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Principle of Least Action and Evolution

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Abstract

As Theodosius Lobzhansky has said, "Nothing in biology makes sense except in the light of evolution." [1] Since the Renaissance, it has been believed that the same laws that govern physics and chemistry in unanimated nature also govern live biology. Instead of looking for a "missing law" in physics to explain evolution, we have the least action principle (or stationary principle). This universal principle, studied since the 1st century and tested in Newtonian classical mechanics, the theory of relativity, and quantum mechanics, establishes that matter does not follow a random path but a minimizing, stationary, or even optimizing path. If processes in physics and chemistry are not random, how are mutations and the formation of proteins in biochemical processes random? If this principle applies to physics and then to biology, we can conclude that chemical processes, mutations, or peptide formation in evolution are not random. I will examine biochemical changes in amino acids that lead to changes that follow the Principle of Least Action (PLA). For this purpose, we have to look into Gibbs free energy. The least action principle has been tested and proven in relativity and quantum mechanics; it can be demonstrated in thermodynamics by transforming the energy equation into an equation of motion. Natural selection, Darwinian, or neo-Darwinian theories try to explain the animated world as a living entity where mutations are random. In recent years, a number of publications have tried to prove that mutations are not random in evolution. Several articles indicate that the formation of dipeptides has a negative free Gibbs energy, suggesting that the reaction is spontaneous and favorable. However, some of these articles do not explain why mutations are not random or spontaneous in the formation of early dipeptides. I disagree with some other papers claiming Natural Selection is entirely dependant on the Principle of Least Action. This paper will offer an explanation, a probable cause of these non-random mutations, not only in animated beings but most important in the early evolution of biochemistry. I will examine a list of papers and explain how the Principle of Least Action is related to evolution and the formation of the first peptides. I will also perform a small computer simulation.

Keywords

Principle of Least Action, Evolution, Cyclic Dipeptides, Mutations, Random

1. Introduction to the Principle of Least Action

The principle of least distance was discovered over 2000 years ago by Heron of Alexandria while he was studying light (Heron 70 a.c.). He found light doesn't necessarily follow a straight path; it doesn't follow a random path; it stays on a path chosen by nature; it follows the shortest distance path. This is the so-called Principle of Least Distance.

In 1657, Pierre de Fermat, studying the properties of light, refraction, found that light doesn't necessarily follow the shortest distance but follows the least time path (Principle of Least Time). About 100 years later, in 1760, Maupertuis and Lagrange extended the principle. Light follows the least action path (the Principle of Least Action), but not only light; they applied this principle to the entire matter of the universe. Lagrange proved that all Newtonian mechanics can be deduced from differential energies by finding a function between endpoints; it was called the Lagrangian (Figure 1). The principle was called the Least Action Principle (PLA).

The expression is formulated in one equation, where terms are S (the action), which is equal to kinetics minus potential energy. In one dimension for x-coordinates, the expression is:

$$\text{For KE: Kinetic energy: } (1/2)mx^2 \tag{1}$$

$$\text{PE: Potential energy: } (1/2)kx^2 \tag{2}$$

$$\text{The Lagrangian is } L = KE - PE = (1/2)mx^2 - (1/2)kx^2 \tag{3}$$

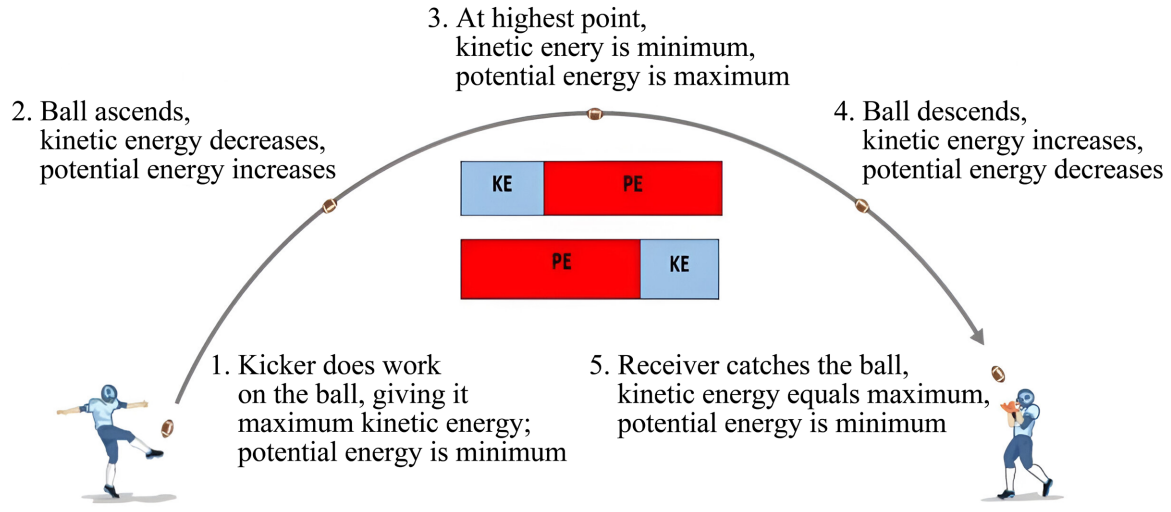

Figure 1. Potential and kinetic energy for the Lagrangian (image from UCF Pressbook University of Central Florida).

