

Projects in Biology I and Biology II

AMALLA, Bon Leif D.

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Part I

Exposition

Chapter 1

Complex systems theory on adaptation and evolution (II)

When studying complex traits (or traits, in general), it has become a reasonable assumption that there must be complex task or operation that requires such traits. Because otherwise, such complex traits, requiring energy to maintain, would be pointless to have. Evolutionary biologists deal with the problem of “teleology” in studying trait evolution (Veloso, 2019). Some questions about the design of organisms and their complex traits can be raised: is there such a thing as a supernatural designer? A similar question relating to teleology, but in a more applied aspect: is it possible to design nature the way humans, as social and intelligent beings, want?

The questions above can be answered in many different ways. Since they will be answered in Part III of the collection, an exposition of concepts leading to the responses are presented in Part I. Syntheses from observations in different biological and ecological systems supporting the introduction from Part I are presented in Part II. Aside from the teleological questions, the axiom that biological and ecological systems are complex adaptive systems (Dong & Fisher, 2019) implies occurrence, given conditions, of catastrophe. A small discussion on catastrophes will also be included in Part III.

In this chapter, connections between complex systems theory and certain biological systems are introduced. Specifically, some aspects of complexity in biological and ecological interactions are discussed. The conclusions from which are crucial to the development of background for later chapters.

A common trait of complex systems is non-linearity (Devaney, 2003). In simpler contexts, nonlinear interaction between different “agents” of a complex system is synonymous to feedback interaction. Such complexity can arise in different levels of organization: from chemical feedback mechanisms within an organism or cell (Chaves & Oyarzún, 2019), to multicellular interaction (Veloso, 2017), to community interactions in different trophic levels (Seibold, Cadotte, MacIvor, Thorn, & Müller, 2018).

1.1 Biological interactions

1.1.1 Biochemical pathways of metabolites

There is a substantial amount of literature describing the different metabolic pathways and their regulation. Among those is a study on the mathematical modeling of feedback and feedforward interactions controlled by genes (Chaves & Oyarzún, 2019).

Biochemical metabolic pathways are a series of chemical reactions catalyzed by enzymes wherein products are used for some operations inside or outside the system. An example of a metabolic pathway is the citric acid (Krebs) cycle. In the Krebs cycle, intermediates in the production of ATP are synthesized. Synthesis pathways in the production of 2-Ketoglutarate, one of the important intermediates of the Krebs cycle, from xylose are studied using a newly developed algorithm (Gupta, Le, Hu, Bhan, & Daoutidis, 2018). The study showed that there are different ways in producing the said intermediate. This would mean that if such different pathways were to interfere with the citric acid cycle, feedback inhibition may occur (Chaves & Oyarzún, 2019). Conversely, the citric acid cycle may interfere with the “different pathways”.

In the nonlinear dynamics model of Chaves and Oyarzún (2019), certain assumptions between interactions of intermediates of metabolite synthesis and enzymes used for metabolism were made. In the study, metabolites in the specific metabolic system can interfere with synthesis in different parts of the pathway. The following were taken into consideration:

- Metabolites regulating enzyme activity;
- Enzyme kinetics;
- Enzyme synthesis by the cell;
- Metabolites regulating enzyme synthesis;
- Concentration dilution as an effect of cell growth

Each of the related considerations were assumed to be parameters of the system, represented as arbitrary functions or numbers. The effects of the parameters on the sustainability of the system can be represented by graphical methods through simulations; however, figures were not present in the article being studied. It is also very difficult to reconstruct the simulation results with the lack of control and knowledge of parameter values. It may be sufficient to know that there exist intricate relationships between the interacting agents of the complex system, indicated by arbitrary parameters. As a consequence from complex systems theory, different settings for parameters can lead to very varied results (Devaney, 2003). The extent of those effects can only be carried out through thorough analysis of the metabolism networks.

1.1.2 Developmental biology and epigenetic landscape

From the complex system described above and the historical assumption that a gene produces one protein, and that synthesized proteins from the gene locus should be identical, why aren't identical twins completely identical? The question posed may not have been one of the questions asked during the development of the Modern Synthesis (Baedke, 2013; Goldberg, Allis, & Bernstein, 2007).

Identical twins have an identical genome (Krasnewich, n.d.), yet their phenotypes aren't exactly the same. It is necessary to conclude that a single genome can give rise to multiple phenotypes. There must be an underlying mechanism for the phenomenon. The notion of *epigenetics* was introduced some time before the Modern Synthesis (Baedke, 2013). This is the mechanism in which different gene networks influence different phenotype expressions in organisms.

In embryo development, portions of DNA are attached with methyl groups to prevent their expression. These markers are inherited from parent organisms through epigenetic inheritance (Goldberg et al., 2007). This is one of the reasons why some offspring features look similar to their parents'. It has also been shown that monozygotic twins share the *very similar* epigenetic markers (Van Baak et al., 2018). This is a very convincing explanation as to how identical twins appear very similar, yet not completely identical.

Going one step further by going back to the conclusion of the previous section, complexity of the system can be assumed by having different gene loci interacting with one another forming a Gene Regulatory Network (GRN) (Goldberg et al., 2007). Similarly, gene interactions can be parametrized, simulated, and studied empirically and computationally. The complex system can still give room to catastrophic outcomes such as one child appearing similar to grandparents from one parent and another appearing similar to grandparents from another parent. (The example is nonsensical, but it shows an extreme possibility given certain conditions).

1.2 Ecological interactions

1.2.1 Population ecology

As organisms grow and reproduce, the resources they require for further growth and respiration increases. Suppose the case of mussels (*Mytilus edulis*) a marine sessile organism (Seibold et al., 2018) (Figure 1.1). It would be quite illogical to clump together as a species since the resource demand of adult mussels is more than the needs of juvenile mussels.

It would be better to disperse offspring, as in the case of seed plants. Yet competition is only one of the mechanisms involved in population regulation. Scale-dependent feedback regulation arises from two mechanisms: distributing resources and lessening stress. A schematic of the feedback regulation is provided in Figure 1.2 (Dong & Fisher, 2019).



Figure 1.1: *M. edulis* and byssal threads

According to the article cited above, mussels maintain a close distance to one another and expel byssal threads onto hard surfaces not exclusive of shells of other mussels. This makes the entire complex difficult to prey upon or be swept by currents. The article notes that there is are optimal patterns in which these kinds of complex systems organize themselves in order to adapt to the environment. This phenomenon is called self-organization (Dong & Fisher, 2019; Veloso, 2017).

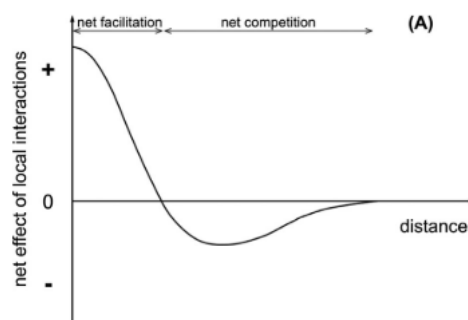


Figure 1.2: Scale-dependent feedback

From the figure, there appears to be a maximum optimal distance wherein the negative effects of competition are minimized. This model does not only work for mussel populations, but has been hypothesized for general populations (Dong & Fisher, 2019).

1.2.2 Community ecology

One of the most common nonlinear system models in community ecology is the Lotka-Volterra model, also known as the predator-prey model (Seibold et al., 2018). Without mathematical modeling, the scenario can be set up as follows:

- Consider two trophic levels: prey and predator
- Suppose there is relatively fewer predators to prey

- Suppose once the prey supply decreases, its consumption also decreases leading to eventual population growth through reproduction
- While prey supply decreases, predator population growth also decreases
- Finally, as prey population increases predator population follows suit

It is evident from the third item that the *sustainability* of the complex system relies on the reproductive rate of prey species and consumption rate of predator species. Suppose the prey species produces at a much slower rate compared to the consumption rate of the predator species. A simulation of the above interaction will intuitively lead to the extinction of the prey species, thus requiring the predator species to occupy a new niche. In other words, changes in environmental or species parameters have led to system death.

Extending from a “population” interaction within colonies, another type of community interaction was discussed by Dong and Fisher (2019), wherein bacteria of different species were placed in one environment. Patterns of self-organization were seen within colonies, which allowed for long-term equilibrium, while none were observed when the different bacteria were introduced. The reviewers compared the observation to the economic “tragedy of the commons”. This may be the case when competing agents do not know how to interact with one another (a broad complex systems theory parameter).

By increasing the scale of the interactions: by increasing the number of trophic levels, by increasing the number of interacting species in specified trophic levels, by increasing the number of interactions being observed, or by combinations of the aforementioned methodologies, more complex interactions can be studied (Seibold et al., 2018). The cited article appeals for more in-depth analysis from community ecology studies through multitrophic approaches. One of the reasons said is worth quoting at length:

We live in an era where the accelerating loss of biodiversity due to overexploitation and loss of natural habitats, invasions, and climate change, as well as the effects of that loss on ecosystem processes and services, requires greater commitment to applied ecology to better provide guidance for dealing with these environmental issues.

