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The formation of proteins revisited

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ABSTRACT

The limitations of the present hypothesis concerning the cellular formation of proteins are discussed. A model of the process of the formation of proteins in biological cells through the dehydrating action of polyphosphoric acids combined with the varying physical and chemical properties of amino acids is described. Polyphosphoric acids exist in various stereochemical forms which act as stereochemical molecular templates. The controlled hydration of these forms give rise to the known variety of spatial forms of proteins.

KEYWORDS

Protein formation;
Polyphosphoric acids.

INTRODUCTION

Cell biology has established that proteins are a product of living cells and that the amino acid sequence composing proteins is constantly and precisely reproduced by the biological cell of origin. This observation indicates the presence of an amino acid selection mechanism in the cellular formation of proteins. Proteins can be produced synthetically by the formation of the peptide bond linking the constituent amino acids by dehydration. The conditions used are not applicable to the cellular formation of these compounds. The present hypothesis of cellular formation of proteins is that identification of a specific amino acid to be attached to the extending protein is through particular three base unit sequences (codons) of the order of bases in the length of DNA. The latter are recorded by the order of linked purine and pyrimidine compounds in a specifically formed length of the RNA present in the nucleus (copying processes). The formation of this RNA is a chemical reaction as the process is stated to involve enzymes. The means of initiating this reaction is not advanced or known. DNA is only present in cell nuclei and amino acids are predominantly present in the intracellular fluid outside of the nucleus. This being the case it is proposed that the RNA migrates to the exterior of the nucleus conveying the order of amino acid linkage to the region of protein formation. This links the order of bases of the DNA to a particular amino acid sequence of a protein.

This is an information transfer system in which the codons are the information and the base order of the RNA transfers information. In any information transfer system there has to be a source of information, a means to transfer of the information and a means of receiving the information. The information leads to or can be used to produce a result, in this case protein formation. In the proposed DNA information transfer system the final function is not precisely defined by the information transfer system. There is, for example, no known physical or chemical attraction between the purine and pyrimidine compounds forming RNA and amino acids. In addition some required information is not generated or

