seemingly impenetrable jungle of biology.

Still, after following the arguments of this book, the student should turn to the excellent, authoritative report of The National Academies of Sciences, Engineering, and Medicine [13] about the engineering principles of biology in all their forms, including the principle of modularity.

CHAPTER ONE

INTRODUCTION

EVERYTHING IS A MOSAIC; HOWEVER, THE TILES OF LIVING MOSAICS ARE MODULES

The world consists of elementary particles, atoms, chemical compounds, sediments, rocks, tectonic plates, planets, stars, galaxies, and galaxy clusters, which all appear, far from being single homogenous things, as mosaics composed of discrete, largely independent parts.

Describing these parts or mosaic ‘tiles’ as discrete objects does not imply that two different tiles of a mosaic cannot share material, symbolic, or functional components. They may very well share components, and yet be quite different objects.

The same applies to all living things. They, too, are mosaics, which consist of a wide-reaching hierarchy of sizes. Their discrete ‘tiles’ may have sizes as different as macro-molecules, polymers, organelles, membranes, cells, tissues, organs, organisms, and populations. However, there is a huge difference between inanimate and living mosaics. The ‘living tiles’ have ‘tasks’ and they are semi-autonomous in carrying them out.

Many consequences of the mosaic-character of living things need still more exploration. Here is a crude rationale for studying one of them.

The conceptual pillars of biology are the theory of evolution, molecular genetics, biochemistry, and the electrical activity of neurons. However, there is a significant divide between them. Their dominant mechanisms are very different from each other and seem to split biology into conceptual domains that are discrete and even may seem incompatible with each other.

The mechanisms of molecular genetics and biochemistry are governed by thermodynamics and quantum mechanics, which only apply to the microscopic world of biological molecules.

On the other hand, the mechanisms behind the electrical pulse-storms of neurons that reverberate through cellular networks and brains, originate from membranes, synapses, cells, and brain domains that are many orders of magnitude larger than molecules. Their dominant concepts and mechanisms relate to membrane biology, cell biology and histology.

Finally, the mechanisms of natural selection only make sense in the even larger world of organisms and ecologies. In exceptional cases, such as in the case of immune cells, there may be a natural selection among rapidly proliferating cells. However, there is no struggle for survival among molecules. They do not need to survive in order to proliferate, as the actions of messenger RNAs and ribosomes guarantee their unchallenged reproduction.

In other words, biology itself is a mosaic of at least three very different conceptual domains, namely the molecular, the cellular and the organismal size levels. Of course, in spite of their differences these ‘conceptual tiles of biology’ have countless mutual contacts and interactions.

Considering that this book is about mosaics, should we not be delighted to find biology itself to be a mosaic that is divided into at least three discrete fields that are semi-autonomous?

Actually, no. At their most fundamental level, all sciences strive to find common ground and unified formulations for all their phenomena. The described divide seems to present an obstacle for the goal of fundamental unity.

Sometimes turning a problem on its head may point to the solution. The concepts and rationales of mosaics may be able to provide the very commonalities that the mosaic character seems to exclude. After all, mosaics are not restricted to certain sizes. Whatever vocabulary describes mosaics, size plays no role in it.

To be sure, another set of size-bridging concepts exist already, namely the concepts and mechanisms of communication and information processing. The advances in neurobiology have demonstrated convincingly how these principles apply equally well to all size levels, be they molecules, neurons, or brains.

At closer inspection, however, we notice that all communication and data processing systems are in particular also mosaics. For example, microprocessors, computers, synapses, neural networks, or entire brains are composite objects. Hence, mosaics may belong to an even deeper level of biological foundation than the principles of communication and data processing.

Their ranking close to the foundations of biology justifies the study of mosaics, their ‘tiles’, and ‘frames’ in considerable detail. They will be called ‘living mosaics’, because they carry out meaningful ‘tasks’ such as metabolism, communication, searches, hunts and other targeted movements.

Obviously, inanimate mosaics such as the rings of Saturn are not capable of any such tasks.

The tiles of living mosaics are parts of these tasks. To be sure, they will always be discrete objects, but as parts of a common task they can never be entirely independent. Therefore, I will consider them as ‘semi-autonomous’, and call them no longer ‘tiles’, but use the name of ‘modules’. They play pivotal roles in all mosaics that carry out tasks. They are at the centre of a fundamental principle of biology, namely the ‘principle of modularity’.

