

tained in a hypothetical framework of prebiological conditions. Added support for a protein-like structure of the polymer is found in positive biuret tests, infrared absorption spectra, and a mean chain weight of 4900.

Shortly after this project on thermal syntheses of peptides was begun, unexpected results under these same conditions led to other investigations (FOX, JOHNSON, and MIDDLEBROOK<sup>18</sup>). There was observed the appearance of amino acids,  $\alpha$ - and  $\beta$ -alanine, not present in the original. This result suggested that our known family of amino acids may have originated by thermal conversion and rearrangement. One biochemical thing led to another and a thermal reaction flowsheet as in Figure 2 was assembled. These are some of the reactions which have been studied; the solid lines represent those for which the details have been published. It was found that aspartic acid can arise thermally from the Krebs Cycle acid, malic acid, by reaction with ammonia or urea and that aspartic acid is converted to  $\alpha$ - and  $\beta$ -alanine. An unexpected product of especial interest was ureidosuccinic acid (FOX, JOHNSON, and VEGOTSKY<sup>9</sup>).

This partial chart includes many thermal products identical to those found in organisms, except for lack of optical activity in some. The reactions are also similar and, most strikingly, the sequences of thermal reactions resemble those of a generalized biosynthesis.

These unified results indicate in principle how the anabolic reactions and protein, somehow functioning as enzyme, could arise jointly. The appearance of ureidosuccinic acid suggests the biosynthesis of genic nucleic acid inasmuch as ureidosuccinic acid is now a recognized biological intermediate for pyrimidines (LIEBERMAN and KORNBERG<sup>19</sup>). From this it is possible to visualize the generation of anabolic reactions, enzymes, and genes in a reflexive chemical memory mechanism (FOX, VEGOTSKY, HARADA, and HOAGLAND<sup>20</sup>). This picture is essentially the reverse of the gene-enzyme-reaction system of BEADLE<sup>21</sup> *et al.* The entire integrated picture is of course incomplete, but it is brought into sharper focus by the finding that all of the common amino acids can be copolymerized under selected thermal conditions into a single product suggestive of protein.

Purely biological evidence for the thermal origin of organisms, although not conclusive, can be found in the literature. The proposal that life began in thermal waters has been offered by several biologists, notably COPELAND<sup>22</sup>. One criticism of chemical or biological theories emphasizing thermal origins is that biological systems cannot withstand such elevated temperatures. One answer to this problem is the fact that some bacteria and algae normally inhabit nearly boiling hot springs. These, according to Copeland, are the most primitive organisms. Se-

condly, GREENSTEIN and HOYER<sup>23</sup>, and also HAMER<sup>24</sup>, showed that many substances inhibit the thermal coagulation of protein; notably nucleic acids do this. In attempting to understand the origin of physiological systems, it may be necessary therefore to understand the special influences of molecular interactions quite as fully as the generation of substances and reactions.

Despite increasing numbers of experimental demonstrations, more than usual uncertainty attends any interpretations in the subject matter of biochemical origins. A true understanding of origins however offers much promise of systematizing the tremendously ramified mass of biochemical knowledge and is to be sought for this reason alone.

At the most the picture which has been inferred represents essentially the way in which biochemical systems originated. At the least, it presents in relatively complete outline an internally and externally consistent picture of how biochemical systems, and by self-directed extrapolation, life (FOX<sup>16</sup>) could have originated, when one invokes a modulation from a hypohydrous magma to an aqueous system.

At the non-interpretative level, the studies have revealed ways and means of producing with relative ease a large variety of peptides which command interest in a number of potential applications.

#### Zusammenfassung

Bei Überschuss von Glutaminsäure und Asparaginsäure werden zahlreiche Aminosäuren thermisch kopolymerisiert. Das Studium der Reaktionen und Nebenreaktionen führt zu einer Theorie über den thermischen Ursprung biochemischer Systeme.

<sup>23</sup> J. P. GREENSTEIN and M. L. HOYER, *J. biol. Chem.* **182**, 457 (1950).

<sup>24</sup> D. HAMER, *Biochem. J.* **56**, 610 (1954).

#### Corrigenda

ROSHAN J. IRANI and K. GANAPATHI: *The Effect of Glycerol on the Biosynthesis of Benzylpenicillin by the Washed Cells of Penicillium chrysogenum*, *Exper.* **14**, fasc. 9, 329 (1958).

The third entry in Table III should read: PA (0.05%) + glycerol (1%) + KCN (0.005 M).

H. GROSSFELD: *Fat Formation and Glycolysis in Tissue Culture. Action of Hydrocortisone*, *Exper.* **14**, fasc. 10, 371 (1958).

There has been an error in the first column of page 372 in line 9 from below. This line should read: ... treated with hydrocortisone in concentration of 125 micrograms/ml.

<sup>18</sup> S. W. FOX, J. E. JOHNSON, and M. MIDDLEBROOK, *J. Amer. chem. Soc.* **77**, 1048 (1955).

<sup>19</sup> I. LIEBERMAN and A. KORNBERG, *Biochim. biophys. Acta* **12**, 223 (1953).

<sup>20</sup> S. W. FOX, A. VEGOTSKY, K. HARADA, and P. D. HOAGLAND, *Ann. N. Y. Acad. Sci.* **69**, 328 (1957).

<sup>21</sup> G. W. BEADLE, *First R. E. Dyer Lecture* (U. S. Government Printing Office, Washington 1951).

<sup>22</sup> J. J. COPELAND, *Ann. N. Y. Acad. Sci.* **36**, 1 (1936).