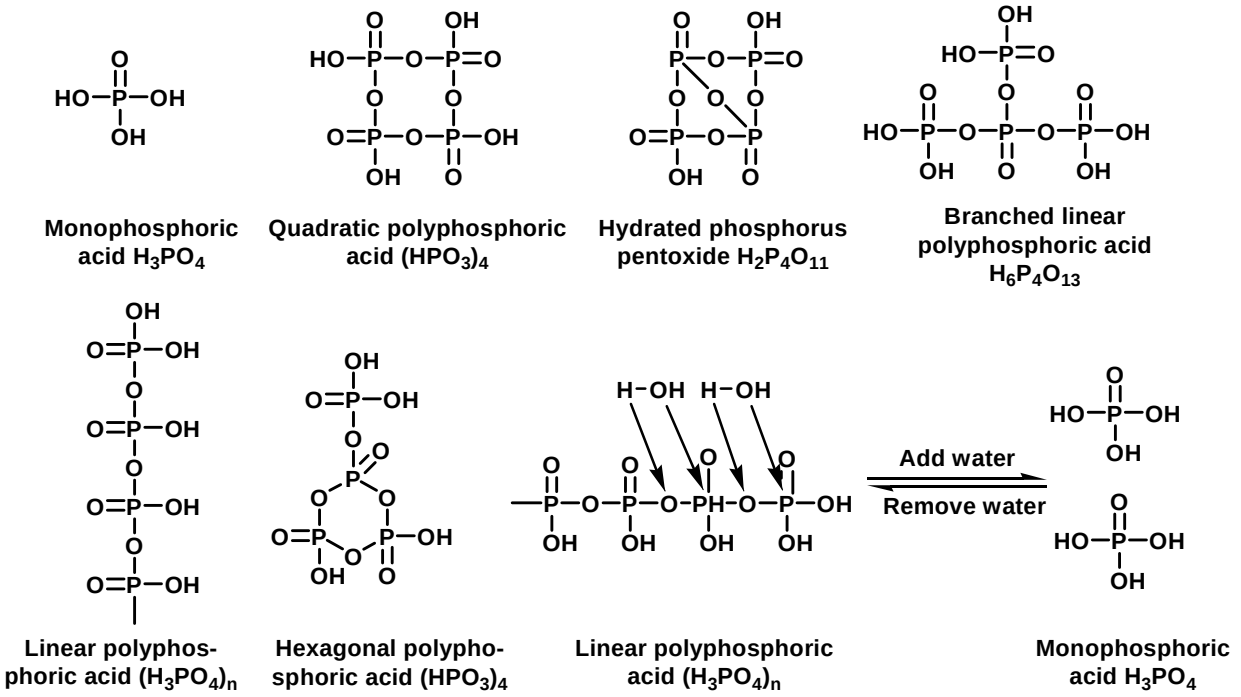

Figure 1 : The forms of polyphosphoric acid

transferred. The formation a peptide bond giving rise to proteins is a chemical reaction involving reacting compounds, compound concentrations, reaction rates, reaction temperatures, the intake or emission of heat and other forms of radiation and involving the production of water. This information is not influenced or derived from the DNA molecules and is not available for transfer. In addition no information is transmitted to identify which of many proteins produced by a particular cell is being formed at any instant and which particular amino acid is required by the protein sequence at this instant. The alternative is that the physical and chemical conditions for the addition of the amino acids is the same for all of these compounds irrespective of any differences in chemical, physical and stereo characteristics and the concentrations of the any one of the individual amino acids is always sufficient to form the relevant protein at the relevant rate and the situation is maintained in this state for the lifetime of the cell or metabolism. This alternative is not viable at least the grounds that the first condition requires the chemical environment to be identical in all biological cells which is clearly not the case and the second condition is contrary to observation. The conditions of molecular motion in the intracellular fluid make precision manoeuvring of the required amino acid to the point of attachment impossible. As a consequence this stage is advanced as being controlled by separate and different lengths of RNA which are proposed as guiding the amino acid to the point of attachment. The amino acid being added to the forming protein is taken to be linked to the ribose sugar molecule of these particular and different lengths of RNA. These units are identified as ribosomes which are cell components. Extensive examination of these units has identified the presence of ribonucleic acid and proteins leading to the present hypothesis that the former is involved in the formation of the latter. A protein formed under these conditions is considered to undergo further processing (post translational modification) in order to form linkages such as cross links between protein strands.

The first observations which are taken to support this hypothesis were the results of experiments on the effects of X- or UV- irradiation of spore cells[1]. The observed effects were a change in the metabolic reactions of the spores. This change was taken to be the result of the formation of a mutation of the gene which controlled the reactions involved such that, "the loss of activity of an essential enzyme could be attributed to gene mutation and that such loss results in "blocks" of essential biochemical reactions. The products of the "blocked" reactions thus become essential growth substances (restoring agents) for the mutants."[2]. This state-