This principle is size-independent. Therefore, our goal of exploring the size-independent vocabulary of mosaics will focus primarily on modules, their properties, actions, and interactions.

The Rarely Mentioned Principle of Modularity

Modern biology has discovered a large number of fundamental principles. Some of the best known among them are the principles of evolution, the laws of genetics, the principle of base-pairing, the so-called ‘central dogma of molecular biology’, the genetic code, nerve excitation, synaptic transmission, ATP-hydrolysis, the ligand-receptor binding, post-translational modifications of proteins, and several others.

Naturally, their claim of universality is - so far at least - restricted to planet Earth. In this limited sense of ‘terrestrial universality’, we need them as the pillars of our scientific explanations. The more such universals we find, the more phenomena of terrestrial life we can explain.

This book focuses on one of the rarely mentioned ones, namely the principle that *all known life forms are composites of distinct and largely autonomous, yet cooperating modules*. In spite of its universality, I could not find any textbooks dedicated to the principle of modularity. Among other goals, the present book is an attempt to close this gap. I hasten to add, though, that the principle of modularity is presented and discussed in the larger context of modern theoretical approaches to biology in the above mentioned excellent report of The National Academies of Sciences, Engineering, and Medicine[13]

The Principle of Modularity as a Requirement of Engineering

The principle of modularity is in plain sight. One can easily observe that all living things have discrete, clearly identifiable, semi-autonomous, yet cooperating parts, such as macromolecules, cells, organs, organisms, or populations.

Why are living things built like that? Building the opposite, namely homogeneous, seamlessly integrated units should serve much better the need of living things to implement body-wide cooperation, integration, communication and the creation of emergent macroscopic properties, should it not?

Actually, it would not. The reason is simple. Eventually, all constructed objects must malfunction or prove inadequate some time. However, once such a failure has happened, any attempt to update or repair a homogeneous object would cripple all its inseparable parts at once. In short, they would violate the vital engineering principle of modularity.

We can observe how dominant this principle is even in our human world. Every successful machine that humans ever built consists of independent modules. For example, every car is a collection of modules such as the engine, battery, transmission, wheels, headlights, etc. All of them are discrete objects, whose removal for servicing will not damage the rest of the car. In addition, they are semi-autonomous, and can be operated and tested outside the car. It is not only true for mechanical objects. Every computer has discrete and semi-autonomous, yet cooperating modules such as a screen display, memory banks, a power supply, circuit boards, microprocessors, integrated circuits, cooling fans, etc. even the computer software contains classes, subroutines, functions, data bases, interrupt routines, patches, etc. Removing them for repairs, upgrades, or diagnosis will not damage the rest.

The definition of modules is ambiguous. Sometimes they contain sub-modules. For example, a car engine, already a module, may contain as its own modules a generator and a starter that are firmly connected and precisely fitted to it. Yet, removing either of them from the engine and operating them separately will not damage the engine.

Alternatively, a complete machine may become itself a mere module of a larger machine. For example, a computer can operate as the single module of a server bank, or a car can function as one ‘detail’ of an entire police fleet. Regardless, modules operate always as identifiable, discrete, and semi-autonomous parts of a larger system.

Living things are no exception. They cannot function for long, let alone survive for millions of years, unless they comply with the principle of modularity. And they all do comply, of course.

Examples of Other Engineering Principles

Modularity is not the only engineering principle. Another important one is the provision of **back-up systems**. For example, the glycogen supply in muscle and liver is a vital back-up for emergency needs of metabolic energy. The fat deposits around the heart have a similar function. During starvation, they are understandably the last fat deposits, which the body depletes.

Already the bilateral symmetry of the body-plan of many organisms provides one back-up system for many body parts. Examples are the second kidney and the second lung we all have, even though a functional body only needs one. The much higher symmetries of the body-plans of most plants and of the parts of plants provide multiple back-ups for their vital organs.

There are exceptions, though, where a back-up system is not feasible. For example, a second independent heart could not pump blood through the vascular system without creating necrotic domains where the pumping of one heart would counteract that of the other.

Yet another important engineering principle is the **storage of spare parts** that may be needed at a moment's notice, whereas their *de novo* construction would be very time-consuming (e.g. the storage of platelets in the spleen; the rotating teeth of sharks). Yet others are the **standardization of parts and processes** that facilitate construction and repair (e.g. the universality of ATP hydrolysis, glycosylation, and phosphorylation), **the shielding from noise** (e.g. the anchoring of enzymes to huge 'cytoskeletal' polymers that are little affected by Brownian movements), the **preparedness for failure** (e.g. the clotting machinery of blood, regeneration of limbs), and so on.