1.3 Self-organization in ecological systems

The review by Dong and Fisher (2019) encompassed different forms of self-organization in multiple levels of ecological organization. Some of them are summarized as follows:

At the organismal level Self-organization at the organismal level is controlled by gene expression and the complex mechanisms behind epigenetics (*ibid.*). Such interactions form patterns that appear as phenotypes may also be called *adaptations* for the specific environment.

At the population level Self-organization of *Mytilus edulis*, as discussed one of the previous sections, is driven by scale dependent feedback regulation (*ibid.*). This is done so that the population can be *sustained*.

At the community level Complex interactions between different organisms and the abiotic environment occur including, but not limited to intra- and intertrophic interactions (Seibold et al., 2018), and competition (Dong & Fisher, 2019). The patterns form from sustainable *niches* occupied by the interacting agents through coevolution.

1.4 Bifurcations and catastrophes

Bifurcations are a special term for significant changes in the way agents may asymptotically approach an optimal “self-organized” system. These happen from significant changes in parameters dependent that control the properties of the agents. In the figure below, a type of bifurcation is shown.

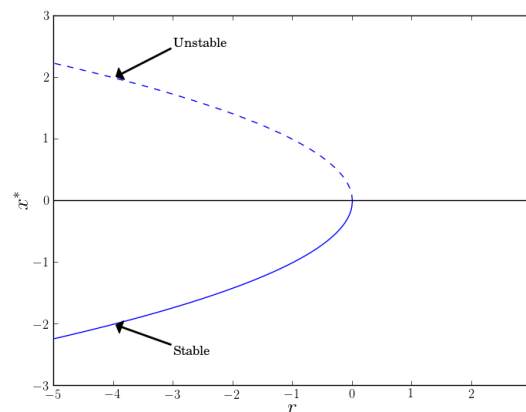


Figure 1.3: A saddle node bifurcation

The saddle-node bifurcation is one of the simplest, yet most important bifurcation models. In the bifurcation model, if the control parameter exceeds a threshold the loss of self-organization capabilities occurs and leads to system death (catastrophe) (Devaney, 2003).

In the case of intracellular systems, one such parameter may be related to the size of the cell and its use of resources. This is an indirect conclusion from the above introduced study on metabolite-enzyme regulation study (Chaves & Oyarzún, 2019). Suppose there were mutations that allow for fast cell growth, requiring fast utilization of metabolites; however, other parameters such as the interaction of enzymes and substrates remain the same (*ceteris paribus*). Then there will come a point that the cell cannot sustain itself, and thus will result to its own destruction. The study of how such parameters affect the system dynamics is in the realm of

bifurcation theory, and will not be explored here (partly due to the lack of deeper knowledge of the researcher).

1.5 Influences of self-organization on adaptation and evolution

From the exposition of biological and ecological interactions between different agents in different levels of ecological organization. Certain, some instantaneous, internal and environmental parameters influence the outcome of these agent interactions. Systems can either organize by themselves forming patterns of self-organization or ultimately lead to catastrophes.

Synthesis What happens if gene mutation rates increased? It depends! There are biological and ecological factors contributing to the complexity of the outcome. What are the organisms? What are they subjected to? How do they interact with their environment before the mutations? Moreover... At what rate does the “increased rate” occur? How will the gene regulatory networks be affected? What will happen to the metabolic pathways of the organism given the unknown changes by the mutations? Complexity in biological systems is ubiquitous, and it *is* difficult to characterize with a lack of parameters of interest.

Chapter 2

Mendelian genetics (I)

2.1 Methodology and Results

Mendel's experiments were done using pea plants. Contradictory to the notion that characteristics of an offspring are due to the blending of the parents' traits, Mendel showed that the traits of the offspring do not appear in intermediate or blended traits.

In his experiment with pea plants, he studied the patterns of inheritance in seven different features of the plant: flower color, flower position, stem length, seed shape, seed color, pod shape and pod color. First, he established pea lines and grew them until they were purebred. That is, the produced offspring are always identical to the parent. He then performed cross-pollination experiments with the different variants of the pea and observed how traits were inherited. He counted the number of offspring pea plants possessing each trait and found similar patterns for each of the seven features.

First, upon crossing peas with yellow seeds to those with green seeds, he observed that the first generation (F1) seeds were all yellow. This shows that in the first generation after the cross, one form of a feature (dominant trait), such as yellow seed color, is visible and the other form (recessive trait), such as green seed color, is hidden.

The F1 generation plants were then self-pollinated. He observed that for the second generation, F2, the recessive trait reappeared in the minority of the offsprings. That is, 3 out of 4 were yellow and 1 out of 4 was green. He then thought that since the recessive trait (green) appeared in F2, the trait must have been present, although not expressed, in F1.

Mendel also analyzed purebred pea plants that differed in pairs of features, such as seed color (yellow and green) and seed shape (round and wrinkled). He crossed yellow round seeds with green wrinkled seeds and observed that F1 seeds were all yellow and round - which shows that yellow and round are the dominant traits. Then, upon self-pollination of the F1, he observed that the F2 generation plants were in the ratio 9 : 3 : 3 : 1 ($\frac{9}{16}$ yellow round, $\frac{3}{16}$ yellow wrinkled, $\frac{3}{16}$ green round, and $\frac{1}{16}$ green wrinkled). This is equivalent to 3 yellow to 1 green and 3 round to 1 wrinkled, which supports the idea that features are inherited independently.

2.2 Synthesis

With these patterns in mind, Mendel proposed that genes can be made controlled by pairs of heritable units (alleles) that came in different versions. That is, genes are made by pairs of heredity units—AA, Aa, and aa where ‘A’ represents the dominant allele and ‘a’ represents the recessive allele. He also theorized that an offspring inherits one unit of one trait from each parent. This has been called the *law of segregation*. Following from the observation that there are independent features, a *law of independent assortment* can be established.

Mendel’s results can be summarized using a tool derived from the two laws described above, a Punnett square (Mason, Losos, & Singer, 2017). A Punnett square for one feature is in Figure 2.1, while a Punnett square for two independent features is in Figure 2.2.

	T	t
T	TT	Tt
t	Tt	tt

Figure 2.1: Monohybrid cross Punnett square

	cP	cp	cP	cp
cP	CcPP	CcPp	CcPP	CcPp
cP	CcPP	CcPp	CcPP	CcPp
cP	CcPP	CcPp	CcPP	CcPp
cP	CcPP	CcPp	CcPP	CcPp

Figure 2.2: Dihybrid cross Punnett square

Chapter 3

Post-Darwin evidences of natural selection and evolution (I)

The role of the notion of epigenetics in the Modern Synthesis (Baedke, 2013; Goldberg et al., 2007) was introduced in the first chapter on complexity. But the study of epigenetics is only a small part relative to the more prominent results from Mendelian genetics, discussed in the previous chapter, and Darwin's theory of evolution through natural selection (Ridley, 2004). Darwin's work *On the Origin of Species* was very important in the unification of concepts in biology (Mason et al., 2017).

3.1 Evidences of “natural selection” and evolution

Since it has been exposed that complexity is ubiquitous in biology, especially in dealing with different scales of organization, evidences towards natural selection should be present in the scales of interest. In this section, complex molecular (HIV evolution) and community (melanism and artificial selection) interactions and their effects on the complex systems are discussed.

3.1.1 HIV evolution and natural selection

Viruses, a complex of nucleic acids encapsulated in protein capsules, are responsible for some important “visible” evidences for natural selection and evolution. One prominent case is the evolution of HIV, the virus responsible for the development of AIDS. HIV reproduces in the human body by injecting reverse-transcribed DNA from its RNA genetic information into the human genome. Since reverse transcription is not usually done by the body, it is safe to assume that the mechanism for reverse transcriptase is provided by HIV. This suggests that one of the ways to stop HIV, “possibly” adverse effects on the human host is by causing the reverse transcription to fail (Ridley, 2004). Indeed, attempts focusing on this objective have been done, one of which is the creation of nucleoside inhibitors. These inhibitors were synthesized such that reverse transcriptase is relatively indifferent to the respective complementary nucleotide in the

viral RNA and the synthesized drug. With these inhibitors, reverse transcription of viral RNA can be stopped.

However, a further study on the implications of the method was shown by Schuurman *et al.* (1995) as cited by Ridley (2004). Apparently, in the first three days of exposure, HIV population dropped, but by then drug-resistant strains of the virus start to reproduce. The drug resistant strain has its reverse transcriptase modified such that it does not bind to the nucleoside inhibitors introduced. This way the virus can reproduce. The non-resistant strains eventually die off resulting in the increase in frequency of the drug-resistant strains. This is *natural selection* at work! The apparent evolution of HIV through natural selection shows that evolution can occur in such scales.