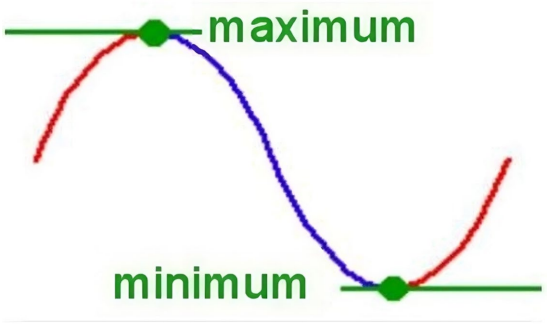

Figure 2. Hamilton principle of stationary action (image from Massey University).

Where m is the mass, k is the force constant, and the action is S.

$$S = \int_{ti}^{tf} Ldt \tag{4}$$

Later, in the 1800s (Figure 2), Hamilton extended the principle of least action. He proposed a stationary principle, meaning matter tends to stay at its minimum or maximum levels of energy (the Principle of Stationary Action). Usually, it's the minimum: that's why it's still called the Principle of Least Action. This principle has been demonstrated for Newtonian physics, relativity, and quantum mechanics (Richard Feynman PhD thesis PLA in quantum mechanics) [2].

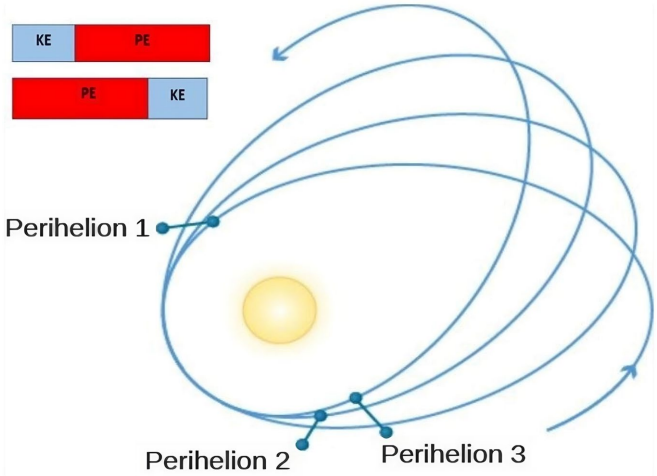

Figure 3. Mercury orbit around the Sun.

One way to prove this experimentally in the theory of relativity, is to calculate the orbit of Mercury. The calculation of the orbit is slightly different when applying Newton's mechanics. Newtonian mechanics failed to predict accurately the orbit of Mercury, and can be accurate calculated using PLA (Figure 3).

The theory of relativity considers the curvature of space. Using proper time, or time of the object in its own reference frame, it can be solved with PLA. The same concept used for the trajectory of the ball; we get the same results as in Einstein's theory of relativity. This is just a special case of Fermat minimizing the least time, a Principle of Least Proper Time.

In Richard Feynman's Quantum Mechanics PhD thesis (1942), Feymann calculates the space shift along each path to its destination in configuration space (shortest path) and reproduces Schrödinger wave function. The path integral (Feynman) is the quantum analog of the Principle of Least Action. Feynman added all possible paths weighted by the quantum action to its destination (Figure 4). The most likely destination is where we have constructive interference (Figure 5).

This premise is a universal principle. It applies to all physics. Some physicists say it is the closest we have to a theory of everything.

2. Thermodynamics

The theory of least action based on Lagrange motion can be formulated in terms of thermodynamics, exchange of energy, kinetics, and potential energy. Probability is a concise concept to denote the state of a system. Forces, *i.e.*, potential energy gradients and differences, drive the system towards more probable states via flows of energy that diminish the differences.

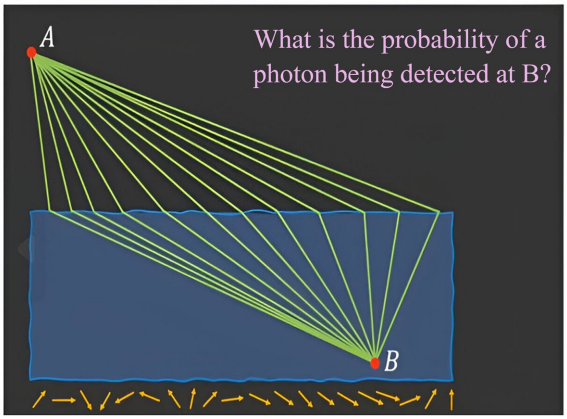

Figure 4. Photon destination paths between 2 points.