These principles of engineering are universal, and they play prominent roles in biological systems and human-made machines alike. However, this book will focus exclusively on the principle of modularity, because its implementation seems to be a fundamental pre-condition for all the others.

The Size Independence of the Principle of Modularity

One of its earliest formulations of the principle of modularity was the cell theory of Schleiden and Schwann. It states that all tissues, organs, and ultimately all living organisms consist of either a single cell, or else are the composite of multiple single cells as their distinct and semi-autonomous modules.

But cells are not the smallest modules of organisms. Cells contain smaller, distinct, and semi-autonomous sub-components and sub–compartments, such as sarcomeres, mitochondria, chloroplasts, cell membranes, nuclear pore complexes, chromosomes, cytoskeletal domains, etc. Even their macromolecules, oligomers and monomers alike, consist of molecular sub-units or domains that are able to exist and function in isolation, and can be modified or even recycled without incapacitating the cell.

Similarly, the principle of modularity applies to the various coding and non-coding segments of genomes that sub-divide into long series of fractal sequences *[02]*. The student of biology will undoubtedly be able to think of many more such examples.

Cells are not the largest modules, either. Entire organisms may function as discrete and semi-autonomous modules of a population of interacting organisms. Every coral reef, herd of caribou, wolf pack, or colony of algae represent a semi-autonomous module within their well-fitted ecology. Ultimately, entire populations of organisms are but modules within Earth's gigantic biosphere.

Modularity as the Source of Emergent Properties of Living Things

Present day biology considers macromolecules as the ultimate elements of explanation. To be sure, they are important modules of cells, and their broad success is undeniable. Yet, the exclusive focus on molecular levels must fail to explain some of their emergent properties.

In biology, we are facing some of the most mysterious emergent phenomena that exist anywhere, such as aging, language, intelligence, meaning, and even consciousness, and creativity. Macromolecular mechanisms are light-years removed from the levels of compounded complexity that may someday explain these ultimate expressions of life.

Perhaps the principle of modularity can point the way. Emergence describes how a collection of units creates a larger object that expresses new properties, which none of the component units had. The phenomenon creates hierarchies of increasing sizes that span many orders of magnitude. In short, *where there is modularity, there is likely emergence as well.*

Modules as Universal Instruments of Scientific Reduction and Explanation

Biological macromolecules can and do combine into larger groups that acquire new functions, individuality, and even autonomy, which elevates them to the level of modules. Examples for such next-higher-level modules are ribosomes, chromosomes, chloroplasts, centrioles, nuclei and so forth.

These, in turn, can group into even larger modules such as cells, which in turn combine into even larger ones such as tissues and organs, and so forth.

Since nature herself offers us a hierarchy of natural modules of living mosaics, they may turn out to be the most appropriate elements for our scientific analyses, even when they are much larger than biological macromolecules [03]. In other words, *macromolecules are powerful instruments of biological explanations, but they are not the only ones. All higher level modules may qualify, as well.*

Of course, many biologists have put this concept to use. Especially, neurobiologists have pioneered elements of analysis that are much larger than neurotransmitter molecules, receptor molecules, or ion channels. The search for the explanation of emergent phenomena such as pain, perception, and cognition employs successfully not only whole neurons, but also groups and networks of neurons and even whole brain domains.

Similarly, the students of DNA have long moved beyond the study of nucleotides, base pairs, polymerases, or transcription factors. They place equal importance on the interactions between the entire double helix and nucleosomes. They have formulated an entire hierarchy of coiled pairings of DNA and nucleosomes, as well as centromeres, telomeres, chromosomes, all the way up to the properties and actions of the entire chromatin and its interactions with the nuclear envelope.

Also, cell biologists have turned their attention to the study of the shapes, dynamics, and functions of a family of very large, linear protein polymers that carry the – misleading - name of the ‘cytoskeleton’.

To be sure, it may not take more than single macromolecules to trigger the *failure* of any of these higher-level modules. On the other hand, single macromolecules, can never explain the complex *functions* of these modules.