3.1.2 Industrial melanism

The peppered moth (*Biston betularia*) has been observed to respond to pollution, an environmental change. Adults of the species have a wide range of phenotypes: ranging from light gray with dark spots (peppered form) and the jet black (melanic) variant. In polluted areas where tree barks are covered by soot, more of the jet black variants were observed compared to the peppered form. A hypothesis was formed by moth collector Tutt around 1896: peppered forms are more visible in sooty trees making them susceptible to predation; meanwhile, the melanic variant is less visible.

This hypothesis on selection for the melanic variant was tested by ecologist Kettlewell in the 1950s. Two populations of peppered moth (with variants of equal population size) were released into polluted and “pristine” environments. From the polluted area, Kettlewell recaptured 19% of the peppered form and 40% of the melanic form. While from the pristine area, Kettlewell recaptured 12.5% of the peppered form and 6% of the melanic form. It appears that there is selection for the melanic variant in polluted areas, implying that there is no reason to reject Tutt’s hypothesis. A similar phenomenon was also observed when the American Clean Air Act was enacted. Yet there was no explanation in regarding the difference in the number of moths recaptured in both books of Ridley (2004) and Mason *et al.* (2017).

Note that the correlation that more peppered forms than melanic forms were recaptured in less polluted environments does not mean the mechanism for the selection, as proposed is correct. Researches according to Mason *et al.* (2017) note that the selection for the melanic form in polluted environment “does not appear to correlate with changes in the abundance of light colored tree lichens.” It is difficult to pinpoint *the mechanism* for selection. As was exposed in the first chapter, there are different interactions in open ecological communities (Seibold *et al.*, 2018), and such can be considered as parameters in complex systems analysis studies. Because of this, different propositions on the mechanism for selection are not necessarily incorrect, but rather may be part of a bigger picture.

3.1.3 Artificial selection

It is known that natural selection occurs when *fit* organisms *reproduce* to leave more offspring in a population with a *varied phenotype* with respect to a certain quality (the criterion for fitness). Considering the historical occupation of humans and the development since the Agricultural Revolution and the ever-growing human population and resource demand, there have been a lot of changes involving artificial selection. Two of which are on the increasing the milk yield of cows (Ridley, 2004) and the taming of the silver fox (Mason et al., 2017).

On increasing the milk yield of cows In a population of cows with differing milk yield, those with higher yield are allowed to reproduce. This method produces a generation of cows with higher milk yield. Continuing this process, it is possible to get a generation of cows with significantly much higher yield than the first generation of cows.

On the taming of the silver fox Similar to how more docile wolves were domesticated as dogs, in order to domesticate the silver fox, Russian scientists selected tamer foxes to mate with each other, assuming that docility is a hereditary trait. The experiment worked; however, there were unexpected results: the domesticated fox behaved similarly to the domesticated dog. The appearance of the domesticated fox also changed by developing curled tails, floppy ears, and shorter legs and tails similar to domestic dogs. It was then hypothesized that the genes responsible for the docile behavior is linked to the expression of the traits described.

3.1.4 Homologous structures

In addition to the evidences of natural selection as a mechanism for evolution, the comparison of homologous structures can also expose an evolutionary trend among species in different classes. Similar to the appendix in humans, there are also structures in other animals that seem to serve little to no function (contrary to teleological arguments) called *vestigial organs*. Aside from these vestigial organs, the universality of a genetic code also shows evolutionary progress (Ridley, 2004).

Homology from skeletal structures The following structures similar to the human arm were observed from different mammals (Mason et al., 2017) (Figure 3.1). A vestigial set of bones in whales homologous to pelvis in four-limbed mammals are found. It can be observed that many of the bone structures are shared across different mammals. This suggests that these organisms share a common ancestor from which the trait was derived. Suppose otherwise, complex systems theory, given conditions, the structures would be completely different (Ridley, 2004). This is further exemplified by analogous structures (wings) of birds, bats, and winged insects where all wing structures have evolved independently (Figure 3.2).

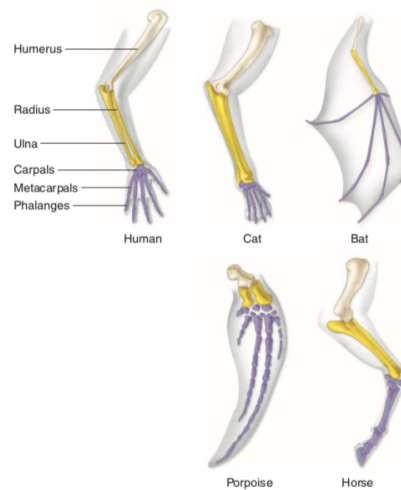


Figure 3.1: Homologous structure in mammal forearms

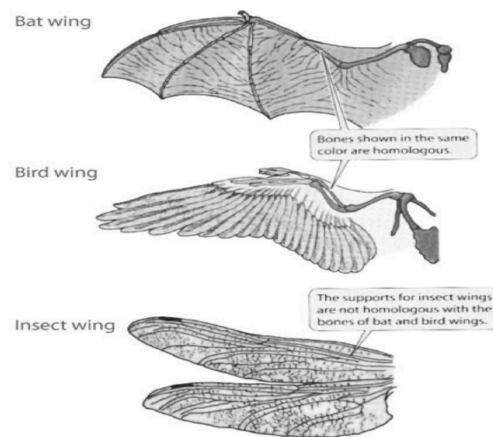


Figure 3.2: Analogous wing structures in bats, birds, and insects from Google Images

Homology from genetic information Regarding the universality of the genetic code, a simple thought experiment was given by Ridley (2004). It is known that tRNAs are responsible for the delivery of specific amino acids to the ribosome for protein synthesis. There are mechanisms in which amino acids bind to the right tRNA. Suppose there were more than one origins of genetic codes and all were equally competent, since all follow the same chemical mechanism. The observation that there is only one observed genetic code suggests otherwise. The only reasonable conclusion is that there must be a single competent origin of the genetic code.

3.2 Complexity behind selection

At this point, it can be summarized that natural selection is a solid mechanism to explain evolution. Following the above cases on HIV and melanism, the complexity behind interactions has been placed under the term “natural selection”. As noted above, natural selection accounts for the complex mechanisms behind natural self-organization in favor of a species variant. Natural

selection is a form of self-organization in the sense that the final allele distribution and niche selection are stable in the long-term.

Carefully following the theory of evolution, it is sufficient to conclude that life has evolved from a single population, and complex interactions with the environment provided the mechanisms for evolution, such as genetic drift and natural selection.

Chapter 4

Theories on the origin of life (II)

Life, has already been introduced, is immensely complex—emergent properties arise in every level of organization. From studies, biologists have developed a certain set of properties that help characterize life.¹ These include:

- complex and highly ordered cellular organization
- able to react and adapt to external stimuli
- able to reproduce and transmit genetic information to offspring

Numerous hypothesis about the origin of life have been proposed including the bubble hypothesis and panspermia. The chapter will tackle the chemical and physical evolution towards the development of the protocell.

4.1 Chemical evolution

Since many biological processes depend on proteins for chemical reactions, it is reasonable to discuss about how the complexity in proteins came to be. This section focuses on the important chemical aspects that were found by certain researchers to be essential for the development of life.

Biochemical pathways are complex. The complexity comes from having multiple feedback mechanisms and many intermediate metabolites coordinated by enzymes, biological catalysts. Sometimes different biochemical pathways can produce and use the same metabolites such as G3P in photosynthetic and respiratory pathways. Amino acids as building blocks of proteins were known to have been generated from a “primordial soup” in the Miller-Urey experiment (Maruyama et al., 2019). The generation of long polypeptides necessary for metabolism in this environment was thought of to be the origin of life. However, research on the shorter peptide

¹Though as I have noted in a midterm exam question that there are some problems regarding reproduction of infertile hybrid species.

amyloids as the possible origin of life has also showed that long polymers are not necessary for the initial development of life (Greenwald, Kwiatkowski, & Riek, 2018).

4.1.1 Amyloids as primitive protein structures

Peptide amyloids are *well-ordered* peptide aggregates with a fiber-like morphology due to its structure. In nature amyloids organize β strands similar in structure to the β sheet secondary structure in proteins. They organize into parallel (or anti-parallel) sheets that do not allow water to penetrate the void between the sheets (Figure 4.1.1 from Greenwald et al. (2018)). Amyloids are considered to have numerous biological functions and consequences including the development of Alzheimer's disease.

