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Evolution

Evolution of the first metabolic cycles

(chemoautotrophy/reductive citric acid cycle/origin of life/pyrite)

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ABSTRACT **There are two alternatives concerning the origin of life: the origin may be heterotrophic or autotrophic. The central problem within the theory of an autotrophic origin is the first process of carbon fixation. I here propose the hypothesis that this process is an autocatalytic cycle that can be retrodictively constructed from the extant reductive citric acid cycle by replacing thioesters by thioacids and by assuming that the required reducing power is obtained from the oxidative formation of pyrite (FeS_2). This archaic cycle is strictly chemoautotrophic: photoautotrophy is not required. The cycle is catalytic for pyrite formation and autocatalytic for its own multiplication. It is a consequence of this hypothesis that the postulated cycle cannot exist as a single isolated cycle but must be a member of a network of concatenated homologous cycles, from which all anabolic pathways appear to have sprung.**

Within the prevailing theory of a heterotrophic origin of life in a presumptive prebiotic broth, the autotrophic processes of carbon fixation are seen as a late invention (1), coming perhaps just in time before the depletion of the broth. A radical alternative, the theory of a chemoautotrophic origin of life, has been outlined in two earlier papers (2, 3). The first of these papers (2) is centered on the problem of the aboriginal source of reducing power for carbon fixation; it sees this source in the oxidative formation of pyrite (FeS_2) from ferrous sulfide (FeS) and hydrogen sulfide (H_2S, or SH^-). In the present paper I shall denote reactions dependent on this energy source briefly as "pyrite-pulled reactions." The second paper (3) is centered on the problem of the requisite physical containment of the organic products of carbon fixation by surface bonding (as a precursor of cell containment), so that they are kept in sufficient proximity for subsequent metabolic interaction. It argues that the products of carbon fixation become in their nascent state anionically bonded to the positively charged pyrite surface, where they establish a growing surface metabolism.

One of the main open problems within this theory of a pyrite-pulled chemoautotrophic origin of life is the constitution of the first autocatalytic cycle, capable of evolving by the grafting of additional cycles. A hypothetical solution to this problem is offered here. The method used is that of a reconstruction of precursor pathways by retrodiction from extant pathways (4). Popper's historical method of situational analysis (5) has been used, as well as his method of evaluating theoretical progress by the increase of the explanatory power (6).

Among the extant metabolisms there are two genuinely autocatalytic carbon fixation cycles, which multiply the CO_2 acceptor in the course of the cyclic reaction: the reductive pentose phosphate cycle and the reductive citric acid cycle (7–11). The former has been considered to be of lesser antiquity, since it is not found to be operative in the kingdom of archaebacteria (12). The latter has been found to be operative in the eubacteria *Chlorobium limicola* (7), *Hydrogenobacter thermophilus* (13), and *Desulfobacter hydrogenophilus* (14) and also in the sulfur-associated archaebacteria *Thermoproteus neutrophilus* (15) and, partly demonstrated, in *Sulfolobus brierleyi* (16). As suggested by Kandler and Stetter (16) and previously by Hartmann (17), it may be considered to be of great antiquity and the evolutionary precursor of the oxidative Krebs cycle. It is here conjectured to be the extant candidate for the reconstruction of the archaic autocatalytic cycle of carbon fixation.

The presently accepted form of the extant reductive citric acid cycle is shown in Fig. 1 in a somewhat unusual representation, twisted in an 8. I am using this representation to draw attention to its inherent simplicity, since it consists of two analogous halves. Beginning with succinate (Su), we find that in the course of one complete turn four molecules of carbon dioxide (CO_2) are converted into a second molecule of succinate. This brings out the important fact that this cycle is autocatalytic: it doubles with every turn.

It will now be shown that starting from this extant enzymatic cycle we can reconstruct the hypothetical archaic nonenzymatic precursor cycle shown in Fig. 2 in terms of five (geo)chemical postulates. It should be stressed, however, that this does not amount to a reduction to chemistry. On the contrary, we arrive at these postulates by retrodiction from extant biochemistry.

POSTULATE 1. *The geochemical setting of the origin of the archaic precursor cycle is an anaerobic aqueous environment, rich in H_2S (or HS^-) and in contact with heavy metal sulfides and pyrite.*

In such an environment, the organic constituents of the extant reductive citric acid cycle coexist with thioanalogues, according to the following chemical theorems, which can be derived from *Postulate 1* in conjunction with well-established chemical facts.