There is no danger that such higher-level approaches will neglect the molecular levels. On the contrary, such analyses will necessarily climb down a ladder of emergent properties all the way back to the properties of single molecules.

The Problem of Identifying Modules

The omnipresence of modules does not mean that they are easy to identify. In spite of their discrete nature, determining the actual borders of modules poses occasionally very difficult problems.

As an example, think of the enormously complex outlines of a Purkinje cell. Another example is our vascular system with all its arteries, veins, and capillaries. It is actually a single contiguous object, and if seen in its entirety, it occupies a space of almost incomprehensible complexity. Or consider an ant nest as one of the modules that comprise the living mosaic of a forest. If one includes all the foraging ants, where does the nest begin and end?

The search for new staining techniques may help. Since Camillo Golgi's most revealing silver stain of neurons, there has been considerable progress of our staining techniques, such as fluorescent in situ hybridization (FISH), immuno-fluroescence in combination with confocal laser microscopy, computerized tomography, imaging of proteins in the live state by green fluorescent protein (GFP), and others. Methods like these are able to outline biological components, in spite of their enormously complex shapes and their intimate intertwining with others. Further improvements of our probing and staining techniques should help outline biological modules better and better.

The principle of modularity as the most universal feature of all life forms

Considering the enormous diversity of modules, it seems that modular architecture not only is one among other basic principles of biology. Arguably, it is the most universally shared property of all life forms on Earth. There is no living thing whose architecture does not comply with it.

In addition, all life forms depend on each other in some way or another, which makes them all tiles of an even larger living 'mega'-mosaic.

The 'Tasks' of Modules

What earns the tiles and whole mosaics of living things the attribute of 'living' is the ability to carry out tasks. i.e. an action with an intent of their own. Therefore, if we encounter *a mosaic that carries out a task, we can decide to describe it as a living mosaic*. It may seem reasonable, because mosaics that could not possibly have tasks, such as moon craters, or sun flares cannot possibly have intentions, because they are not living.

On the face of it, this definition seems to exclude mosaics that carried out tasks in the past, but are no longer functional (e.g. a skeleton), or that will carry out tasks in the future (e.g. pro-insulin), but are not yet active. Therefore, we will call *all mosaics as living mosaics, which are used, have been used, or will be used to carry out tasks*. This includes former tiles of a living mosaic, as well as objects that were collected, fabricated, or modified by a living mosaic in order to be used as 'tools', provided their task is to participate as one of its tiles in the performance of the living mosaic's task.

Philosophically speaking, we are moving here on very thin ice. The definitions of words like 'living', 'task', and 'intent' are ambiguous and even circular. Still, their common sense meaning is clear. In chapters 9, 10, and 28 we will discuss the concept of tasks in more detail. For the time being, we notice that tasks are using material objects, but they themselves are not material objects. Instead, *tasks are composed of instructions, data, and 'markers' for processes and functions that are placed in specific order.* All living mosaics are associated with one or several such tasks. The non-material components of tasks may be called 'symbols' as they stand for certain material objects.

Hence, tasks are composed of parts, which are not material and, therefore, they may be categorizes as 'symbolic' mosaics, themselves. Examples are patterns, texts, languages, and programs, whose discrete tiles are symbols such as signals, body markings, pulses, letters, numbers, functions, etc. In his recent book, Harari [08] describes them as organic 'algorithms'.

Symbolic mosaics do not stand alone, but interact with members of yet other categories of mosaics, which use logical functions as their nodules. They process information by discrete sets of rules that constitute yet other symbolic mosaics. And so forth.

The Problematic Concept of 'Tasks' and Other Forms of Teleology

Maybe, engineering is in our blood. From our earliest childhood on we love building things. Conversely, when we chance upon an unknown object, we cannot help but trying to decide whether it was built intentionally or whether it is an accidental product of nature.

All this applies to mosaics. Regardless whether the mosaic is a painting, a symphony, or an unfamiliar machine, if all the parts fit perfectly well, one is immediately convinced that there was great effort behind it, and therefore the mosaic must have a purpose.

These are, of course, teleological thoughts, which science banned long ago. However, to be fair, only the sciences about inanimate nature rejected teleology. Should biology ban it, too?

It will not be easy to do. As long as we only look at inanimate nature, we can easily agree that (say) moon craters have no purpose, and inventing one will not help us explaining their properties, let alone the moon.