Minireview

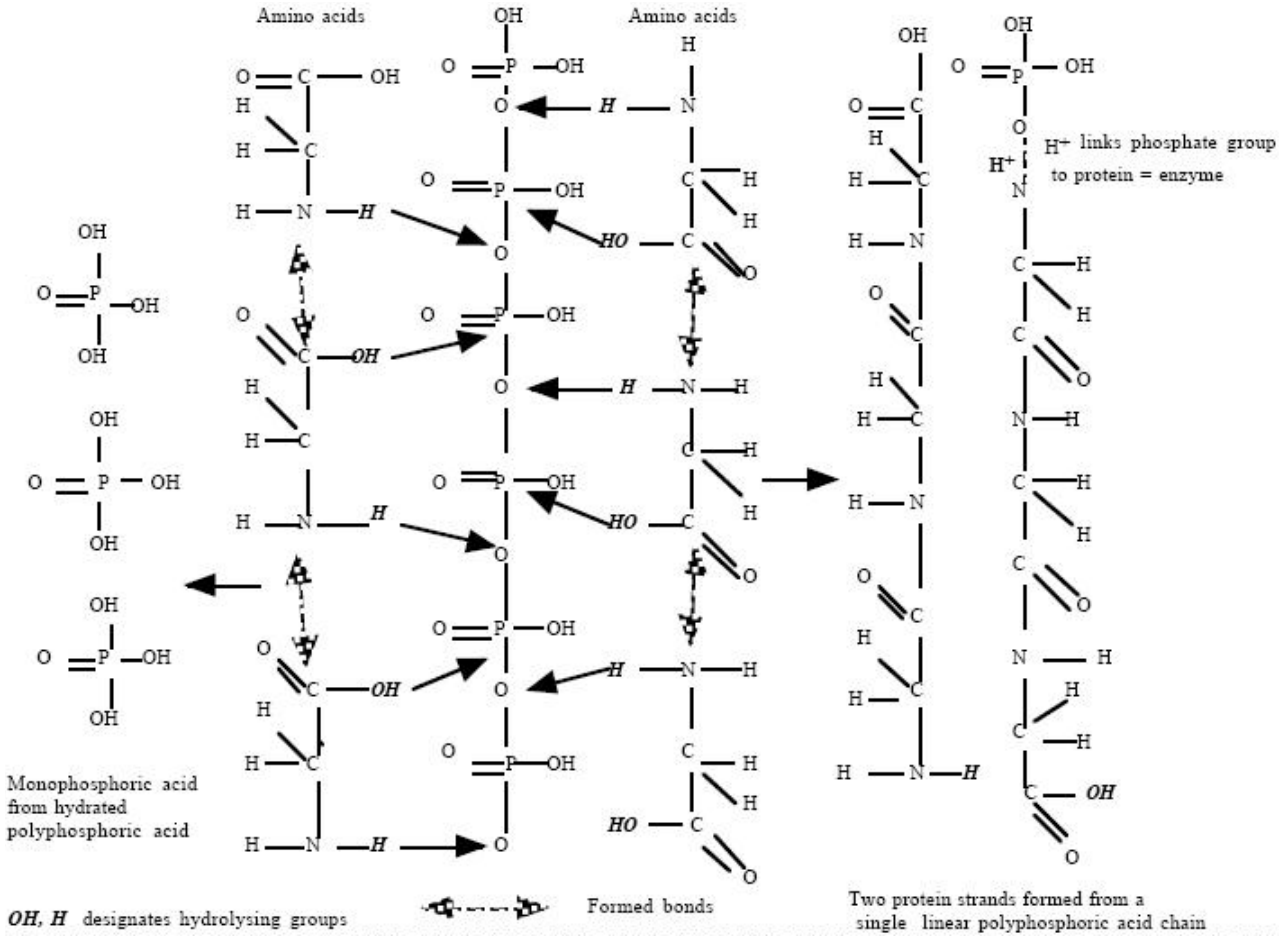

Figure 2a : The formation of proteins by dehydration involving polyphosphoric acid

ment assumes that genes controlled the formation of enzymes. Enzymes are proteins and from this genes controlled the formation of proteins. However the radiation used in the experiments above would also have resulted in the formation and/or discharge of inorganic and organic ions (betaines) in the system being studied causing the cessation of normal reactions in which these components were involved or the induction of detrimental biological reactions. Under these conditions the compounds used in experiments and which acted as "restoring agents" e.g. amino acids, therefore became a source of the required ions when decomposed by biological reactions such as decarboxylation and /or deamination. Particular lengths of DNA of the above model are identified as the genes. A gene is advanced as a unit which conveys information concerning a particular characteristic of a lifeform from generation to generation.

The entire process is considered to involve a series of enzymes. For example the formation of DNA and RNA are considered to require the presence of an enzyme to separate DNA strands prior to the proposed copying processes above. Enzymes are proteins. The copying process envisaged means that DNA cannot duplicate until a separating enzyme is present and a separating enzyme cannot be formed until DNA is separated. A protein is part of a ribosome and it follows that a ribosome cannot form until a protein is formed. In effect a protein cannot form until a protein is formed. These paradoxes are considered to have no relevance on the grounds that DNA in any cell of present times is not formed de novo and is derived from an ancient lineage of the particular type of cell and it is advanced that whatever the origin of living cells in the remote past the chemistry of these cells has evolved over time to give the situation described above. However the formation a peptide bond giving rise to the proteins is, as stated above, a chemical reaction involving reacting compounds, compound concentrations, reaction rates and so on. This will have been the case from the origin of life forms. If it were to be otherwise this means that