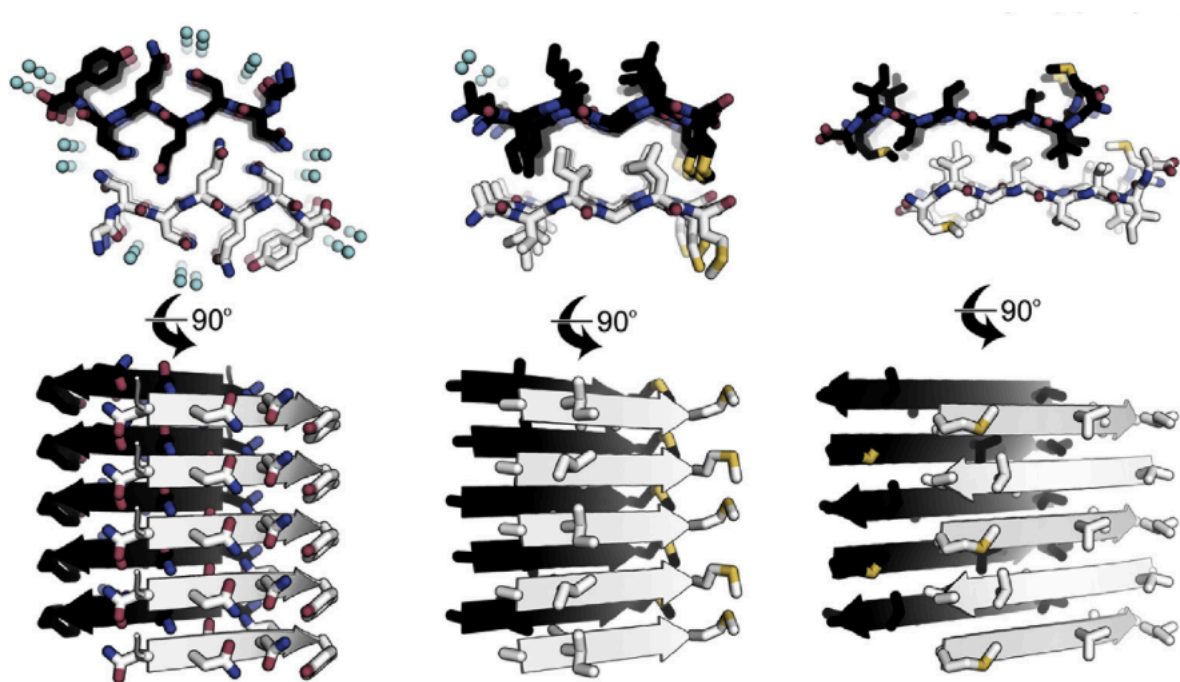


Figure 4.1: Structure of amyloids showing possible configurations.

The following are important properties of amyloids that have been shown through experimentation (Greenwald et al., 2018): 1) they can be formed from simple sequences of short peptides; 2) they are more stable than isolated peptides; 3) they can catalyze reactions; 4) they can act as templates of their own replication; 5) they can interact with RNA, DNA, and polysaccharides.

The first and second properties possibly indicate that due to the simple and easy formation, there could be more amyloid peptides than sophisticated protein chains. The catalysis of reactions is important in establishing simple metabolic pathways by interacting with DNA, RNA, and polysaccharides (sugars). Finally, the ability to act as templates of their own replication may have also given cells the ability to reproduce. These properties of amyloids can be related

to the functional definition of life, in that it is able to carry out metabolic reactions and that it can reproduce amyloids (and as a possible consequence, genetic material).

4.1.2 Proposed requirements for the origin of life

Maruyama et al. (2019) propose the following requirements for the origin of life:

- a reliable energy source;
- a supply of nutrients and elements found in living systems;
- high concentration of reduced gases;
- dry-wet cycles;
- non-toxic aqueous environment;
- “cyclic conditions”

The proponents stated that some studies refute the possibility of the reduced atmosphere because they did not agree with the numerical calculations for the early atmosphere of the Earth. However, they did not disagree with the fact that organic molecules have come from the reduced gases. If the reduced gases were not found in the atmosphere, a possibility is that the gases are dissolved. Furthermore, they have asserted that the only reasonable place for the origin of life is from the vicinity of natural nuclear reactors. One of such has been found in Africa. The theory is similar to the bubble hypothesis in a way that organic molecules have their origins in the sea.

The possibility of panspermia based on the proposed requirements cannot be falsified and hence may be dismissed until further factors are known (Maruyama et al., 2019). The study is important since they have proposed necessary requirements for the possible origin of life. This creates a scaffolding for future arguments on the topic.

4.2 Cell origin

The origin of the living cell is a complex phenomenon. There are numerous theories in its development, such as the development of the membrane first before the necessary cellular faculties (Matveev, 2019). In this section, the development of the primitive cell environment (the protocell) without the cellular phospholipid bilayer is discussed. Biophysical arguments will primarily come from the hypothesis of Matveev (2019) on the development of the protocell. Along with it, the general properties of life (Mason et al., 2017, p.15) will be used to strengthen the hypothesis.

Matveev (2019) defines the protocell the precursor of the cell. Experiments have shown that the interior of the biological cell (the cytoplasm) has a different liquid “phase” relative

to bulk water ². A difference in phase was explained to be the difference in the dissolving power of water in and out of the cell. This observation was caused by the adsorption of water into hydrophilic groups of proteins in strong hydrogen bonds, increasing the energy required to dissolve substances. Though this phenomenon is not observed in all proteins with hydrophilic groups, Matveev (2019) proposed that to ensure water adhesion, the substrate protein should have pockets with fixed charges where water can accumulate. It was however noted that the energy difference is only slight compared to the bonding in bulk water, it was sufficient to reduce solubility!

The model of the protocell is capable of producing concentration gradients by pushing aqueous particles into and from different phases. This can be thought of as primitive homeostatic regulation and adaption. It can also be thought of as cell growth through material exchange with the outside environment. The model also can split into two in response to chemical cues in the environment which possibly a primitive form of reproduction.

Finally, from the development of the protocell with the important properties of life, the phase can be enclosed in the fluid mosaic phospholipid bilayer membrane through possible self-organization with present phospholipids in the aqueous environment forming *the cell*.

²regular liquid water

Part II

Observations

Chapter 5

Endosymbiosis of mitochondria and chloroplasts (I)

Most of life on Earth was composed of prokaryotes. After some event eukaryotes were created. The endosymbiotic theory explains the origin of mitochondria and chloroplasts in eukaryotes as well as the possible origin of eukaryotes (Bodył & Mackiewicz, 2013; Mason et al., 2017).

5.1 Origin of eukaryotes

Fossil evidence of cell bodies much bigger than prokaryotes have been dated to be around 1.5 BYA (Mason et al., 2017). A nucleus, the organelle, has been found in the fossil cells, which suggests that evolution of eukaryotes from prokaryotic bodies. It has also been noted that in prokaryotes have cell membrane *invaginations* that may have led to the formation of the endoplasmic reticulum and the nucleus.

There are two models on the origin of eukaryotes (Bodył & Mackiewicz, 2013):

- Eukaryotes have evolved from cell bodies with compartmentalization
- Eukaryotes have evolved from the process of endosymbiosis itself.

The first model says that a Gram-positive bacterium has lost its peptidoglycan cell wall. Next, invaginations of the cell membrane enveloped the bacterial DNA forming a nucleus and formed the endoplasmic reticula. The second model says that an peptidoglycan-less bacterium engulfed bodies around it which resulted in further compartmentalization within the cell forming a nucleus and endoplasmic reticula (Bodył & Mackiewicz, 2013). Without the cell wall, there are two factors relating to cell growth worth noting: cell growth is possibly only limited by resource distribution efficiency, and there is a less restricted transfer of matter with the environment.

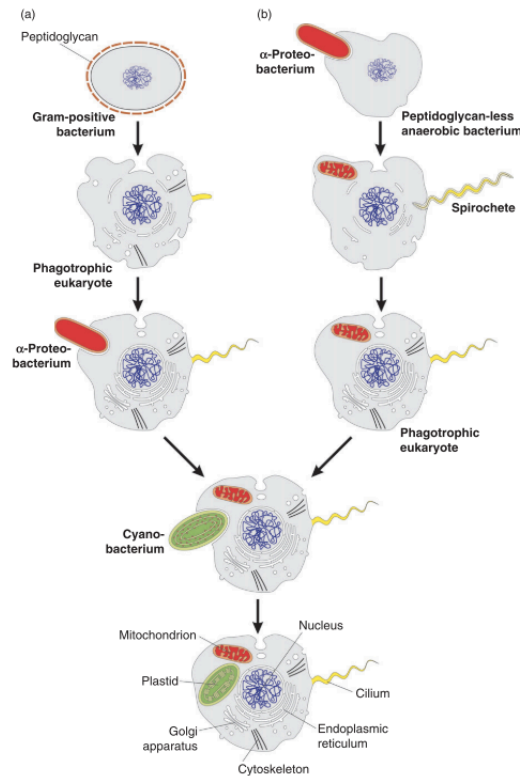


Figure 5.1: Two models of eukaryote origin

Following this development, Gram-negative energy-producing and/or photosynthetic bacteria may have entered the larger eukaryotic cell prototype described above. The above is summarized by Figure 5.1 (Bodył & Mackiewicz, 2013). In addition to the increase of mass of the eukaryotic cell, complex systems theory posits that there must be interaction between the engulfed cells and the host cell. This interaction is called endosymbiosis.