The situation is quite different in biology. We cannot effectively investigate biological objects without considering their interlinked functions, because biology is all about engineering; and engineering is all about purpose, albeit about human purposes. Even Rube Goldberg machines 'have the purpose' of demonstrating none is needed.

For instance, teaching the histology of the human kidney without reference to the purpose of the medulla, the basement membrane of the glomeruli, the shape of the podocytes, the proximal convoluted tubules, the loop of Henle, etc. would be an endless stream of unrelated, meaningless statements. Certainly, no medical student reading it would be inspired to devote his/her life to nephrology and kidney pathology. Teaching the kidney organization without linking it to its biological purpose would be as effective as teaching students the entries in a telephone book.

However, the concept of 'purpose' cannot exist in isolation. Every purpose is supposed to be in the service of a superior level purpose. Conversely, whenever we claim to know the 'purpose' of a machine, we look at the component parts and look for the way, in which they contribute to the purpose.

In other words, one cannot ascribe a purpose to a 'part' without justifying it by the purpose of the higher-ranking 'whole'. For example, each nephron, whose purpose it is to serve the kidney function, would ultimately be useless, if the whole kidney had no purpose. Surely, the steering wheel of a car is useless, if the car is a dysfunctional wreck.

Hence, every time we want to justify the purpose of an object, we must go up the scale of sizes, and find out whether the next higher level still has a purpose. Unfortunately, along the way even biology reaches quickly a limit where teleology becomes meaningless.

Take again the example of the kidney. Moving up one level of organization, we can identify its purpose to filter blood plasma and to adjust the blood pressure. We will also be able to find a 'purpose' for the maintenance of 'healthy' blood conditions of a whole mammal like a horse. However, when it comes to naming a purpose for the whole horse, most people will struggle to name one in objective terms. However, even if a cavalry enthusiast could name an objective purpose for horses, we would have to continue further up the scale of sizes. Eventually, we would have to demonstrate the purpose of mammals in general, or of animals, or of life on Earth per se. At the latest at this level in the hierarchy of life, we have to admit that we cannot name a purpose for life on Earth that science can prove. There are too many counter-examples of planets without life, even in our own solar system, and they seem to be doing quite well without it.

Although biology must eventually reject teleology as a global concept, it remains indispensable for our understanding, teaching, and heuristics of biology on countless levels of size and evolution. Adopting a compromise, we may resort to 'local' versions of teleology, i.e. versions, which work up to certain levels of biological organization, but stop making sense at the next higher levels. The compromise allows us to interpret biological configurations and networks of interactions by their ‘local’ purposes, and consider them correspondingly as tools, scaffolds, developmental precursors, food sources, signals, etc., while we do not try to identify a ‘global’ purpose for their higher levels in the hierarchy.

Jigsaw Puzzles as the Most Trivial Examples of Fitted Mosaics

The simplest examples of fitting and fitted objects are mosaics of rigid, flat tiles with variable shapes. Before any misunderstandings arise, this book is not comparing life forms with jigsaw puzzles. *Fitting a mosaic is a much more challenging task than restoring a set of fragments to its original order!*

In the first place, unlike the pieces of a jigsaw puzzle, the tiles of a fitted mosaic are not fragments, but autonomous or at least semi-autonomous individuals. Most of all, they do not carry any attached clues of ‘the final picture’ on their faces that may help decide whether a piece was put in its right place.

Worse, *there are no single ‘right’ places for any of them.* Many different mosaics may contain each of the tiles in many different locations and functions, as the same set of components can yield very different functional and perfectly fitted mosaics. Only the conditions of tessellation must remain fulfilled:

1. Every tile must fit perfectly its neighbours.
2. All tiles combined must fill the frame exactly.

Differential Calculus, the Antithesis of Modularity?

The discontinuity between their precisely fitted parts distinguishes mosaics quite dramatically from the favourite conceptual tools of physics. Hamiltonians, entropy, electro-chemical potentials, wave functions, electromagnetic and gravitational fields etc. are infinitely smooth and even differentiable mathematical functions and fields. Even *particles* are formulated as quantities that are inseparably linked to differentiable fields and wave functions. Their very requirement of differentiability guarantees that most points of such infinitely smooth objects expand all the way to infinity.

Mosaics are not only dramatically different objects, but differentiable functions and fields are not important for biology. At best they play peripheral and auxiliary roles. For example, they may occur as time courses, temperature dependencies, concentration gradients, or current-voltage relationships. Although important for specific disciplines, they are not central objects of biology.