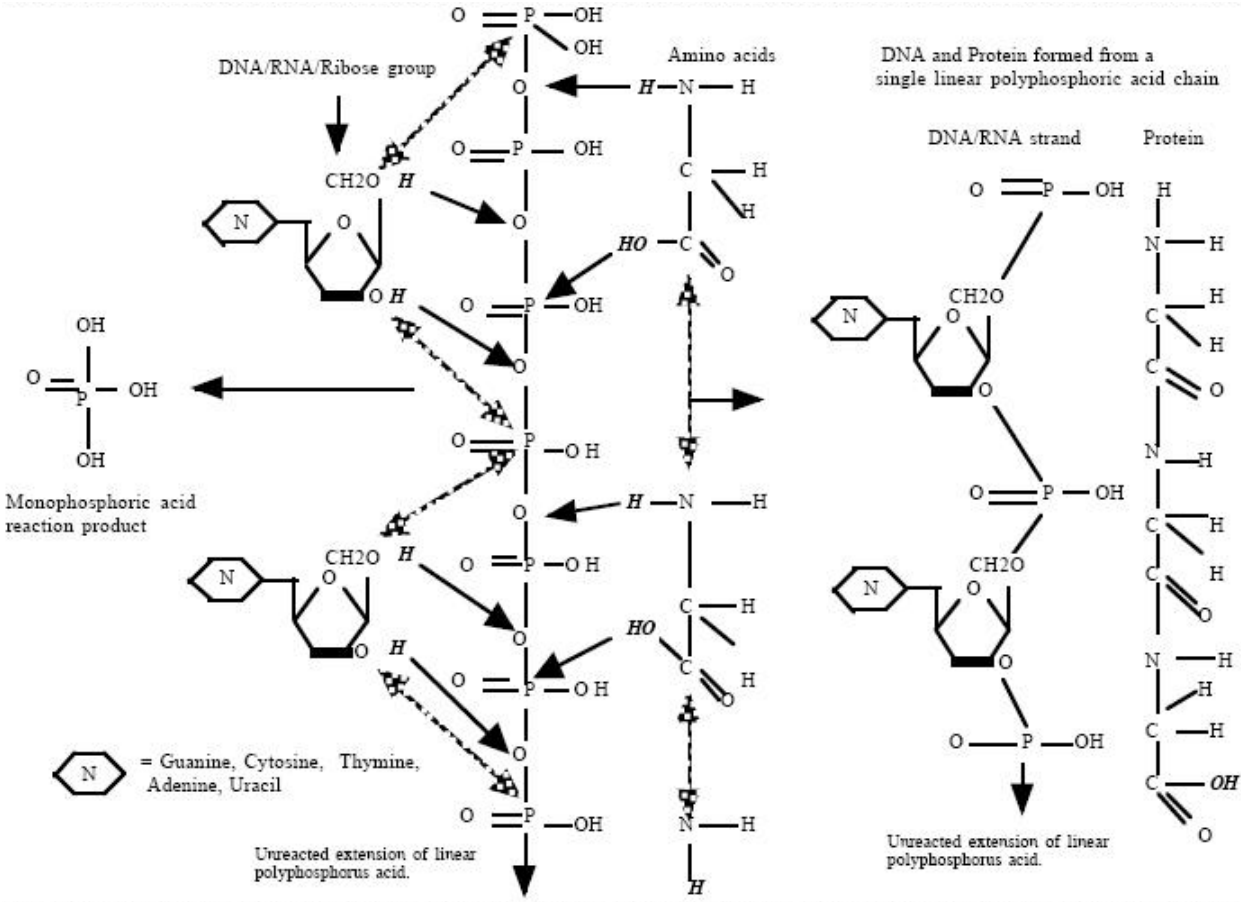

Figure 2b : DNA and Protein forming from a single linear polyphosphoric acid chain

there exists or has existed a completely different and unknown set of chemical reactions leading to the formation of proteins. This implies that the laws of chemistry changed over time. Such a postulation is without support.

The formation of proteins

It is proposed that proteins are formed by the normal chemical reactions in biological cells. The principle chemical reactions in biosystems are hydration and dehydration in the breaking and forming of peptide and glycosidic bonds, dehydration in the formation of esters, reduction, oxidation, the release of carbon dioxide from the carboxylic acid group (decarboxylation) and the removal and decomposition of amino groups (deamination). The spatial arrangement of molecular groups forming organic compounds is also involved in these reactions. In order that hydration and dehydration reactions can proceed an effective hydration/dehydration agent whose properties also involve stereochemical characteristics must be present in cells. Polyphosphoric acid is the only known compound which exists in biological cells and which possesses the correct chemical and physical properties to be the principle compound in cellular hydration/dehydration reactions.