THEOREM 1. *The carboxylate groups (—COO^-) are in equilibrium with thiocarboxylate groups (—COS^-)* (3).

THEOREM 2. *The compounds with carbonyl groups (and their hydrated forms and* enol *forms) coexist with thioanalogous compounds, as shown in Fig. 3a.*

THEOREM 3. *The dehydration–hydration equilibria via aconitate and fumarate* (Fig. 1) *are in competition with reactions of addition of H_2S* (Fig. 2).

THEOREM 4. *The positively charged surfaces of the heavy metal sulfides and of pyrite bind the anionic organic constituents of the archaic cycle via their anionic carboxylate (—COO^-), thiocarboxylate (—COS^-), or thiolate (—S^-) groups in the nascent state* (3).

Theorem 4 was introduced (3) as a main postulate of the theory of surface metabolism. The recent demonstration by Dameron *et al.* (18) of a strong surface bonding of the pentapeptide $(\gamma\text{-Glu-Cys})_2$-Gly onto CdS crystallites at around pH 7, but not below pH 3.5, is regarded as an experimental corroboration of this theorem.

THEOREM 5. *The surface-bonded organic constituents establish a nonenzymatic surface-bonded reaction system (surface metabolism)* (3) *in which all reactions are class reactions* (cf. refs. 19–21) *and in which all surface-bonded products are*

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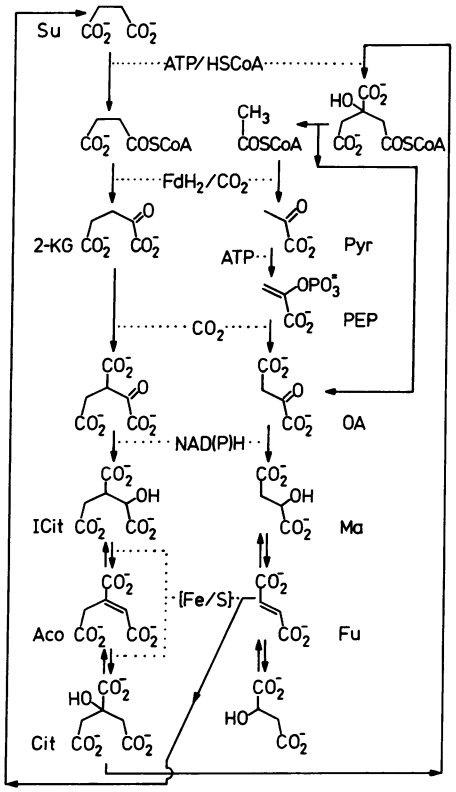

FIG. 1. Twisted representation of the extant reductive citric acid cycle. Su, succinate; 2-KG, 2-ketoglutarate; ICit, isocitrate; Aco, aconitate; Cit, citrate; Pyr, pyruvate; PEP, phospho*enol*pyruvate; OA, oxaloacetate; Ma, malate; Fu, fumarate; FdH_2, reduced ferredoxin; [Fe/S], enzyme with an iron-sulfur cluster; HSCoA, free coenzyme A. (The reactions are not shown as stoichiometrically complete.)

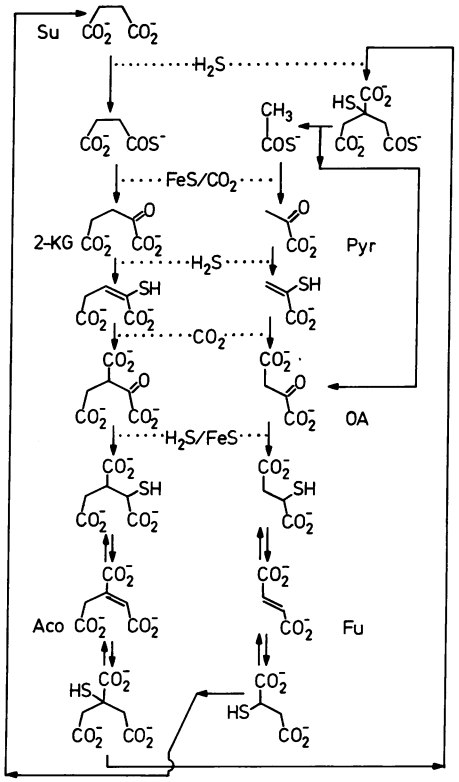

FIG. 2. Proposed archaic reductive citric acid cycle wherein the compounds with SH groups coexist with those having OH groups (not shown) and wherein the carbonyl groups coexist with thio-derivatives (partly shown).

subject to further reaction, giving rise to recursive reaction sequences.