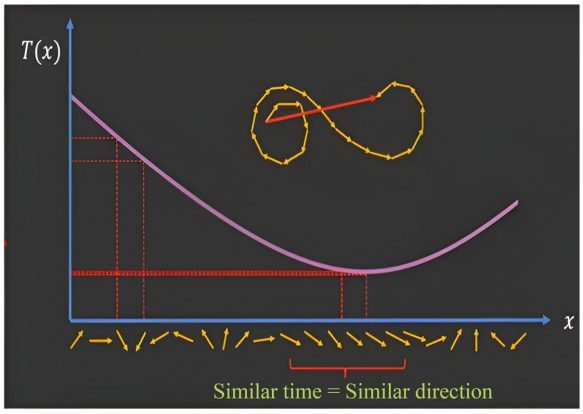

Figure 5. Final destination path.

The 2nd law of thermodynamics is often praised as the supreme among the laws of nature. Yet, the general principle is seldom pronounced explicitly in diverse

disciplines of physics, *i.e.*, in basic, continuum, and quantum mechanics, in fluid and electrodynamics, or in optics. Likewise, the law is rarely related directly to other universal imperatives, e.g., to the principle of increasing "entropy", minimum energy, minimum time, least action, or the maximum power principle.

The second law of thermodynamics is the starting point for the equivalence of the differential equation of evolution and the integral equation of dissipative motion in Hamilton's principle. The optimization of energy, Ville R.I Kaila and Arto Annila ("take the steepest gradient in energy", "take the shortest path in energy") [3] is clear. The optimization of energy is also discussed in Boltzmann (1905) [4] and Stöltzner (2003) [5].

Since the late 1800s, researchers in thermodynamics have been trying to connect the theory of evolution with natural selection. Boltzmann applied statistical mechanics to chemical thermodynamics. In terms of the principle of least action, which at the present is well established in terms of energy Maslow 1991 [6].

The first and second laws of thermodynamics were combined into one equation by Josiah Willard Gibbs:

$$\Delta H = \Delta G + T\Delta S \quad or \quad \Delta G = \Delta H - T\Delta S \tag{5}$$

In a chemical reaction, ΔG can be negative or positive. Gibbs negative (ΔG), which is spontaneous, is called exergonic, and emits energy. A $\Delta G > 0$, positive, is endergonic, the reaction needs energy. An enthalpy (ΔH) < 0 is called exothermic; an $\Delta H > 0$ is called endothermic.

In terms of proteins, the so-called thermodynamic hypothesis, or, in other words, Amfisen's dogma, means that the native state, or working state, of a protein should be the global minimum of free energy.

With negative ΔG, we have a spontaneous reaction. No additional energy is required to complete this process. We also need to study the kinetics of the reaction. A reaction to completeness might take millions of years in evolution. According to the Arrhenius formula, the speed of the reaction depends on the temperature (T) and the activation energy (E_a), with A and R constants. Higher temperatures result in higher speeds (red curve); lower activation energy means the barrier is lower to complete the process, and the rate constant k is higher. See below:

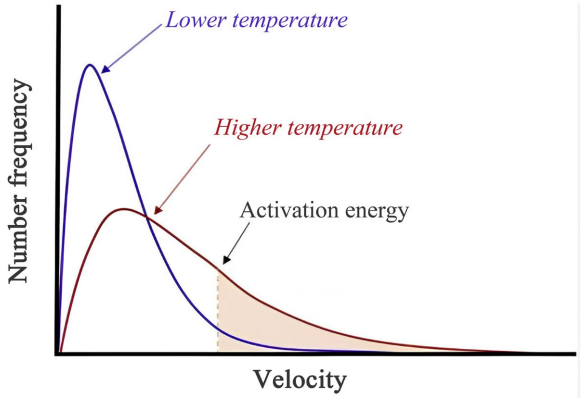

Figure 6. Bolzmann distribution.

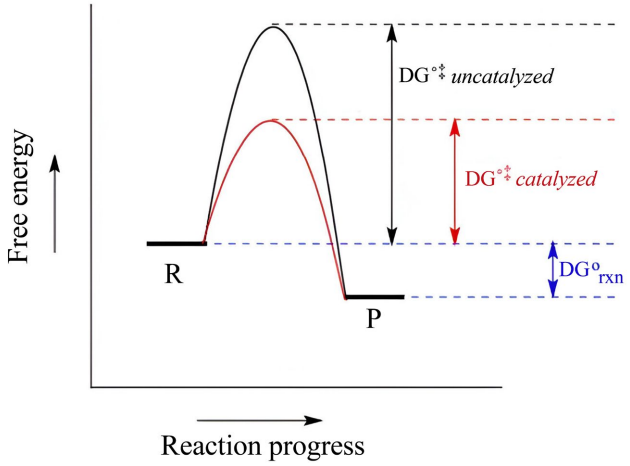

Figure 7. Transition state energy.