The central objects of biology are almost the opposite. They are heterogeneous, complex, discrete, individual objects such as evolutionary trees, skeletons, protein structures, nucleotide sequences, nucleosomes, chromosomes, nuclear pores, microtubules, cells, organs such as lungs, networks of blood vessels, of neurons, brains, individual organisms, ecologies, and so forth. Invariably, other, similarly discontinuous objects and environments surround them, *not* forming graded, continuous transitions between them.

These core objects of biology may interface and interact with others like them. The interactions may rely directly on contact or indirectly on surrounding, often circulating media, or a chain of other individuals. Each may have their own specific evolution, development, replication, and molecular machinery. Yet, no matter how complex their compositions, shapes, and functions, they are always limited in size and reach, and can be recognized as distinct objects that are exquisitely well fitted together.

It is no surprise that the above line of reasoning justifies us again to treat the objects of biology as living mosaics.

Chemical Compounds, the Particularly Important Implementations of Mosaics

In contrast to physics and its world of mathematical functions, chemistry had always played a much closer role in biology. Already the alchemists of many centuries ago entertained strange ideas about matter linked to other strange ideas about life. Eventually, biochemistry and molecular biology dominated modern biology, both of which are, of course, sub-specialties of chemistry.

Seen from the vantage point of this book, the close relationships between chemistry and biology are not too surprising. After all, chemical compounds are a subset of mosaics, namely all the mosaics that are composed of atoms as their fitted tiles.

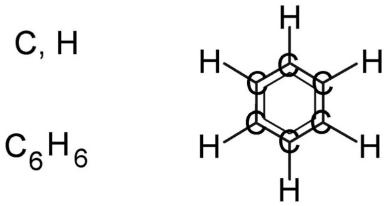

Fig. 1-01. The method used by chemistry to describe a chemical compound (= spatial mosaic of atoms) such as benzene as mosaics. The example defines as tiles the common elements C and H, describes their content by a summary formula C_6H_6 of the numbers of linked atoms, and depicts their spatial fitting by a stick-graph that images the presence or absence of their interactions. As to its classification, benzene is assigned to the class of aromatic hydrocarbons.

As far back as the eighteenth centuries, chemistry developed a language to describe and classify chemical compounds as composite objects, i.e. as mosaics.

1. Chemistry assigns each compound (mosaic) to a class of compounds such as salts, acids, metals, polymers, hydrocarbons, etc.
2. It describes each such mosaic by a summary formula that lists the atoms and counts their numbers.
3. It describes the fitting of the tiles using a stick-graph that depicts which atom forms bonds with which other by what valence (figure 1-01).

Chemistry expresses the fitting of the tiles through the concept of chemical valence: The stick-graphs in the figure depict the valence requirements for each atom in well-known ways by the number of edges (including ‘partial’ edges), which emanate from each node (figure 1-01).

As much as it would be tempting to take advantage of the century-old legacy of chemical mosaics, the chemical approach is too specialized to apply to all mosaics: Chemical valence is the consequence of the laws of quantum mechanics, whereas the fitting mechanisms of mosaics in general share no such common natural laws. Their fitting employs mechanisms as diverse as physical laws, geometry, formal logic, celestial periodicities, accidents of evolution, and numerous others.

The Principle of Modularity as Justification for Biological Research

Whether biologist are aware of it or not, they frequently apply the idea that organisms consist of discrete, semi-autonomous units whenever they take the organisms apart in the name of research. In these situations, researchers assume that - at least in principle - the parts of living things work in their natural context essentially the same way, as they do in isolation after an experimenter has removed and purified them. What other justification is there, but to assume that living systems consist of discrete, semi-autonomous units?

Researchers are often rather reluctant to mention the assumption explicitly, because it is controversial and quite vulnerable. Nevertheless, its best justification is the principle of modularity. Indeed, if the investigated objects are modules of a mosaic and thus be at least semi-autonomous, many of their functions should work in isolation the same way as in their natural context. Isolating them or at least observing them in isolation may not alter fundamentally the results.

Nevertheless, it is a questionable assumption. In the first place, the experimenter cannot know *a priori* which of the functions of a living module are truly autonomous and will work unaltered in isolation, and which are not.

In addition, there is a logical danger. By splitting the living mosaics conceptually into semi-autonomous parts, their modularity becomes a self-fulfilling prophecy. What, if there are living mosaics and expressions that defy the logical or practical isolation of modules?