THEOREM 6. *In the archaic surface-bonded cycle the aldol–retroaldol equilibrium of the surface-bonded thio form of citrate shown in Fig. 2 is less favorable for cleavage than in the corresponding solution equilibrium* (cf. ref. 3).

POSTULATE 2. *In the geochemical setting of the origin of the archaic precursor cycle, pyrite (FeS_2) is the thermodynamically most stable iron sulfur compound, but its formation by hydrogen evolution (e.g., $FeS + H_2S \rightarrow FeS_2 + H_2$) is slow relative to the reactant feeding rate.*

POSTULATE 3. *The geochemical setting of the origin of the archaic precursor cycle is rich in CO_2 and pyrite formation is accelerated by the reductive carboxylation of surface-bonded thiocarboxylates* (3), *as notionally shown in Fig. 3b.*

POSTULATE 4. *In the geochemical setting of the origin of the archaic precursor cycle surface-bonded 2-thioketocarboxylates undergo β-carboxylation, as notionally shown in Fig. 3c.*

POSTULATE 5. *In the geochemical setting of the origin of the archaic precursor cycle pyrite formation is accelerated by the reductive desulfuration of surface-bonded thioorganic constituents, replacing —SH with —H, as notionally shown in Fig. 3d.*

Postulate 5, when applied to the thioanalogues of the extant cycle, gives rise to the following chemical theorems.

THEOREM 7. *The (thio)carbonyl groups undergo pyrite-pulled reduction to alcohol groups* (3) *or thiol groups.*

THEOREM 8. *The thiol groups undergo pyrite-pulled desulfuration (e.g., $\rangle CH—SH \rightarrow —CH_2—$).*

Incidentally, a reduction of a carbonyl group to a methylene group by the oxidation of H_2S to elemental sulfur has been demonstrated to occur with α-diketones but not with monoketones (22). One of the interesting aspects of this reconstruction of the archaic cycle by these postulates is the replacement of the relatively weak reducing agents [reduced ferredoxins, NAD(P)H, FADH] of the extant cycle by the strong reducing agent FeS/H_2S. This has the important consequence that an energy coupling to ATP hydrolysis is obviated. It will now be shown that the overall archaic cycle

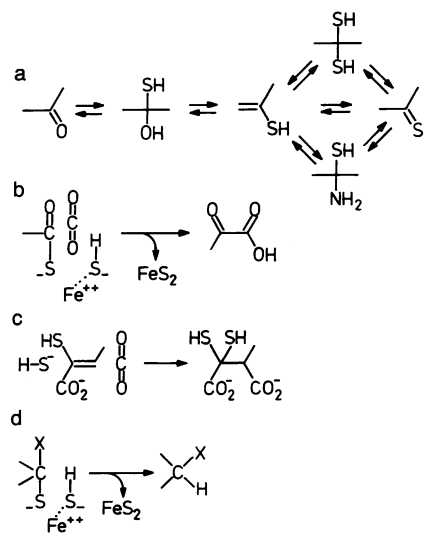

FIG. 3. Notional reaction mechanisms for explaining theorems. (*a*) *Theorem 2* (the reaction components H_2O, H_2S, and NH_3 are omitted). (*b*) *Postulate 3*. (*c*) *Postulate 4*. (*d*) *Postulate 5*; X = OH or SH (*Theorem 7*); X = H (*Theorem 8*); X = NH_2 (*Theorem 9*); X (jointly with a free bond) = O= (*Theorem 10*); or X = H_2O_3PO— or H_2O_3PS— (*Theorem 11*).

is indeed exergonic. The thermodynamic calculations rely on the formulae given by Thauer *et al.* (23) and on the standard free energies of formation ΔG_f°. In contrast to my earlier papers (2, 3), here I use the most recent data (rounded) of ΔG_f°(pyrite) = −160.1 kJ/mol (24) and ΔG_f° (FeS α) = −93.8 kJ/mol (25), ΔG_f° (H_2S aqueous) = −27.9 kJ/mol, and ΔG_f° (HS^- aqueous) = +12.1 kJ/mol (26). We obtain for the evolution of gaseous hydrogen at pH 0 and 25°C:

$$FeS + H_2S \rightarrow FeS_2 + H_2 \quad \Delta G^\circ = -38.4 \text{ kJ/mol}.$$

The reaction is exergonic. With increasing pH, SH^- participates increasingly. However, up to about pH 8, the value of ΔG° does not change substantially. Above pH 8, the reaction becomes increasingly less exergonic. It is of interest that in the acidic pH range a temperature increase (e.g., to 125°C) renders the reaction more exergonic, as calculable from the values of the standard enthalpy of formation (ΔH_f°) (24, 26). This means that the energy source of pyrite formation is thermoacidophilic and suitable for the thermophilic universal ancestors proposed by Woese (27).