K: rate constant

A: pre-exponential factor

Ea: activation energy (in the same units as RT)

R: universal gas constant

T: absolute temperature (in kelvin)

$$k = Ae^{-Ea/RT} \tag{6}$$

We can get a better idea with the Bolzmann distribution (chart to the left) (**Figure 6**). The curve in blue has lower temperatures and a lower speed; fewer particles are at a lower speed. The curve in red has a higher temperature, more particles are moving at a higher speed, and the area under the curve is greater. The curve to the right, **Figure 7** shows a higher curve with a higher activation energy (uncatalyzed). The lower curve (red) shows a lower activation energy.

There is a distinction between thermodynamics and kinetic stability. Activation energy, or the energy required for the reaction to be completed, is what determines kinetic stability. When we describe a response as kinetically stable, we imply that it proceeds slowly. The rate at which the reaction proceeds is independent of the amount of energy introduced into the system. In order to counteract this, our bodies produce more enzymes, like DNA and RNA polymerase. These increase the turnover rate by lowering the activation energy and decreasing the kinetic stability when added.

In order to connect thermodynamics with natural selection and evolution, it is not necessary to explain the entire process of natural selection through thermodynamics as Ville R.I Kaila did. Thermodynamics and current theories explain the effects of biochemistry; there are other effects that cannot be explained by thermodynamics and/or the principle of least action. These effects are caused by living beings, Darwinian or neo-Darwinian theories.

3. Amino Acids and Cyclic Dipeptides

The probability of forming amino acids must be amazingly small, but as Stephen

Fried has said, "The universe seems to love amino acids", and "Maybe if we found life on another planet, it would be based on amino acids" [7].

However amino acids forming proteins have a ΔG (Gibbs free energy) positive, non-spontaneous and unfavorable. In our body peptide bonds formation and proteins is thermodynamically unstable, unfavorable, but kinetically stable.

Bond formation of proteins with amino acids is an endergonic process that requires energy. Endergonic processes are those that absorb energy; the joining of two peptides takes energy; and the product's free energy is $\Delta G > 0$. Any time that ΔG is positive, the reaction is non-spontaneous, which means that the reaction will not occur unless energy is added to the system. Our bodies do this by coupling peptide bond formation with ATP hydrolysis. The high-energy phosphate bond can be broken, releasing the necessary energy to activate peptide bond synthesis.

According to Yeting Guo *et al.*, "Simpler forms must have originated at the origin of life, given their versatility" [8].

The simplest form of a peptide is a dipeptide. Simpler cyclic amino acids (DPKs don't need ATP for the formation of a dipeptide). Cyclic dipeptides offer appealing structural and biological diversity; they offer better biological activity due to conformation rigidity. Cyclic dipeptides can bind to targets with higher affinity than linear dipeptides. They offer stability, have lower energy, and are more energetically favorable.

One of the simplest cyclic amino acids is Proline. It's special because a penta structure in a ring form. If we could pair this amino acid with the simplest of all amino acids, Glycine, we would have a simpler, more stable dipeptide.

Recent studies (Yeting Guo *et al.*, Cyclic Dipeptides Formation from Linear Dipeptides Under Potentially Prebiotic Earth Conditions) have proven that cyclic amino acids not only show a ΔH (enthalpy) negative, but a ΔG (Gibbs free energy) negative (no need of ATP).

Negative enthalpy is very convenient for early dipeptide formation. Because, at any temperature, if $\Delta S > 0$, ΔG (Gibbs free energy) will be negative, therefore spontaneous and favorable to the reaction.

$$\Delta G = \Delta H - T\Delta S \tag{7}$$

ΔH	ΔS	
-	+	Spontaneous at any temperature

According to the Yeting Guo study, they tried experimentally several combinations of linear Pro-AA and found both linear Pro-Gly and linear Gly-Pro could form cyclo-Pro. In this study, the linear Proline-Glycine and Glycine-Proline ended with enthalpies of −608.976 to −609.039 kcal/mol. The free Gibbs energies range from −609.022 to −609.0913 kcal/mol (**Table 1**). These are favorable energies for the formation of dipeptides (without ATP), and if the kinetics are favorable in the aqueous solution, we can see that the Least Action Principle is working through the free energy to form dipeptides.

See supplementary Table 1 Energy value for the Linear-Gly-Pro and Linear-Pro-Gly to form cyclo-Pro-Gly from Yeting Guo *et al.*, Cyclic Dipeptides Formation from Linear Dipeptides Under Potentially Prebiotic Earth Conditions.

Table 1. From Yeting Guo *et al.*

	OPT/B1		OPT/B1+ZPE		G		H	
RC-LPG	**−609.23851**	**1.4**	**−609.03852**	**1.1**	**−609.07861**	**−0.2**	**−609.02554**	**1.1**
RC-LGP	**−609.24077**	**0.00**	**−609.04005**	**0**	**−609.03875**	**0**	**−609.02734**	**0**
TS-LGP	**−609.18458**	**35.30**	**−608.98720**	**33.2**	**−609.02215**	**35.3**	**−608.97605**	**32.2**
PC-LGP	**−609.25186**	**−7.00**	**−609.05267**	**−7.9**	**−609.09137**	**−8.2**	**−609.03950**	**−7.6**
RC-LPG: Linear Pro-Gly								
RC-LPG: Linear Gly-Pro								
TS LPG: Linear-Gly-Pro								
PC-LPG: Linear-Gly-Pro								

Absolute energies are in au units and relative ones are in kcal/mol^{-1} units.