Polyphosphoric acid exists in various stereo forms and all of these forms undergo reversible hydration/dehydration[3]. as shown in figure 1. Phosphate is the dominant ion in mammalian intercellular fluid (TABLE 1). The presence of polyphosphates in the intracellular fluid of cells in the human and other mammalian metabolisms has been established[4-8]. In addition the next most dominant ion in mammalian cells is potassium. The concentration values given in the table show that 0.15 mole of potassium ion requires 0.05 mole of phosphate ion to form the normal potassium orthophosphate, namely $K_3(PO_4)$. The concentration of phosphate ion is in excess of this requirement. The concentrations of other cations present are insufficient to account for this discrepancy. These results mean that an alternative form of some phosphate ion exists in cells. It is known that potassium dihydrogen phosphate (KH_2PO_4) and dipotassium hydrogen phosphate (K_2HPO_4) possess a

Minireview

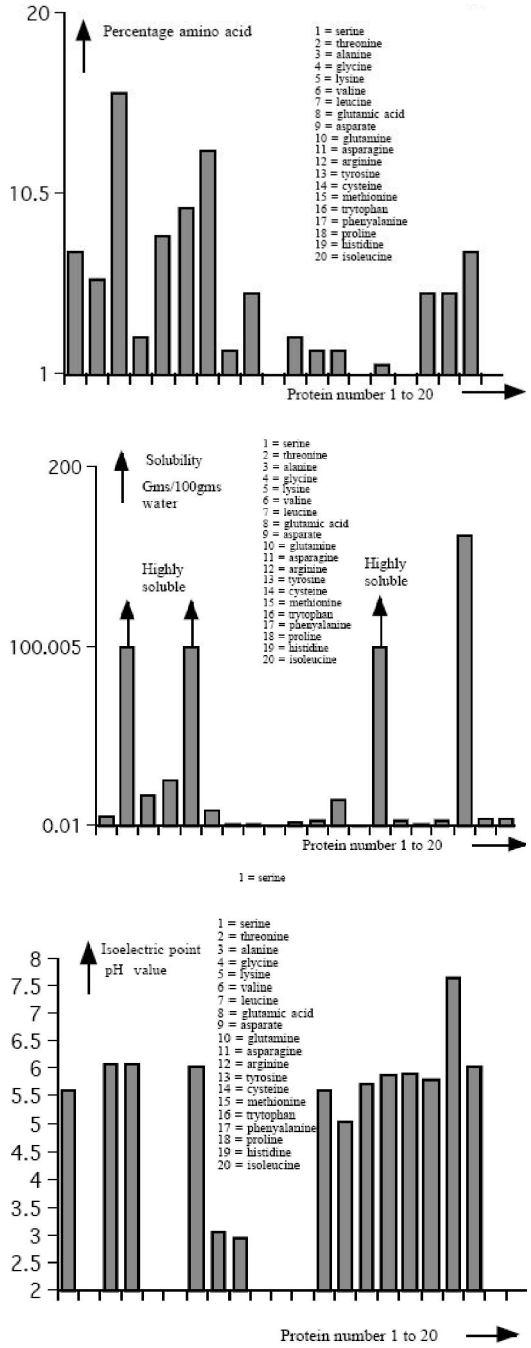

Figure 3 : The variation of solubility, isoelectric point and percentage of various amino acids in the amino acid sequence of a-haemoglubin protein