Next, we calculate the overall free energy of reaction of the proposed archaic cycle, based on the free energy of formation data compiled by Thauer *et al.* (23), whereby all carbon constituents are taken in the aqueous state, while H_2O is taken in the liquid state. One obtains the following values of ΔG° (for pH 0) and $\Delta G^{\circ\prime}$ (for pH 7) with hydrogen as reducing agent:

$$4CO_2 + 7H_2 \rightarrow (CH_2\text{—}COOH)_2 + 4H_2O$$

$$\Delta G^\circ = -151 \text{ kJ/mol}$$

and

$$4HCO_3^- + 2H^+ + 7H_2 \rightarrow (CH_2\text{—}COO^-)_2 + 8H_2O$$

$$\Delta G^{\circ\prime} = -160 \text{ kJ/mol}.$$

The pyrite-pulled cycle is much more exergonic:

$$4CO_2 + 7H_2S + 7FeS \rightarrow (CH_2\text{—}COOH)_2 + 7FeS_2 + 4H_2O$$

$$\Delta G^\circ = -420 \text{ kJ/mol}$$

and

$$4HCO_3^- + 2H^+ + 7H_2S + 7FeS \rightarrow$$

$$(CH_2\text{—}COO^-)_2 + 7FeS_2 + 8H_2O$$

$$\Delta G^{\circ\prime} = -429 \text{ kJ/mol}.$$

For concentrations of CO_2 (≈5.7 mmol/liter) and H_2S (≈7.5 mmol/liter) that are typical for vent waters (28) the values are still highly exergonic: $\Delta G = -284$ kJ/mol; $\Delta G' = -293$ kJ/mol. With increasing temperature, this reaction becomes less exergonic. However, the overall cycle is still highly exergonic at the typical growth temperatures of thermophilic bacteria. This result is of the greatest interest. It means that the proposed archaic cycle in its overall operation is far from chemical equilibrium. It therefore satisfies the condition of irreversibility which has been established by Prigogine (29) and Eigen (30) as a necessary condition for all forms of life.

The thermodynamic feasibility of the proposed cycle depends not only on the overall free energy but also on that of the individual steps. An exergonic cycle will not run if it is very "bumpy." In the extant cycle, the conversion of succinate to 2-ketoglutarate is endergonic and it requires the formation of a thioester by coupling to ATP hydrolysis. In the proposed archaic cycle, this conversion is close to equilibrium without such energy coupling, since it is pulled by pyrite formation. For pH 7, we obtain $\Delta G^{\circ\prime} = +6.6$ kJ/mol and the free energy approaches a minimum value close to zero if the pH is lowered.

The two most endergonic steps in the proposed archaic cycle are the two β-carboxylations. For the β-carboxylation of pyruvate at pH 7, a value of $\Delta G^{\circ\prime} = +27$ kJ/mol is calculated. It should, however, be remembered that, in the presence of H_2S, pyruvate and oxaloacetate exist (partly) in their enethiol forms (*Theorem 2*), whose β-carboxylation may be less endergonic than that of the keto acids. In the extant cycle, the endergonic step of the β-carboxylation of pyruvate is overcome by energy coupling with ATP hydrolysis via phospho*enol*pyruvate (PEP). It is of interest that for nucleophilic condensations of PEP, Ganem (31) has proposed that PEP is first converted to an enethiol ether of pyruvate with a cysteinyl group of an enzyme and that this enethiol ether is the actual nucleophile. In any event, each of the two β-carboxylations in the archaic cycle is followed by an exergonic pyrite-pulled reduction which pulls the β-carboxylation over the hill.