Now we need to consider the kinetic effect of this reaction. As we mentioned before, the formation of peptides is kinetically favorable and stable. According to Yeting Guo, the activation energy may be high, and the formation of cyclic dipeptide may be too slow in the experiments with P_3m. They suggest the promoting effect of trimetaphosphate P_3m on cyclization is kinetic rather than thermodynamic. The TS barrier is low; for linear Gly-Pro (LGP), it is 33.2 kcal/mol^{-1} lower than Pro-Gly, where no transition state was found (Figure 8). The yield of cyclo-Pro-AA from linear-AA-Pro as the reactant was increased compared with that from linear-Pro-AA as the reactant.

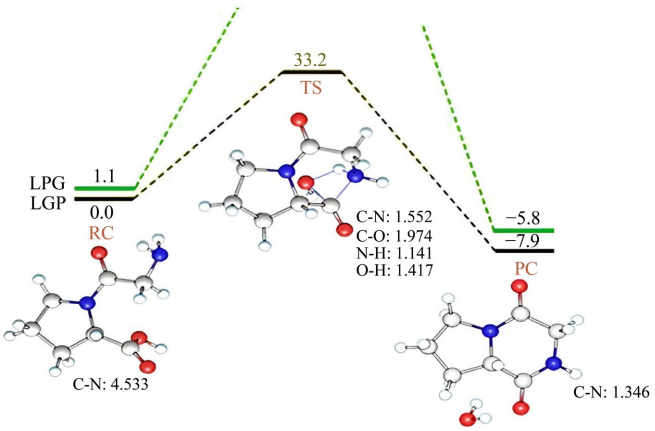

Figure 8. Transition energies in kcal/mol^{-1}, distances in Angstroms units From Yeting Guo *et al.*

The yield of cyclo-Pro-AA could also be promoted by the presence of P_3m in the reaction. They found that the transition state is lower for linear Glycine-Pro-

line than for Proline-Glycine. It was therefore implied that P_3m had a positive effect on cyclo-Pro-AAs formation.

According to A. Solis [9] prebiotic sequences are amenable to mutations that significantly lower native conformational energies. In this study, prebiotic sequence mutations lower the energy of activation.

Camilo Mora and Andres Gonzales [10], performed a computer simulation using the group contribution method (GMC) to calculate free energy for the dipeptides based on molecular dynamic simulation (MD). They implemented multiple simulations with the 20 amino acids in dodecane water.

Table 2. Gibbs free energy (G) for the 20 amino acids dipeptides from C. Mora and A. Gonzales simulation.

Amino Acid	ΔG[KJ/mol]	+/−	Pair	ΔG[KJ/mol]	+/−
Asp	−388.4	2.87	Ala-Asp	−413.69	4.03
Glu	−356.4	0.82	Ala-Glu	−384.85	2.06
Lys	−294.61	2.34	Ala-Lys	−373.32	2.42
Arg	−270.66	1.31	Ala-Arg	−255.87	1.31
Tyr	−177.3	2.22	Ala-Tyr	−235.97	8.07
Trp	−168.78	1.69	Ala-Asn	−229.8	2.17
Gly	−166.48	0.76	Ala-His	−220.27	3.65
Gln	−166.19	1.15	Ala-Gly	−219.52	1.11
His	−165.46	1.71	Ala-Cys	−218.76	2.7
Ala	−164.27	1.61	Ala-Leu	−218.45	0.77
Asn	−161.24	2.19	Ala-Ala	−218.35	1.49
Leu	−158.99	1.58	Ala-Gln	−217.31	1.47
Val	−157.54	1.74	Ala-Pro	−215.99	0.79
Phe	−157.47	1.18	Ala-Val	−215.68	0.84
Ile	−156.9	1.23	Ala-Ile	−215.08	0.95
Cys	−151.74	1.16	Ala-Ser	−213.13	1.2
Ser	−150.28	0.98	Ala-Phe	−210.77	1.56
Thr	−146.34	0.72	Ala-Trp	−209.8	1.54
Pro	−144.78	1.05	Ala-Met	−207.59	3.6
Met	−138.63	1.58	Ala-Thr	−206.68	1.63

As we can see in Table 2, the formation of dipeptides is spontaneous ($\Delta G < 0$).

I performed the same simulation (**Figure 9**), just for verification, using Avogadro and ORCA for Glycine-Proline dipeptide with water as a solvent. My results using Avogadro as a viewer, optimizing the geometry with ORCA for enthalpy and Gibbs free energy calculations. The result for the enthalpy of the reaction was −684.51621 kcal/mol. The free Gibbs energy, after subtracting the temperature multiplied by the entropy, was −684.57 kcal/mol.