In principle, there are. The most obvious exceptions are some of the fractal mosaics, which we will discuss in chapter 8. These are all the mosaics that are made *entirely* of tiles that are mosaic themselves, which in turn only contain tiles that are also mosaics, and so forth. In the limit, such mosaics clearly contain no more distinct or semi-autonomous tiles. Instead, their ‘inside’ is completely continuous. Experience tells us that no other mosaics violate the modularity principle. Besides, they only violate it at their infinite limit, whereas all real living mosaics only have a finite number of components.

Holistic approaches to biology such as traditional Chinese medicine or the Indian Ayurvedic medicine present a number of different kinds of exception to modularity. There are also accepted examples for holistic approaches in Western medicine, such as hypnosis and the so-called ‘placebo effect’.

In a sense, even these approaches define their own kind of modules, such as a life force chi, a meridian, and selected points, as in the example of acupuncture. However, as long as there are no reproducible assays and experiments to isolate these postulated modules, we consider these systems as having no modules, at least for the time being.

The most radical exceptions to the principle of modularity in biology are presumably emotions like love, faith, fear, wrath, or grief, but also expressions of creativity in art, music, poetry, or mathematics, as they have no isolatable parts. On the contrary, they emerge as indivisible, new whole entities from their underlying sources and carriers.

To be sure, their sources are brain domains, and thus mosaics of neurons. Yet, one may argue that they have no discrete parts, but express variable intensities and are subject to undercurrents, similar to bodies of water or air. Nevertheless, psychologists and poets alike have offered analyses of these very elusive feelings, although their nature as perceptions makes the objective and reproducible identification of parts very difficult.

Obviously, it does not help trying to exclude these exceptions as unbiological, because, naturally, we only find these phenomena with certainty in the living mosaics of biology, and only there. Yet, for millennia, they have resisted successfully every attempt to break them into distinct, tangible elements that would allow us to study them in isolation.

For the time being, these most challenging properties of living mosaics must remain unexplained, at least in experimentally verifiable terms. The present treatise will settle for much more practical questions, such as questions about some of the logical consequences, if a system *is verifiably,* a mosaic composed of modules.

Natural Selection as a Driving Force behind the Principle of Modularity

Naturally, the definition of modules also raises the question of their origin. At first, it may seem that we can settle this question rather quickly. The origin of discrete, autonomous objects needs no explanation, unless life began in a featureless continuum. There is no evidence for such beginnings. On the contrary, a billion years ago, as today, all matter on Earth consisted of discrete objects that had existed and acted in isolation for some time before groups of them aggregated to initiate life. Hence, like all other initial matter, the seeds of life had also to be discrete, and associated with each other from the start.

However, this argument does not explain why the manifestations of life remained modular for millions of years, and even evolved their modules to ever-higher levels of complexity and efficiency. Therefore, we should ask whether there is a selective advantage of a living mosaic for having a modular architecture. If so, evolution would quite likely have improved and enhanced modularity in all its manifestations.

As was mentioned multiple times before, effective engineering always uses modules, because systems with a modular architecture are more robust, effective and reliable than non-modular ones. The latter are prone to continuous cross-talking and cross-reacting. They cannot confine the damage caused by perturbations, and therefore tend to freeze, disintegrate, or flip into detrimental actions upon suffering trauma.

In addition, the evolution of modular systems can proceed faster than non-modular ones, because the modular system can evolve its modules one at a time. In contrast, non-modular systems need to revamp their entire body at the risk of rendering it dysfunctional, even after a relatively insignificant change.

Therefore, generally speaking, systems with a modular architecture operate more predictable, less error-prone, and adapt faster to changing conditions. Hence, modularity is most certainly a major selective advantage.

There are several other definitions of modules. For example, one may define them as the morphological characters and homologues of organisms [25]. As these quantities are the markers and road signs of evolution, they offer much greater objectivity. Supported by the fossil record, and as natural evolutionary concepts, they suggest right from the start quite detailed scenarios of their evolution. On the other hand, they are less obvious choices to describe the inner architecture of these morphological characters and homologues, especially the molecular architecture of single cells, organelles, viruses, and prions, for which there are few morphological characters and no fossil records.