The above considerations show that from a thermodynamic point of view the archaic cycle may operate best at a pH below about 8. The requirement of surface bonding seems to exclude a pH below about 3. The most favorable pH range can be specified further if we consider kinetic requirements. The nucleophilicity of HS^- is much higher than that of H_2S. Therefore, the pH should be sufficiently high for the existence of a sizable HS^- concentration. This is true at 25°C for a pH above about 5.5 and at 125°C for a pH above about 4.5. Also, the β-carboxylation and retroaldol cleavage reactions are promoted by pH increase. Of course, the influence of the reaction conditions [pH, pressure, temperature, reactant concentrations, salinity, catalytic trace elements such as Se or heavy metal ions (notably Co^{2+} and Ni^{2+}), and cofactors such as surface-bonded basic or lipophilic constituents (3)] on the performance of this archaic cycle can be determined only by a program of theory-guided experiments. But once these conditions are known, they may indeed be used for tuning the cycle into rotation in an attempt to initiate an artificial origin of life.

So far, the archaic cycle (Fig. 2) has been reconstructed as a notional analogy to Fig. 1. It requires, however, corrections in view of the fact that in a nonenzymatic surface reaction system all reactions are class reactions (*Theorem 5*), so that the constituents undergo not singular reactions but several competing reactions. Turning first to citrate, we note that the surface-bonded thioanalogue of citrate may undergo reductive carboxylation and subsequent β-carboxylation prior to retroaldol cleavage. Indeed, such alternative pathway should predominate in view of *Theorem 6* and the facilitation of retroaldol cleavage by additional carboxylations. It is of interest that the products of this alternative pathway are stronger surface bonders as compared to weakly bonding acetate. In another alternative pathway, malate may acquire a $—COS^-$ group and undergo reductive carboxylation leading eventually to citrate and thus bypassing the formation of succinate.

A number of alternative reactions of this kind are possible. Jointly they establish a complex cyclic reaction network. A most important aspect of this network has been singled out in Fig. 4. It consists of a concatenation of a recursive series of chemically homologous cycles. *Theorems 7* and *8* apply not only to oxaloacetate but also to 2-ketoglutarate which gives rise to glutarate. This in turn is subject to the reaction of *Theorem 1* and *Postulate 3*, which means that the archaic succinate-based citric acid cycle $\mathcal{C}^1$ is concatenated with a glutarate-based homocitric acid cycle, $\mathcal{C}^2$. A portion of this cycle in the oxidative direction is still found in the aminoadipate pathway to lysine. In $\mathcal{C}^2$, the retroaldol cleavage

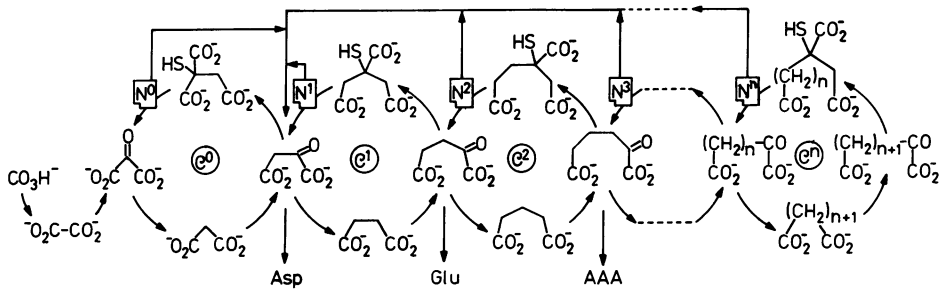

FIG. 4. Concatenated series of chemically homologous archaic cycles $\mathcal{C}^1$ to $\mathcal{C}^n$ and a priming pathway including for formal completeness the unlikely norcycle $\mathcal{C}^0$; all are in simplified representation, wherein $N^0, \ldots, N^n$ denote the reaction pathways involving retroaldol cleavage. AAA, aminoadipic acid.

leads to the regeneration of 2-ketoglutarate and to the formation of oxaloacetate which enters $\mathcal{C}^1$. Therefore, $\mathcal{C}^2$ is autocatalytic via $\mathcal{C}^1$. Generalizing this scheme, we come to a concatenation of higher and higher homologous cycles ($\mathcal{C}^3$, $\mathcal{C}^4$, . . . $\mathcal{C}^n$) proceeding via 2-ketopimelate, 2-ketosuberate (32), . . . , to longer and longer dicarboxylates up to those akin to diabolic acid, which is found in the cell membrane of *Thermotoga maritima* (33), and thus to a self-lipophilization of the pyrite surface (3). These homologous cycles may be seen as producing also the precursors for such important coenzymes as cofactor B (32), lipoic acid, and biotin.