strong tendency to form poly-forms and adenine triphosphate is found in all cells and is a salt of polyphosphoric acid. It has been shown that in mixtures of water and phosphorus pentoxide the various forms of polyphosphoric acid are dominant when the molecular ratio of these two compounds is one to one.[3] Biological fluids are hydrophilic colloidal fluids and as a consequence the free water content of cells is low. These conditions will therefore encourage the existence and support the structural forms of polyphosphoric acids particularly in intracellular fluids. Polyphosphoric acid is formed from monophosphoric acid by the removal of water from the latter. Water exits cells by osmosis or electro-osmosis. The former mode of transfer is supported by the observation that sodium ion is dominant ion in the intercellular fluid and the potassium is partly complexed as polyphosphates in the intracellular fluid as proposed. The later mode of transfer is supported by concentration and electrochemical potential differences of sodium ions and potassium ions (sodium-2.711volts, potassium -2.924 volts[9]) give rise to a potential difference known as the membrane potential which has a value of the order of 70 mV and which results in water leaving the cell by electro-osmosis. Either of these processes converts any monophosphoric in the cell to polyphosphoric acid giving rise to a continuous process. The movement of water towards the cell membrane will give rise to a gradient in the concentration of phosphoric ion such that the concentration of polyforms is highest at points remote from the cell membrane i.e. towards the centre of the cell[10]. The minimum stable length of linear polyphosphoric chains has been found to be 10 monophosphoric acid units linked together. Chains with more than 500 units are considered to convert to cyclic form and long linear chains are also considered to exist in the form of spirals[5]. The conditions in a given fluid (pH value, temperature, nature and concentration of cations present) are the factors which decide whether monophosphoric or polyphosphoric acid is the stable form[5]. The long chains of polyphosphoric acids become more stable against hydrolysis as the pH of the medium in which they exists increases.

Hydration and dehydration reactions involving this compound consist of the transfer of water (H^+ and OH^- ions) to and removal of water from cell compounds. This is demonstrated in the figure 2a which shows the formation of a protein under the control of polyphosphoric acid acting as a molecular template. Also shown is the formation of a link between the formed protein and monophosphoric acid. A similar link is possible involving polyphosphoric acid. Proteins containing these linked molecules function as enzymes[11] The percentage of a given amino acid varies from protein to protein. Ionic properties and solubility of amino acids

TABLE 1 : Cellular ions

Intercellular				Intracellular			
Cations	Mol/L	Anions	Mol/L	Cations	Mol/L	Anions	Mol/L
Na^+	0.14	Cl^-	0.105	Na^+	0.01	Cl^-	0.002
K^+	0.004	HCO_3^-	0.05	K^+	0.15	HCO_3^-	0.008
Mg^{++}	0.004	PO_4^{--}	0.006	Mg^{++}	0.05	PO_4^{--}	0.285
Ca^{++}	0.01	SO_4^{--}	0.002	Ca^{++}	0.006	SO_4^{--}	0.05
Organic acid	0.006			Organic acid	0.008		
Protein	0.012			Protein	0.055		

Data from reference 17

TABLE 2 : The physical and chemical properties of amino acids

Amino acid	First ionisation constant pK_1	Isoelectric point pH	Solubility 25°C, 100gms water	Crystal structure
DL-Alanine	9.866	6.07	16.72	Orthorhombic
L-Aspartic acid	3.86	2.98	0.5	Rhombic
L-Cystine	8	5.02	0.01096	Hexgonal
L-Glutamic acid	4.07	3.08	0.864	Orthorhombic
Glycine	9.788	6.064	24.99	Monoclinic
L-Histidine	9.18	7.64	4.19	Not known
Hydroxy-L-Proline	9.73	5.82	36.11	Not known
DL-Isoleucine	9.758	6.038	2.229	Not known
DL-Leucine	9.744	6.036	0.991	Not known
DL-Methionine	9.21	5.74	3.31	Hexagonal
DL-Phenyalanine	9.24	5.91	1.411	Not known
DL-Serine	9.15	5.6	5.023	Monoclinic
L-Tryptophan	9.39	5.88	1.136	Not known
L-Tyrosine	9.11	5.63	0.0351	Not known