5.2 Endosymbiosis of mitochondria

The first step in the evolution of mitochondria was the manifestation of the complex interactions between the interior of the host cells and the engulfed bacteria. Originally, following a traditional model of phagocytosis, the engulfed bacteria might have been thought as food for the eukaryotic cell, but that did not happen to be the case. Somehow, the α -proteobacterium may have managed to disturb the digestion process of the host. The fact that the symbiont has remained in the host allowed for sustainable symbiosis between the two organisms (Bodył & Mackiewicz, 2013). This is a result of internal self-organization!

There are two processes in the symbiosis mentioned above: endosymbiotic gene transfer (EGT) from symbiont to host genome, and the transfer of transport proteins (translocons) on the membranes of the symbiont to the envelope surrounding it (Bodył & Mackiewicz, 2013). The number of protein-encoding genes in present mitochondria are significantly less than those found in the hypothesized predecessors. Some of these genes were either transferred to and

incorporated with the host genome or may have been lost completely. Again, the interacting organisms will have to adapt to such environment. Bodył and Mackiewicz (2013) say that a possible reason for the decrease in number of such genes is to prevent complications from mutations.

The transfer of translocons improved the efficiency of protein transport between the host cell and the symbiont. Moreover, such protein transport between mitochondria and the host has evolved from “molecular tinkering” (Bodył & Mackiewicz, 2013). At this point the mitochondria have already been integrated with the host cell and are officially organelles.

5.3 Endosymbiosis of chloroplasts

Meanwhile, chloroplasts have been thought to evolve from cyanobacteria. Similar processes, as with mitochondria, have occurred in the incorporation of the chloroplast. However, there was more than one case this might have occurred since photosynthetic organisms don't belong to one group (Mason et al., 2017).

The secondary symbiosis events created chloroplasts with more than two envelope membranes (Bodył & Mackiewicz, 2013). The explanation for these secondary symbiosis events is the endocytosis of green and red alga containing primary chloroplasts (*ibid.*). The evidence for this is well preserved by cryptophytes. However, this begs the question: What happened to the nuclei and organelles of the green and red alga? The question was not answered in both sources used above, but it can be hypothesized that a similar mechanism, as with the endosymbiosis of mitochondria with hosts: the organelles of the symbiont are incorporated to the host, EGT occurs between host and symbiont chloroplast and symbiont nucleus (Bodył & Mackiewicz, 2013), the mitochondria of the symbiont die off, possibly because the EGT between symbiont and host nucleus, making the organelle unlikely to survive without its needed proteins.

Evidences for endosymbiosis Mason et al. (2017) notes that mitochondria and chloroplasts have circular DNA and that they divide through binary fission similar to bacteria. This proves that the organelles have bacterial origins! A recent study has also shown that the method of binary fission of mitochondria (through protein ring pinching) is preserved in all eukaryotes, suggesting that there is only one event of mitochondrion endosymbiosis (Kato et al., 2019).

Chapter 6

Plant defense mechanisms (II)

Defense mechanisms are traits used by certain species to prevent others from attacking them. These can be thought of as adaptations for survival. Being adaptations, such are results of complexities in the growth and development of the individual and their interactions with the environment. Relating to relative fitness, plants with more successful defense mechanisms, consequently leaving more progeny, are considered to be more fit. Purposefully leading to the discussion on teleology as a point of view in studying evolution, defense mechanisms provide a wide array of expression and questions.

6.1 General overview

As given by Mason et al. (2017, p.792-802), there are different kinds of plant defense mechanisms for different kinds of situations. These include: physical defenses such as protection of the inner tissues with the epidermal cells, chemical defenses such as producing toxic substances to herbivores (including humans), pathogen recognition and plant cell death to prevent spread, and signaling pathways for plant immunity. As said, plant defense mechanisms can be very complex.

Physical defenses The epidermal layer of the plant serves as a layer of protection of the “internal organs” of the plant. Plants develop strong bark and waxy cuticles for structural integrity and maintenance of internal environments (by preventing water loss). Those structures also double as protection. The strong bark of the plant makes the material difficult to mechanically digest, requiring a lot of energy, and thus may not be an efficient source of nutrition for some organisms. The waxy cuticles, being thick layers of lipids, make it difficult for pathogens to infect the internal structures of the plant. Some plants also develop thorns from lateral meristems to prevent large herbivores from eating the plant.

Chemical defenses through secondary metabolites Many plants produce chemicals that can potentially kill herbivores such as poisonous substances. These include cyanogens which pro-

duce cyanide when metabolized by the herbivore. Plant secondary metabolites can also change the behavior of the herbivores. Such include caffeine, cocaine, and morphine. Humans have learned to use the metabolites in medicine by observing herbivores under effects of the drugs (Mason et al., 2017, p.794-796).

Pathogen recognition and defenses When plants get wounded, they become susceptible to pathogens such as bacteria invading the interior of the plant. Wounded leaves produce a peptide sequence called systemin which travels through the vascular system of the plant. This leads to the production of jasmonic acid activating the transcription of defense genes. It was also observed that plants have a kind of “immunity” by recognizing pathogens, but the mechanisms are quite different from animal immune systems (Mason et al., 2017, p.799-800).

6.2 Evolutionary effects on herbivory and the ecosystem

As has been said, being adaptations, plant defense mechanisms are crucial to protect the plant from ecological stresses such as herbivory. The interactions of herbivores with the plant with two types of defenses, as studied by ? (?), have been found to have quantitative effects on the fitness of the plant with respect to the herbivore environment. The theoretical simulations, variables and parameters will be reviewed in this section.

6.2.1 Summary of the study

With the general overview of general plant defense mechanisms in the previous section, such can be divided into two categories: *quantitative* and *qualitative* defenses. Quantitative defenses are those that require energy and dose to have effects on the herbivore or pathogen that threatens the plant. Qualitative defense on the other hand only determines herbivore deterrence or attraction by the presence or absence of the characteristics. As was assumed in the aforecited study, these defense mechanism *bundles* have no energy cost for the plant.

The objectives of the study were to determine the effects of plant defense strategies to herbivory, to simulate whether the evolution of the defense strategies has a role in the diversification of strategies, and to study the effects of defense evolution in ecological diversity and dynamics.

The variables used in the development of the simulations were the following:

1. Plant and herbivore respective biomasses
2. Plant quantitative and qualitative defenses
3. The “preference” and “generalism” of the herbivore to the plant defenses

On the other hand, the parameters used were:

1. Plant basal carrying capacity
2. Conversion efficiency
3. Plant growth rate
4. “Benefits” of plant quantitative defenses in terms of reduced plant consumption
5. “Costs” of quantitative defenses
6. Herbivore mortality rate
7. Basal herbivore consumption
8. Variance of competition kernel

The Lotka-Volterra system ¹ was used in modeling population dynamics. The choice of the model for the description of population dynamics is reasonable since, plants act as prey and herbivores act as predators. The biomass growth of both system actors (plant and herbivore) were based on the growth of each, their mortalities, competition, and assumed basal carrying capacity. Since the variables are dynamic (they change with respect to each other), the proposed representation seemed adequate for the system.

The evolution of the plant defense strategies were said to be from the pressure exerted by herbivory, which relates to the fitness of the plants (resident and mutant), and was modeled based on a “canonical equation of adaptive dynamics”. Fitness was defined as the rate at which the biomass grows given the defense traits of the plants present. This accounts for the “evolutionary” definition of fitness (Ridley, 2004). The canonical equation regards (small) mutation rates and the fitness benefit of slight changes in characteristics.

At the end of the simulations, it was found that the evolution of quantitative defense traits helps to maintain or increase diversity of defense traits, while the evolution of qualitative traits have detrimental effects on the coexistence of plants and herbivores.

Though the study was successful in achieving their objectives, there were parts of the model that were unclear ².

6.2.2 Critiques and comments on the study

The critiques on the study are mainly based from the assumptions of the researchers ³. The first concern is related to the use of a single number to represent the defense mechanisms of the plant. As noted above, plants have developed a wide variety of defense mechanisms against herbivory including physical and chemical defenses. Quite similarly to human behavior, herbivores in the

¹see Chapter 1 for an overview

²This is an opinion on the parts of the article that were unclear to me. Unfortunately, I have not found answers anywhere else, so I have decided to put them in the next section.

³This subsection is primarily based on my knowledge on the topic.

study were assumed to be able to ascertain preferences in the kinds of plants they ingest. The herbivore preferences were also represented as numbers. If the number representing the defense trait of a plant variant B is farther than that of another plant A, then the herbivore would prefer eating plant A.

Consider the following thought experiment ⁴. Given two defense traits that the herbivore is averse to, it will not want to be exposed more to them but rather receive less of them. Suppose there exists a set of combination of traits such that the herbivore does not prefer any one of those. In other words, the herbivore is indifferent to those combinations.