The proposed archaic cycle requires for initiation the availability of molecules of at least one of its constituents. The initiation time (induction period) depends on the probability with which one such molecule can be assumed to be produced by a priming reaction within the geochemical setting of the archaic cycle. Fig. 4 shows an example for such a priming reaction sequence in which all constituents are surface bonders. Without introducing any additional postulate, Fig. 4 merely assumes a small but finite propensity for a molecule of carbon dioxide to undergo (via thiocarbonate) a pyrite-pulled reductive carboxylation to oxalate, which is again converted by a sequence of pyrite-pulled reductive carboxylations and reductions via ketomalonate and malonate to oxaloacetate. For the sake of formal completion, Fig. 4 includes a norcycle $\mathcal{C}^0$, in which, however, the carboxylation of oxaloacetate is highly unlikely.

The above priming sequence follows the same pattern of carbon fixation as $\mathcal{C}^1$, whereby reduction occurs in conjunction with C—C bond formation. A completely different priming reaction pathway (not illustrated) is thinkable, whereby a sequence of reductions of one-carbon units down to the level of methylmercaptan (methanethiol) occurs, followed by C—C bond formation with carbon monoxide (CO) to produce thioacetate. This priming reaction sequence is suggested by the extant pterin-dependent reductive acetyl–CoA pathway, which is found in eubacteria as well as in archaebacteria (12).

One of the most important requirements for an evolution is the possibility of branch reactions. From the point of view of the archaic autocatalytic cycles, these are reactions of decay since they lower the multiplication rate. If they predominate, the autocatalytic cycles become extinguished. However, from the point of view of the extant autotrophic metabolisms, these branch reactions serve as starting points for all anabolic pathways.

A most important class of branch reactions is caused by the presence of ammonia units, due perhaps to a process of pyrite-pulled nitrogen fixation (3), leading to the formation and accumulation of amino acids and other nitrogen bases (which may even be required for priming the autocatalytic cycle). The formation of amino acids can be explained by *Theorem 2* (Fig. 3*a*) and *Theorem 9* (Fig. 3*d*), which is derived from *Postulate 5*.

THEOREM 9. *Geminal thiol-amino groups* ($H_2N—\overset{|}{C}—SH$) *undergo pyrite-pulled reduction to amino groups* ($—CHNH_2—$) (Fig. 3*d*).

In this fashion, the archaic cycle $\mathcal{C}^1$ produces aspartate and glutamate, which are surface bonders, and alanine, which is a non-surface bonder. The homologous cycle $\mathcal{C}^2$ produces 2-aminoadipate, the precursor of lysine.

Next, we consider that many extant anabolic pathways involve the reduction of carboxylate groups via phosphoanhydride and thioester activation to aldehyde groups. This reaction can be retrodictively converted into an archaic precursor reaction by *Theorem 10*, derivable from *Postulate 5*.

THEOREM 10. *Thiocarboxylate groups* ($—COS^-$) *undergo a direct pyrite-pulled reduction to aldehyde groups* ($—CHO$) (Fig. 3*d*).

By virtue of *Theorem 10*, we arrive not only at the glutamate and aspartate families of the amino acids but also at the origin of the tetrapyrrole pathways. More importantly, by virtue of *Theorems 10* and *7*, the carboxylate group at one end of a long-chain dicarboxylate may be reduced to a primary alcohol group. This gives rise to the first bipolar lipids, akin to the long-chain ω-hydroxyalkanoic acid found in the cell membrane of *Thermotoga maritima* (34). These are detached from the surface at the alcohol end, and they accumulate to form monolayer membrane patches attached to the pyrite surface. As an amendment to my earlier proposal (3), these may well be considered the oldest membranes in the history of life. Finally, even the origin of substrate-chain phosphorylation may be reconstructed as a branch of the archaic cycles by means of the following theorem, derivable from *Postulate 5*.

THEOREM 11. *Geminal thiol-phosphate groups* ($H_2O_3P—\overset{|}{Y}—\overset{|}{C}—SH$; $Y = O$ *or* S) *undergo pyrite-pulled reduction to phosphate ester or thioester groups* ($\rangle CH—Y—PO_3H_2$).