Yet other definitions of modules can be derived from biological networks [04]. Every living mosaic is in particular a network of interacting components. By counting the local density of nodes, one can derive a definition of modules that seems entirely objective. On the other hand, its linkage to known evolutionary pathways appears more difficult to establish. Nevertheless, a linkage to evolution can be argued quite credibly, especially by a model study [25], which demonstrated the emergence of modularity in such networks depending on the ’cost’ of its connections.

Living Mosaics: A New Vantage Point and a Wealth of New Questions

Considering organisms and their components with the metaphor of living mosaics offers a number of new perspectives. Here are some of them in no particular order.

The ‘Islands’ of the Fitted Solutions in a Gigantic ‘Ocean’ of Failed Ones

Anybody who tries to assemble manually a mosaic will soon realize that the task is a surprisingly difficult and counter-intuitive. And it is not an entirely dispassionate one.

Actually, the fitting of mosaics can evoke quite strong emotions. Initially, one is easily frustrated. One may not always be aware of it, but ‘fitting’ requires the adjustment of huge numbers of linked, multi-dimensional variables. Hence, the number of ‘failures’, i.e. the number of non-fitting tile configurations is usually enormous. In other words, failure *is the rule*.

Conversely, the completion of a perfectly fitted mosaic solution, and even the mere encounter with one may evoke profound delight. The completely fitted solution projects a strong sense of inner logic. One may even feel that only this solution is a possible one.

Yet, in most case, this impression of uniqueness would be entirely wrong. There may be hundreds or even thousands of different ‘sibling’-solutions for the same fitting task, in spite of seemingly impossible odds for finding even a single one.

Still, regardless how many perfectly fitted solutions exist, the non-solutions always outnumber them. They are like tiny islands, distant from each other, and surrounded by an ‘ocean’ of non-solutions.

The ‘Seeds’ of Mosaics and a New Kind of Determinism

The surprising number of different sibling solutions of most mosaics poses an intriguing question. If the assembly is successful, what decides which sibling-solution it yields? The decisive factors cannot be the frame or the tiles, because they are the same for all sibling-solutions. Do the location and orientation of the first tile decide whether the assembly leads to a solution, and which one it is? Or is it the second tile? Do all tiles matter equally much for the solution?

The answer is surprising, too. Each fitted mosaic gives rise to several small groups of initial tiles that have a very special property: If assembly starts with any of them, the fitting mechanism leads unerringly to one and only one mosaic. Chapter 11 will describe these determinant groups as '*key-seeds*' of their mosaics in greater detail. It will turn out that there are many more key-seeds than there are sibling solutions.

If it starts with a key-seed, the assembly of a mosaic is entirely a matter of necessity, no matter how large and complex the mosaic may be. Therefore, it presents a special kind of determinism that is neither intuitive, nor is it a matter of some universal law. Instead, it reflects intriguing and highly individual implications of the fitting process.

The driving forces of fitting are *logical* rather than *physical.* For example, the fitting may apply trial-and-error methods, which offer no force-intensity or force-distance laws, or any other explicit formula. Instead, they use information gleaned from look-up tables and other ways of relating individual actions to individual consequences.

Nevertheless, during assembly, the tiles experience and create some peculiar kind of 'action at a distance' that applies to the inside of the mosaics. For example, the key-seeds contain tiles in locations all over the frame, far away from the place where the next tile is to be added. Yet, they influence the location and orientation of all others. Actually, this 'action at a distance' of tiles is not exactly an 'action'. In reality, the distant tiles merely restrict the possible locations and orientations of tiles elsewhere. In general, no single tile from the earlier stages of the assembly is able to *dictate* the placement of the successor tiles. After all, the very existence of multiple sibling-solutions proves that fitting can follow many alternate paths. Only all pre-placed tiles together are able to restrict the possible choices so much that they amount to enforcement.

By definition, the logical relationships between mosaics and their key-seeds leave no room for alternative paths, but lead from key-seed to mosaic in a progression of necessity. Thus, it represents a peculiar kind of mechanism that drives the assembly: It follows a *path of necessity without any physical mechanism that involves the interactions between the tiles.* At this stage, the statements may sound rather abstract, but chapter 11 will offer several simple examples.

The progressions by necessity involve the exact fitting requirements, the boundary conditions imposed by the frames, and the exact consequences of misplacing any one of the tiles. Obtaining this knowledge may be no problem in cases of human-designed mosaics. Nevertheless, it is the very essence of biological research.