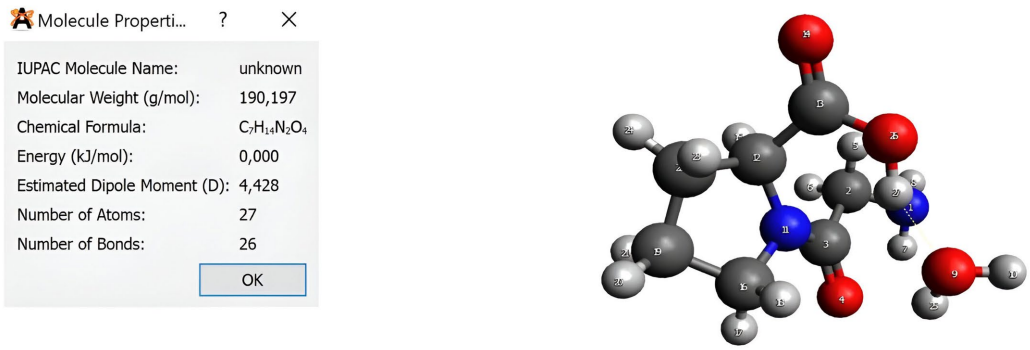

Figure 9. Condensation glycine-proline avogadro.

4. Extraterrestrial Meteorites

In order to find a connection between the formation of dipeptides and the existence of amino acids, I have to mention how amino acids, even dipeptides, have been found. In particular Glycine and Proline.

Is the formation of amino acids rare in the universe?

We have found extraterrestrial meteorites with similar amino acids found on earth, and, according to some authors, the basic amino acids formed early in life. In the Murchinson meteorite (1969), there were a total of 86 amino acids (Toshiki Koga & Hiroshi Naraoka, 2017) [11]. Out of these 86 amino acids, up to 10 of them are the same amino acids that formed life on earth (**Table 3**). Others are totally new. But what are the chances of finding 10 out of the 20 amino acids in the universe? They are probably very low.

These amino acids include Glycine and Proline. The Murchinson meteorite, which fell in 1969, contains the early prebiotic AAs and what is believed to be the early amino acids. These 10 AAs could have started the formation of the rest of the amino acids and other complex molecules, including dipeptides.

Table 3. Extraterrestrial amino acids.

	Early Amino Acids	Meteorites
		Extraterrestrial
1	**Alanine**	Murchinson
2	**Aspartic Acid**	Murchinson
3	**Glutamic Acid**	Murchinson
4	**Glycene**	Murchinson
5	**Isoleucine**	Murchinson
6	**Leucine**	Murchinson
7	**Proline**	Murchinson/Murray
8	**Serine**	Murchinson
9	**Threonine**	Murchinson
10	**Valine**	Murchinson

Although individual amino acids have been found in abundance in carbonaceous meteorites, there have only been two reports of polymers, the first being diglycine and a more recent one of large polymers of mainly.

Glycine in the CV3 class carbonaceous chondrite Allende. Thanks to these findings we can assume that early prebiotic soup included Glycine and Proline.

5. Mutations

Recent studies have found that mutations have a bias, and the probabilities of forming proteins from amino acids are astoundingly small. The chances of forming one protein of 150 amino acids (small length) are 1 in 10^{164}, which is unlikely, even considering the age of the universe (13 - 15 billion years).

Some researchers have found that not all mutations are random in humans [12]. In a recent study with plants, it was found that mutations are not random (J. Monroe *et al.*, 2022) [13]. Mutations reflect natural selection in Arabidopsis? After observing thousands of mutations, there is a mutation bias. The mutations were definitely not random. They found a prevailing paradigm: mutation is a force in evolution; some mutations try to protect an essential gene; beneficial mutations. They don't follow a natural selection path. Plants evolve in certain directions.

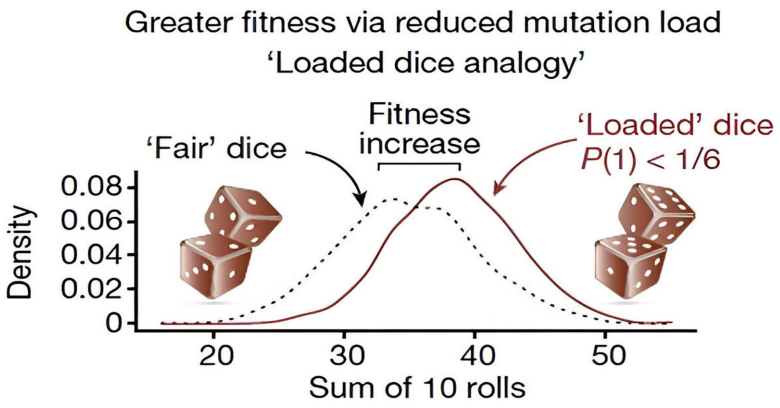

Figure 10. From J. Monroe.