Then, even if the defense traits of the plants are different (thus represented by different numbers), the “preference” of the herbivore should not change (should still be represented by the same number). With this scenario, then there is a contradiction with the methodology of the researcher, *i.e.* it would be impossible to study the evolution of plant and herbivore traits.

The problem is observed to arise when the multidimensional problem of trait preference is simplified into a single non-operational representation. Of course there are a lot of dimension reduction studies in statistics⁵ and in other fields. Yet such studies admit to the loss of “explainability” at the cost of modeling capability.

The second concern, related to the first, is on the generality of the assumptions used in modeling. The study does not go anywhere specific and that may be the reason why the equations, parameters, and variables appeared too vague. It is understandable that it is for the sake of simplicity and getting the desired results as were described in the objectives. But it hides the logical structure that underlies the mechanism of defenses.

⁴I have devised this on my own based on consumer economics

⁵such as principal component analysis and partial least squares regression

Chapter 7

Animal defense mechanisms (I)

7.1 General defense mechanisms

Chemical defenses ¹ Chemical defenses are widespread within different groups. Comparing two major animal groups, chemical defenses are more extensive in invertebrates. These chemical defenses include toxins, or chemical with noxious odors, which affect the sensory systems some predators use to capture prey. Chemical defenses, similar to plant secondary metabolites, are synthesized in the bodies of animals. An example of a chemical defense is the secretion of ink of a cephalopod when it is threatened. ² This results to a reduction of visibility (if the predator relies on light), protecting the animal. There are accounts of usage of cephalopod ink for commercial sources. ³

Immune systems The human immune system is a very complex defense mechanism against unrecognized pathogens in the body. Multiple organs work together in order to keep the unwanted pathogens away from the body. Humans have two kinds of immunity: innate and adaptive immunity. Innate immunity given by the presence of the skin, mucous membranes, antimicrobial substances, and natural killer cells (Tortora & Derrickson, 2015, p.396-398). Adaptive immunity on the other hand is an adaptation from the production of antigens that the system recognizes and terminates foreign material (Tortora & Derrickson, 2015, p.399-407).

Predator evasion Predator-prey relationships are ubiquitous in nature. Naturally, for the prey to survive, it must have mechanisms to stay away from predators in order to be considered fit. An example of which is given above on ink secretion of some cephalopods.

¹ from <https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/chemical-defense>

² <https://www.theguardian.com/science/2017/aug/09/why-do-cephalopods-produce-ink-and-what-on-earth-is-it-anyway>

³ *ibid.* as above

7.2 Theoretical study on defense phenotype variance

In this section, a theoretical study by Wang, Cornell, and Speed (2019) on the evolution of defense phenotypes will be summarized and discussed. The study revolves around the evolution of two defense phenotypes that organisms can use sequentially *i.e.* one defense is executed after another given that a first one fails. As summarized above animals have a wide variety of defense mechanisms to choose from and they are not limited to only one defense trait (as was seen with plants). These traits may also have variety across the population, given the possibility of genetic drift (Ridley, 2004). The study aimed to propose a potentially predictive explanation for kinds of defense variation.

7.2.1 Model description

Sequential traits “must be crossed in turn”, therefore it is reasonable to assume that selection biasedly acts on the first defense trait executed by the organism. In order to study the time evolution of traits, the following variables were introduced.

1. defense phenotypes;
2. average phenotypes;
3. phenotype variances;
4. total population

Defense phenotypes and their variances were studied for each defense trait. The total population was also held constant since the *frequencies* of individuals with *defense traits* are studied. Ideal defense phenotypes were assumed, and that deviations around these ideals (tolerance) were accounted for. Though it was not explicitly stated, it is likely assumed that only one agent is being acted upon by the defense traits. The effectiveness of the phenotype is given as a constant value, which supports the assumption. Variant fitness was based on the *conditional effectiveness* of the defense phenotypes. This relates indirectly to the evolutionary definition of fitness as an ability to leave healthy offspring (Ridley, 2004).⁴ And finally, mutation strengths were also considered.

The distribution of the effectivity (of phenotypes), mutations (of phenotypes), and phenotypes are assumed to be Gaussian (*normally* distributed).

⁴It is reasonable to assume that if defense mechanisms did not work, then the variant cannot leave healthy progeny.

7.2.2 Results

Based on model simulations it was found that because of trait selection defense phenotypes moved towards the ideal phenotype. These was caused by the following mechanisms: 1) mutation; 2) order of defense execution; 3) trait effectivity.

If there were no mutations in the population then all of the defense phenotypes were the same. Stronger mutations also resulted to high phenotype variance. As the traits evolve, it was found that the variance of the first trait is lower compared to the second, and this evolution is independent of conditional fitness.⁵ It was also observed that as a the effectivity of a defense trait increases, its variation decreases, while the variation of the other trait increases, regardless of execution order.⁶

⁵Though this likely to be a circular argument since the equation was modeled such that this selection is biased towards the mutation of the first defense trait executed.

⁶With the previous sentence, an interplay of effectivity, mutation, and variance results from the complex system.

Part III

Beyond

Chapter 8

Teleological arguments and intelligent design (II)

As has been exposed in Part I, selection can be classified into two groups: natural and artificial selection. The two concepts will be reintroduced in this chapter to give a possibly sound discussion on the validity of natural selection. The infallability and logical flaws ¹in the main arguments of intelligent design are also discussed. Other arguments (and respective counter-arguments) against natural selection are also exposed.

8.1 Selection

8.1.1 Natural selection

Natural selection is a concept wherein a species variant that is considered to be more fit for the environment is selected for its characteristics. Charles Darwin has thought that natural selection is one of the major mechanisms for speciation and the evolution of traits. It has been shown that it can operate on the different scales of ecological organization, as in the case of HIV evolution (Ridley, 2004) and industrial melanism (Mason et al., 2017; Ridley, 2004).

Though the mechanisms for some natural selection occurrences are not easily determined as in the case for industrial melanism, correlations between variables have been established and has shown that natural selection persists (Ridley, 2004). An example of such correlation is between the frequency of each variant and the local environment. It has been shown that the melanic variant is considered to be more fit in the polluted environment, while the normal variant is more fit in the less polluted variant. Given this information, there can be a lot of factors that can cause the selection: first is predation (camouflage as a defense mechanism), a second is toxin immunity (effect of pleiotropy). ² Experiments can be made to determine the mechanism for selection.

¹This is based on personal opinion and knowledge.

²from https://en.wikipedia.org/wiki/Industrial_melanism

8.1.2 Artificial selection

Artificial selection was done by humans as a part of niche occupation in order to adapt to the environment. Examples of experiments are on increasing the milk yield of cows (Ridley, 2004) and on the taming of a fox (Mason et al., 2017). Increasing cow milk yield has purposes in economics and agriculture, while fox domestication is for aid. Both experiments have shown that trait selection increases the frequency of the selected trait (Ridley, 2004).

Artificial selection would not be possible if natural selection does not happen. The simplest argument would be that they follow the exact same mechanism but at different rates. Since artificial selection can be controlled, the most of the parameters in which it operates can be manipulated to give some expected results. Though there may be some exceptions as in the change in appearance of the domesticated fox described above (a [hypothesized] result of pleiotropy) (Mason et al., 2017).

8.1.3 Misunderstanding maths

One of the common misconceptions in inferential statistics is the belief that correlations may be causations.

Correlations and causations From above, one interesting case is of pleiotropy in peppered moths. Suppose there is a gene that has effects on wing color and pollutant resistance. Experiments were conducted such that wing color is related to the mechanism of selection. As a hypothesis on selection mechanism, pleiotropy can be justified or falsified through further studies on the peppered moth genome.

Even without concrete examples, the statement can still be proven false. Strong correlation between two variables can be observed if changes in one of the variables produces a determinate change in another. Correlation is a statistical description, while causation is a logical description. This means that correlations *always* have two-way relationships (and *vice-versa*), it does not matter which is a dependent or independent variable ³, while a causation may not work both ways (the converse of the statement is false). Take for example the following statements: “very high sugar intake causes diabetes” and “very high sugar intake has strong relationships with signs found in diabetes”. The difference in nuance is precisely the difference between causation and correlation.

³though hypotheses should properly state which makes the more logical sense

8.2 Intelligent design

8.2.1 Irreducible complexity

Irreducible complexity is an argument of intelligent design where adaptations are fine tuned to operate with each other in the sense that if one component were missing, the system would collapse. This can be observed in some developing blastula, wherein if one cell has been taken away, then animal development will stop. ⁴ The argument has been related to the *Watchmaker analogy*.