I will now sketch briefly how the proposed archaic autocatalytic cycle could have evolved into the extant reductive and oxidative citric acid cycles. The general course of biochemical coevolution from a surface metabolism with the appearance of semicellular structures, a genetic machinery, and competent enzymes has been previously outlined (3). In the course of this coevolution, at least the archaic cycle $\mathcal{C}^1$ and a portion of the homologous cycle $\mathcal{C}^2$ become "enzymatized" step by step and lifted off the pyrite surface. For this evolution, the appearance of polyanionic constituents (peptides, coenzyme A) with thiol groups ($—CH_2—SH$) is decisive. The thiol groups compete with hydrogen sulfide in its reactions with various constituents. Thus, surface-bonded anionic peptides with a plurality of cysteinyl units give rise to an evolutionary progression which proceeds from simple surface bonding through the capping of cluster-like microcrystallites (18) to the ligand-determined minimum clusters of the extant iron-sulfur proteins. Such clusters are still found in

the enzymes for the conversions between isocitrate and citrate and between fumarate and succinate, reminding us of their origin in a pyrite-bonded surface metabolism. One subclass of enzymes with iron-sulfur clusters, the ferredoxins, are of particular importance, since they can undergo reversible redox reactions. This means that ferredoxin cycling replaces pyrite dumping. Upon the appearance of ATP, activated CoA-thioester formation competes with thioacid formation. Now, a ferredoxin-dependent reductive carboxylation of a thioester, analogous to the pyrite-pulled reductive carboxylation of a thioacid, can be effected by reducing agents that are weaker than FeS/H_2S. The formation of the disulfide dianion (S_2^{2-}) of pyrite gives way to an intermediary formation of organic disulfides. Also, the formation of the heterodisulfide of coenzyme M and cofactor B in the conversion of fumarate to succinate (39) replaces the pyrite-pulled reduction. In the cytoplasm the (enzymatic) retroaldol cleavage via acetyl-CoA is favored, and the subsequent ATP-dependent formation of phospho*enol*pyruvate from pyruvate is the starting point for a large variety of anabolic branch pathways.

With the appearance of pterins, the extant reductive acetyl—CoA pathway comes into existence as a second carbon fixation pathway and as a supplement to the reductive citric acid cycle. It is linear in terms of the carbon fixation reactions and cyclic in terms of the recycling pterin carriers. It is autocatalytic only with respect to the biosynthesis of the pterins from the primary products of carbon fixation. This huge autocatalytic cycle includes the reductive citric acid cycle or a portion thereof. Further evolution is characterized by a number of takeovers. One of the two carbon fixation pathways is opportunistically interrupted by the abandonment of individual enzymes with a concomitant improvement of control functions. With the appearance of heterotrophic practices, the anabolic reductive carbon fixation pathways are reversed and converted into catabolic combustion pathways: the oxidative acetyl-CoA pathway (35) and the oxidative citric acid cycle which, in its oldest known version, uses ferredoxins as electron acceptors and the same ATP-citrate lyase as the reductive citric acid cycle (36) and whose dependence on lipoic acid with S—S bond formation is reminiscent of the formation of the disulfide ion of pyrite in the archaic cycle.

The reductive citric acid cycle has its origin in an extremely reducing anaerobic environment rich in H_2S. Its many later evolutionary modifications and the appearance of the acetyl-CoA pathways allow a stepwise emancipation from the narrow chemical confines of the original homestead of life. The conquering of environments, low on H_2S but still reducing, is at first accompanied by processes of biogenic H_2S formation from sulfur and sulfate, processes that serve for the acquisition of energy and for the establishment of a milieu sufficiently rich in H_2S. Finally, the conquering of nonreducing or even aerobic environments was possible only after the appearance of an entirely new autocatalytic cycle of carbon fixation, the Calvin cycle, or perhaps a variant thereof viewed by Kandler (37) as proceeding via the bisphosphate of the widely occurring branched sugar hamamelose. Through all these expansions by which life has become precariously detached from its original homestead and from the aboriginal metabolic processes, life seems to have conquered this world partly by changing it and partly by adapting to it (38). In this overall process, biochemical evolution and biogeographical expansion are seen as mutually dependent.

My gratitude goes foremost to my mentor Sir Karl Popper, on whose theory of situational analysis and scientific methodology my paper is based and without whose help it would have been neither begun nor finished. I am also deeply indebted to Georg Fuchs, especially for his suggestions concerning the presentation of the postulates, and to Otto Kandler, to Walter Siebert, and to Carl R. Woese, who proposed the search for the universal ancestor, the progenote.

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