The adaptive value of this bias can be conceptualized by the analogy of loaded dice with a reduced probability of rolling low numbers (that is, deleterious mutations) and thus a greater probability of rolling high numbers (that is, beneficial mutations) (**Figure 10**).

In a recent study of malaria with an innovative method, researchers found that the generation of human hemoglobin (HbS), which protects people from malaria, is higher in people from Africa than in Europe. In this second study, human hemoglobin (Daniel Melamed *et al.*, 2022) [14]. They applied a method to measure the origination rate of the target mutation. According to the authors, the data suggest "a complex picture of mutation rates involving mutation-specific influences". Thus, the significance of these patterns is more likely due to the independent origins of the mutations, mutation-specific rates being influenced by genetic and/or

epigenetic factors, giving advantages in a population, mutations favoring certain traits, etc., neo-Lamarckism?

According to A. Solis, "mutations might not only be favorable for lowering the activation energy but also help the correct fold of early peptides" [9].

In biology, recent studies have found that mutations are not random, and the probabilities of forming proteins from amino acids are astoundingly small during the prebiotic soup. Even when proteins form or produce genes, the traits expressed are not the ones expected by Darwinism or neo-Darwinism, where the changes are harmful to species. There are some other explanations that try to be compatible with the random mutation theory. But what if the mutations are not random? What if they follow a path?

According to Ruth Hershberg "But mutation is challenging to study; it is complicated by the effects of natural selection" [15].

These two studies show that mutations, in some cases, are not random. Second, they have a tendency. What has to do with the PLA? The tendency may be due to different factors; one of them is PLA.

Mutations might be connected to PLA. PLA offers an explanation. There are two papers that relate PLA to evolution, but they treat mutations as the only cause. Kaila VRI and Annila A. in "Natural selection for least action", suggest PLA causes natural selection. In this paper, natural selection (including survival of the fittest, adaptation, gene flow, neutral evolution, etc.) is caused by PLA in animated beings. However, natural selection processes are not only physicochemical or biological; they even include social and cultural behavior, because adaptation is a social process. This doesn't necessarily happen to humans. There are proto-human species that might have become extinct due to a lack of social and cultural adaptation, as Boyd, R., and Richerson, P. suggest in their article "Culture and the Evolution of Human Cooperation" [16].

Another paper I need to mention by Cllr. Clive Neal-Sturgess, "Natural Selection as the Sum over All Histories" [17], claims the only trend valid is the PLA as the "ultimate causal direction". I agree there is a direction, but for animated beings, it is not the only one. When animated beings enter the process of evolution, there are many factors, including PLA, biological, chemical, survival of the fittest, adaptation, social/cultural factors, etc.

Before animated beings, physiochemical processes were "the only game in town", as we know it. I will suggest the PLA has been fundamental in the evolution of a prebiotic soup and/or inorganic matter. I would agree with Cllr. Clive Neal-Sturgess: PLA is the ultimate causal direction in this context.

But most important, these two papers don't offer a possible path to evolution. I have mentioned some papers that make this path possible in a prebiotic soup, with the formation of dipeptides and with PLA as a probable cause.

The results are important because dipeptide molecules have the properties of peptide elongation and chiral catalysis without the intervention of an enzyme. These could be the early peptides during prebiotic conditions.

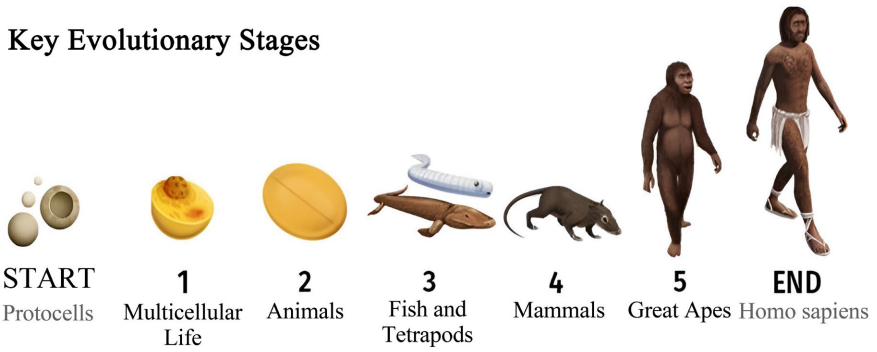

Figure 11. Evolution from Protocells to Homo sapiens.

6. Evolution

Do we have evolution before biology? Or natural selection? The evolution of life-giving chemicals before DNA, RNA or other complex molecules.

The evolution we are now studying is primarily in animated creatures, possibly multicellular life. Not in the formation of amino acids and proteins. The principle of least action effect has been at work since the Big Bang, the formation of amino acids and the first peptides.