Data from reference 9

also varies (TABLE 2). The solubility is a function of pH[12,13] and has a minimum at the isoelectric point. The pH value of the intracellular fluid in mammalian cells has a value of 6.9[14] and the pH value of the isoelectric points of most amino acids varies around a pH value of 6.0. A given amino acid will undergo dehydration to form a peptide link at the pH value of the isoelectric point as a result of the peptide bond formation involving the transfer of both hydrogen and hydroxyl ions (H^+, OH^-). At the isoelectric point the concentrations of these ions is equal. Polydiphosphoric acid has four replaceable protons with the values of the dissociation constants pK1 = 1.7, pK2 = 1.95, pK3 = 5.98 and pK4 = 8.74. Monophosphoric acid has three replaceable protons and the values of the dissociation constants are pK1 = 2.12, pK2= 7.21 and pK3 = 12.3[3]. Comparison of the same constants for each acid shows that when the monophosphoric acid groups are formed the pH of the volume of intracellular fluid in which proteins are forming increases. Alternatively when dehydration of the monophosphoric acid giving rise to polydiphosporic acid occurs the pH of the same volume of fluid decreases. These conditions apply to all the polyforms of this acid. It follows that protein formation, that is, removal of water by polyphosphoric acid to give the peptide bond and monophosphoric acid, results in a change in the pH of the intracellular fluid. Where the resulting in a change of pH is small and a sufficient concentration of molecules of the same amino acid are available these will continue to link. When a sufficient change in pH value occurs this prevents the same amino acid joining by altering the relative amounts of the hydrogen and hydroxyl ions associated with the structure at pH values removed from the isoelectric point. The next amino acid with characteristics compatible with the new pH conditions joins and releases another monophosphoric acid molecule. Further change in pH has the result of defining the characteristics of the next amino acid to join. It is also possible for the pH value of the intracellular fluid to return to the value which favors the joining of previously linked amino acids to the forming protein. The length of a protein will cease to extend when the change in pH gives rise to a value which is not favorable to the isoelectric pH of any of the amino acids in or reaching the cell. In the case of amino acids displaying side chain carboxylic and amine groups, for example lysine and arginine, peptide linkages between protein strands are formed under the dehydrating action of polyphosphoric acid. Side chain carboxylic and amine groups are not ordered with the same linear separation and at the same spatial angle in all amino acids. Peptide linkages formed between these groups in different protein stands will result in links between main strands giving rise to a complex three dimensional structure.

The percentage of a given amino acid varies from protein to protein as shown in figure 3 for a-haeomoglobin which allows the spatial concentration of cell amino acids in the intracellular fluid during the formation of a-haeomoglobin can be assessed. Glycine with a high solubility occurs in a lower percentage of the protein than leucine with a low solubility. This indicates that leucine is present in the cell at a higher concentration. Specified

Minireview

sequences of the purine and pyrimidine bases composing either DNA, RNA or both are recorded as being related to specific amino acids by direct observational comparison of a sequence of bases in the nucleic acid from particular cells alongside the sequence of amino acids in a protein produced from the same cells[15]. On the basis the model above both of these compounds (nuclei acid and protein) can be produced simultaneously and in relation to one another. This is shown in figure 2b and any relationship between the bases of the nucleic acid and a particular protein or proteins is the result of the physical and chemical characteristics plus the stereo nature of components in conjunction with the physical and chemical conditions in the volume of intracellular fluid where the reaction takes place. This is the case for the formation of histone proteins in the cell nucleus.

DISCUSSION

From the above it is concluded that normal chemical reactions take place in the cells of human, mammalian and other metabolisms and that the nucleic acids are products of these reactions and play no part in the organisation and control of the nature and concentration of other compounds produced in these cells. The properties of polyphosphoric acids and the dominance of phosphate ions in living cells indicates that this element plays an important role in the formation of proteins in living cells. The repeated experimental observation that monophosphoric and polyphosphoric acid groups are persistently associated with proteins and other cell products supports this conclusion. The particular amino acid sequence in any protein produced in a living metabolism is the result of the relative concentrations of amino acids reaching the cells by transport in metabolic fluids such as the blood circulation in animals. The origin and concentration of these acids are metabolic reactions or the diet which in turn is specific to the lifeform involved. The transfer of this mechanism between generations derives from the arrangement and resulting physical repulsion of the DNA molecules in the cell nucleus which defines the nature and characteristics of the lifeform. The arrangement means that the formation of these molecules eventually results in cell division. It has been shown that the rate of division of any cell cell decides the number of these cells in the metabolism and the amount of the cell product e.g. proteins, which result in amount of muscle, bone and tissue present in the metabolism[16]. The actual base sequence of DNA in an individual metabolism is decided by the linking of DNA molecules or separate lengths of these molecules present in the sperm or equivalent male component with the same units present in the ovum or equivalent female component at the time of fertilisation[16]. This is true of both animal and plant lifeforms. From this it follows that any natural phenomena which interferes with and alters the nature and nucleus arrangement of these units will produce evolutionary effects.

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