The Watchmaker Analogy In the same way that a functioning watch has been designed by its intelligent craftsman wherein all of its components are doing their respective functions, the Universe must also have been created by an intelligent being. ⁵

There are two keywords to note from the analogy: design and function. Structure and function cannot be entirely isolated from each other (Tortora & Derrickson, 2015), and hence it has then become reasonable to use the terms together. In studying the logic of design, each part present in the system (*e.g.* in organisms), must have uses if it is included. Obviously, the observation of structures *not having function* immediately breaks the watchmaker analogy. Vestigial organs/structures are such structures. Examples of which are pelvic bones in whales and hindlimbs in snakes (Ridley, 2004), which can be explained through natural selection and genetic drift.

Another implication of the argument of irreducible complexity is the observation of emergent properties. If the rules of mathematics are considered as universally true, then so would be the observation of emergent properties in some complex adaptive systems. An example of application of maths is the study of (Veloso, 2017) on self-regulation in multicellular systems, wherein individual cells adapt in the presence of other cells.

8.2.2 Specified complexity

Specified complexity is observed when information of apparently very low probability has been observed. ⁶ In the sense that the probabilities make the existence of such information improbable (but not impossible). An example of which is the genetic code in the genes that code for proteins. Suppose there is an intelligent deity that has made the genetic code so that it codes complex systems of proteins with emergent properties. Was the intelligent being also responsible for mistakes in mutations causing genetic drift for natural selection to occur?

⁴from one of the lectures in Bio II on animal diversity

⁵from https://en.wikipedia.org/wiki/Intelligent_design; some words were changed and omitted

⁶from https://en.wikipedia.org/wiki/Intelligent_design

Synthesis In both arguments, irreducible and specified complexity had logical weak spots, and that the second argument is not falsifiable. Natural selection is a statement of correlation on the nature of interaction between agents, while intelligent design is a statement of causation of design and function. As said, correlations and causations have different nuances and hence are not equivalent. In any case, conclusions from correlations are bound by certain mathematical laws, and that such laws agree with Darwin's natural selection. On the other hand, intelligent design sought a logical causation that had unjustifiable holes.

Chapter 9

Genetic engineering (I)

The genetic disease to be discussed in this chapter is the α -1-antitrypsin (AAT) deficiency. As the name implies, it is caused by a deficiency of properly functioning AAT. The causes of the deficiency and its treatment, augmentation therapy and gene therapy are discussed. Most of the information in this chapter is retrieved from the review of Stockley and Turner (2004) on the assessment and treatment of the disease.

9.1 α -1-antitrypsin and the deficiency

9.1.1 α -1-antitrypsin (AAT)

AAT is a glycoprotein primarily synthesized in liver cells, though it can also be produced by cells in the lining of the respiratory airways. Its expression is controlled by two alleles present on chromosome 14 (an autosome). The primary function of the protein is to protect the lungs from a protease (neutrophil elastase) secreted by white blood cells for immune response¹. It does so by binding to the protease. Hence if there is a deficiency in functioning AAT, the lungs will be attacked by NE causing respiratory disorders such as emphysema.

9.1.2 The deficiency AATD

AATD is a gene disorder that is caused by abnormalities in the genes responsible for the production of AAT. Such are caused by mutations. Stockley and Turner (2004) lists insertion and deletion mutations on the gene being contributors; however, the most common mutation is the missense from a point mutation causing a supposed glutamic acid to be replaced by a leucine amino acid. Upon examination of the amino acids, glutamic acid (Glu) has a carboxylic acid in its R group making it acidic, while leucine (Leu) has an aliphatic R group. This allele variant has been called the PiZ variant. The acidic nature of Glu makes it charged under normal blood plasma pH, while Leu being aliphatic contributes no charge. By changing the R group, a change

¹from https://www.kamada.com/therapeutic_areas/alpha-1-antitrypsin-deficiency/

in protein charge occurs, which in this case causes a reduction in the binding capability of the mutated protein to neutrophil elastase. Another effect of the substitution is the “destabilization” of the resulting protein causing it to undergo “polymerization” which causes it not be secreted outside the cell. Resulting to an overall deficiency of AAT.

The genetic nature of the disease was also studied in participating families. It has also been established that environmental conditions can affect the expressions of the PiZ variant. The term used to describe this observation was “gene-environment interaction” resulting from epigenetics. It was found that individuals homozygous for the allele did not need environmental stresses to contract respiratory disorders, while those heterozygous (containing normal variants) needed environmental stresses. Another interesting result was also found: even if individuals have the same genotype and were subjected to the same environment, results were different. This suggested that there are mechanisms other than genetics, the environment, and their interaction (epigenetics). This was not highlighted in the study.

9.2 Therapies

9.2.1 Augmentation therapy

Since the deficiency in the amount of the protein causes diseases, a reasonable treatment is replenishment to normal amounts of the protein. This is termed augmentation therapy. It was deemed to be a feasible form of treatment given weekly infusions of doses of the protein. Though it was found that testing for disease severity is impractical, the biochemical treatment (through doses) is sufficient such that it normalized the amount of AAT in lung plasma.

9.2.2 Gene and stem cell therapy

The classical form of gene therapy is the insertion of the normal gene into the affected cells, *i.e.* those with the PiZ variant. The studies reviewed used viral vectors to transfer genetic material. It was found that adeno-associated viral vectors with functional AAT gene are capable of achieving higher levels of AAT in the lung plasma. It was also noted that: it was less likely to induce inflammation compared to other viral vectors used.

There were proposed routes of administration (RoA) for the viruses: through the hepatic portal vein, through airways, and intramuscular injection. Injection of the virus vectors through the hepatic portal vein seemed reasonable since the liver is where bulk of AAT is synthesized. However, this was thought to be impractical if a patient needed many doses of injection to be treated. The portal vein is difficult to inject material to being found within the liver ². Use of nebulization for administering vectors through airways was recognized as a viable alternative.

²Found through consultation of 3D anatomic model in <https://www.healthline.com/human-body-maps/portal-vein#1>

The most successful route of administration among those reviewed was the intramuscular injection of vectors. The direct addition of vectors to hepatic cells has been shown to be effective *in vitro*, and *in vivo* methods have yet to be developed and assessed.

The capability of treated stem cells to deliver corrected genes to many tissues has been studied on mice. It was shown that it was effective, and clinical trials on human patients are to be expected. One possible method is the injection of vectors into the bone marrow, where stem cells are produced. These bring hope for advancement of treatment methods.

Chapter 10

Extinction events (I)

Five major mass extinctions have been recognized. The most well-documented of which is the Cretaceous–Paleogene (KPB) mass extinction, which happened about 65Ma (Mason et al., 2017, p.456). ¹ Shortly following the KPB mass extinction is the Paleocene–Eocene Thermal Maximum (PETM), which is an event marked by a rapid temperature increase, resulting to global climate change that happened approximately 56Ma (Keller et al., 2018). This chapter will focus on the two events and how they are linked to the current climate crisis and “mass extinction”.

10.1 Effects of KPB and PETM on general global biodiversity

10.1.1 Cretaceous–Paleogene Boundary (KPB) mass extinction

Though the KPB mass extinction was not the most severe mass extinction known, it is the most documented and thus most famous mass extinction event. ² A prevailing hypothesis for the mass extinction was that it was triggered when a meteor fell into the Chicxulub crater in Mexico (Keller et al., 2018; Mason et al., 2017, p.456). This caused debris to accumulate in the atmosphere and reduced the average amount of solar energy influx to the Earth, decreasing the amount of light and heat. Since sunlight is vital for photosynthesis of terrestrial plants, which act as primary sources of food, the deficiency of it will result to poorly functioning ecosystems. There are other hypotheses regarding the KPB extinction event. These include an eruption of a volcano (Deccan volcano) (Keller et al., 2018).

Keller et al. (2018) have pointed out criteria for the transition between the Cretaceous and the Paleogene periods. First is the mass extinction of planktic foraminefera, which was observed from fossils. Another criterion is the sudden increase of iridium (Ir) in the transition phase. This is known as the Ir anomaly. The proponents have argued against the meteor impact theory using the two criteria above by stating that the impact theory dismisses them. The meteor impact

¹Ma here means Mega (million) years ago

²Numerous films and documentaries focus on the depiction and extinction of dinosaurs.

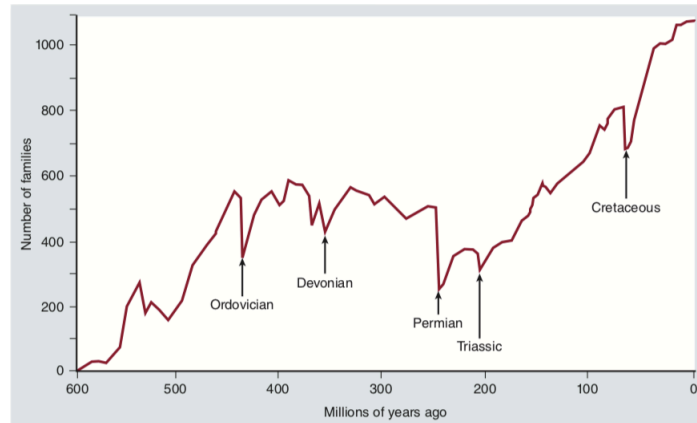


Figure 10.1: Number of families with respect to number of years ago. Image shows five major extinction events pointed to by arrows.

theory, though was formulated based on the observation of the Ir anomaly, ignored the fact that Ir can accumulate in “redox boundaries in clay layers” and that volcanic eruptions from the deep mantle can spew out Ir (Keller et al., 2018). The proponents have also shown evidence of the other criterion using fossil images and comparison, giving validity³ to the Deccan volcano hypothesis. They have also suggested that the Chicxulub impact happened prior to the mass extinction crisis, and was not the cause of mass extinction.