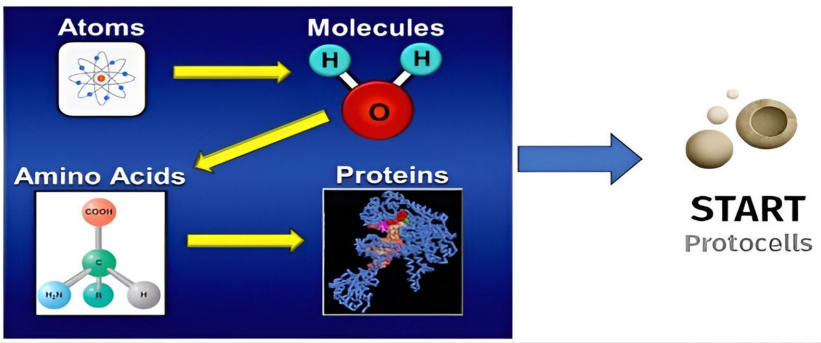

Figure 12. Evolution in unanimated nature and animated nature.

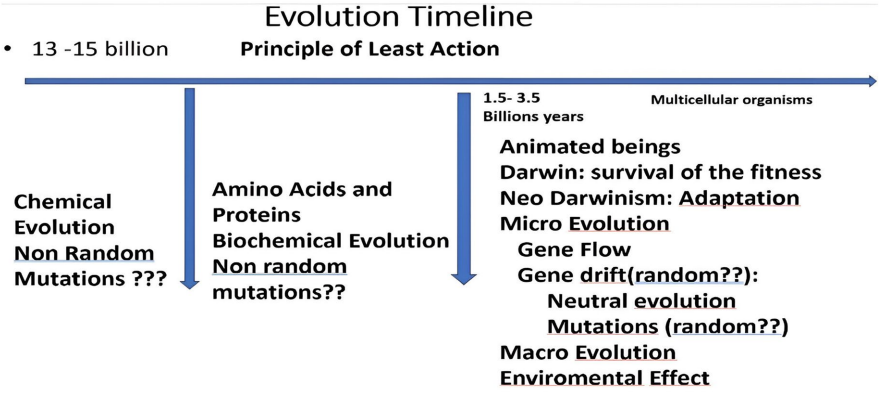

Figure 13. Evolution timeline in unanimated nature and animated nature.

We can see this in Figure 11. It's difficult to pinpoint when natural selection,

Darwinian, neo-Darwinian begins. Nevertheless, the PLA has been modifying atoms and molecular structures since the beginning of the universe.

In Figure 12, we can see the evolution of unanimated nature and organic nature, after the big bang.

In Figure 13, I present the same idea of evolution in a timeline and the impact of theories on the evolution of organic materials, or unanimated nature.

7. Conclusions

If processes in physics and chemistry are not random, how can mutations, the formation of proteins, and biochemical processes be random?

The PLA is the closest to a theory of everything; it works with Newton (classic mechanics), relativity, and quantum mechanics.

This paper starts with the existence of amino acids because we have found them in carbonaceous meteorites. In my opinion, the PLA also affects the formation of amino acids. The basic ones, needed for the early formation of life.

Some research has been done on the effects of quantum tunneling on biological systems. They can be fundamental to the formation of early amino acids, dipeptides, and proteins.

This paper doesn't offer a solution to evolution, but offer, like Darwin did, circumstantial evidence. PLA favors a path to the creation of the main components of life. It also points that once life is formed; PLA is still affecting evolution.

The Principle of Least Action doesn't replace natural selection as we know it; natural selection doesn't tell the whole story in animated beings; PLA adds more complexity to evolution. It adds one more factor to the evolution of animated beings. It extends the principle of natural selection. In a world before the existence of animated beings, it is a fundamental factor in the creation of amino acids and the formation of dipeptides.

I would change the famous Einstein metaphor to "God plays dice with the universe, but the dice are loaded". The evolution of the universe has a trend, and that trend is pointed in the direction of the Principle of Least Action. There is a book by Coopersmith J. with a very pertinent title, "The Lazy Universe" [18]. The title by itself is telling matter "chooses" a path.

Some researchers are looking for a "missing law", but the principle of least action is almost 2000 years old and has been tested. This principle leads to biological and natural evolution. There are "bubbles" of quasi-random behavior in evolution, and later, with the impact of animated beings, comes what we know as natural selection, Darwinian or neo-Darwinian. The effects (survival of the fittest, adaptation, social, etc.) complicate the distinction between the Principle of least Action and the other effects.

We cannot compare evolution after the emergence of animated beings, or so-called natural selection, survival of the fittest, or adaptation. The real natural selection starts at the beginning of the universe because the Principle of Least Action has been working since day one after the Big Bang. With the Principle of Least

Action, a physics law of the universe, the formation of amino acids and proteins is part of the trend in the natural selection process.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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Some Other Figures and Material

Figure 4, **Figure 5** PBS Space Time hosted by Matt O'Dowd, Youtube, Nov 2021, Is ACTION The Most Fundamental Property in Physics.
https://www.youtube.com/results?search_query=Is+ACTION+The+Most+Fundamental+Property+in+Physics
Hossenfelder, Sabine, 2023, Youtube, The Closest to a Theory of Everything
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