Though non-avian dinosaurs got extinct, they were not the only ones to do so (Mason et al., 2017, p.456). Other groups include marine and flying reptiles and ammonites (a type of mollusk). The biodiversity of angiosperms, birds, and planktons were severely decreased. However, the biodiversity of turtles, crocodiles, and amphibians were estimated to have remained the same. The same pattern was also observed in other mass extinctions, which led scientists to believe that mass extinctions do not need to affect all groups of organisms equally (Mason et al., 2017, p.456). Figure 10.1 below shows the five major mass extinction events.⁴

As a consequence of this, previously dominating groups may perish, thus changing the direction of evolution. This can be related to bifurcation models in complex systems analysis.⁵ Non-dominant groups may dominate depending on the conditions following the mass extinction.

10.1.2 Paleocene–Eocene Thermal Maximum (PETM)

The Paleocene–Eocene boundary (PEB) was remarked by the following criteria:

1. Disappearance of some benthic foraminefera
2. Occurrence of some planktic foraminefera

³My opinion given the evidence.

⁴Image lifted from (Mason et al., 2017, p.456).

⁵Introduced in Chapter 1 on complexity

3. Diversity of *Apectodinium*

A high carbon footprint was found in the atmosphere and oceans possibly coming from volcanic eruptions through methane (Keller et al., 2018), a greenhouse gas. It was also marked by a global temperature increase of $5 - 9^{\circ}\text{C}$ over a course of 30,000 years and ocean acidification. The high amount of greenhouse gases in the atmosphere may have been responsible for the global temperature increase. From closer inspection of Figure 10.1, it can be seen that there is a steep increase in diversity about 10My after the KPb mass extinction. Fossil records also agree that mammalian migration and diversification happened after the PETM.

10.2 Implications in the Anthropocene “mass extinction”

From the two events above, Keller et al. (2018) summarized that rapid increase in global average temperature can cause two things: mass extinction or pseudoextinction. In both cases there were still extinction events but pseudoextinction in the Eocene period brought diversity. One of the differences between the Anthropocene mass extinction and the KPb mass extinction is that human niche occupation and economics play vital roles in aggravating the effects of climate change. Another crucial difference is that humans are aware that they are an agent responsible for the rapid increase in greenhouse gas flux in the atmosphere. Humans are also able to develop solutions that can alleviate effects and slow down climate change.

Chapter 11

Global climate change (II)

11.1 Human niche construction

11.1.1 Historical perspectives

Throughout history, there have been important events that have altered the economic lifestyles of our species. These include the Neolithic revolution and the Industrial revolution. In the Neolithic revolution, man has discovered how to utilize agriculture to maintain a sedentary lifestyle. Plants, livestock, and pollinators were used to increase the yields of agriculture. There were many “experiments” on the artificial selection of animals, including the domestication for use as aids in farming and human consumption. Such use and alteration of niches of species other than one’s own to suit their needs is termed *niche construction*¹. However, as remarked economies were stuck in what was called a “Malthusian trap” (*i.e.* no economic growth)².

The Industrial revolution marked the start of rapid economic growth. This meant that more resources will have to be retrieved and processed for human consumption. This further implies the creation of goods and services from natural resources. Greater volumes of material processing implies that more waste is produced, and such can lead to large amounts of environmental polluters. One of the effects of which is *global climate change*. As noted in the previous section on mass extinctions there are two possible outcomes, either there will be a rapid mass extinction similar to the Cretaceous-Paleogene boundary or a period of diversification as a result of pseudoextinction similar to the Paleocene-Eocene boundary.

11.1.2 Pollution and global climate change

One of the problems faced by society nowadays is global climate change, with anthropogenic greenhouse gases as primary suspects. It has been said that human activities constitute to about

¹from https://en.wikipedia.org/wiki/Niche_construction#Humans

²from <http://assets.press.princeton.edu/chapters/s8461.pdf>

90% the global greenhouse gas flux (Sumi & Mimura, 2011). Because of this various considerations on the next actions will have to be made.

Anthropogenic global climate change (GCC) is a problem with many dimensions affecting different aspects of ecosystems and societies. Two of the most important factors interacting in GCC are the global system (biosphere) from which humans as an animals species obtain our necessities and human systems including philosophies, psychologies, and politics (Sumi & Mimura, 2011). These subsystems are dependent on each other, so it is necessary to understand and act. GCC, having to manifest its effects in the future ³ produces inequity between generations. To help in understanding the extent of climate change in later generations simulations are being done; however, they are not necessarily reliable (has a non-deterministic nature) since weather is chaotic. To further complicate issues, changes in economic situations especially in producer and consumer dynamics can also affect climate (Sumi & Mimura, 2011).

Water circulation (hydrologic cycle) is an important part of the geochemical cycles (Mimura, 2011). The effects of global climate change on the hydrologic cycle have been studied. It has been found that GCC has effects on average temperature, amount of precipitation, evaporation, and the sea level. Runoff was observed to be and predicted to increase in some areas. Glaciers are threatened. The frequency and intensity of drought and precipitation were found to increase in simulations. Finally, water quality is also affected by causing ocean acidification and salination. This further decreases the amount of freshwater available for consumption.

Organisms in ecosystems are also affected. There are observations of biodiversity losses in tundra, boreal forest, and coral reef ecosystems (Mimura, 2011). Many more environments are stressed. It is estimated that there will be larger biodiversity losses since 20 – 30% of studied species are at high risk of extinction.

11.1.3 Proposed solutions

Generally, two forms of solutions are proposed and implemented: solutions to mitigate the effects of GCC and to adapt to GCC. Mitigation measures opt for the reduction of emissions and increase in absorption of greenhouse gases. These are done by the establishment of mitigation policies, but the effects of these policies are only expected to be manifested for the next several decades (Mimura, 2011). Adaptation measures on the other hand increase the “preparedness” of humans and ecosystems for the adverse effects of GCC. Since the effects of mitigation effects are not directly manifested, adaptation measures are also important to improve on.

One thing to note is that the effects of climate change cannot be suppressed and that impacts are certain to manifest, and this problem is more serious in developing countries (Mimura, 2011; Sumi & Mimura, 2011). As noted in Chapter 1, it is important to study the factors affecting the complexity of the problems in order to make better decisions, in the case of ecological complexity to help in adapting to GCC. With this in mind, new paradigms in economics are

³possibly to a much greater intensity as is experienced now

being developed to create new schools of thought under the name “ecological economics”.

11.2 Ecological economics

On the law of scarcity One of the most fundamental laws in economics is the law on scarcity which states that there will never be enough resources to satisfy the needs of every person. Neoclassical economics (NCE, the standard economic paradigm) says that there is no limit to the growth of economies (through production). This contradicts with the law of scarcity, upon which most of microeconomic theory is built upon. Ecological economics (EE) on the other hand, proposes an *optimal scale* where economic growth can be limited (Daly & Farley, 2004, p.15-18). The limitation of economic growth, while focusing on development is crucial for maintaining the sustainability of economies and ecologies.

The optimal scale Utility is can be defined as the amount of satisfaction one receives upon consumption of the good. This is usually considered in modeling consumer/producer dynamics in microeconomic NCE, but it is not considered in macroeconomics. Daly and Farley (2004, p.15-18) propose a concept of disutility which is a form of negative satisfaction caused by a reduction of “ecological welfare”. The optimal scale exists when satisfaction is the same as dissatisfaction.

Synthesis Due to the rapic increase in greenhouse gas flux primarily caused by human niche construction, global climate change is observed. Similar to the most recent mass extinction and the Paleocene-Eocene thermal maximum (PETM), the average global temperature increases rapidly (Keller et al., 2018). This means that climate change may proceed to two extremes: mass extinction and pseudoextinction. In both cases, there are massive biodiversity losses. Global climate change has already done numerous effects on abiotic (water) and biotic (ecosystem) resources. This has serious impacts on the economics within ecosystems and of man-made economies as well. Three kinds of solutions are being studied: adaptation, mitigation (Mimura, 2011), and philosophical strategies (Daly & Farley, 2004). Though GCC is a natural phenomenon, knowing the intricate relationships between ecologies, economies, and societies, the manifestation of effects may be lessened.

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