P r e b i o t i c c h i r a l i t y

http://en.wikiversity.org/wiki/Prebiotic_chirality
http://en.wikiversity.org/wiki/Prebiotic_chemo-osmosis
http://en.wikiversity.org/wiki/Prebiotic_Petroleum

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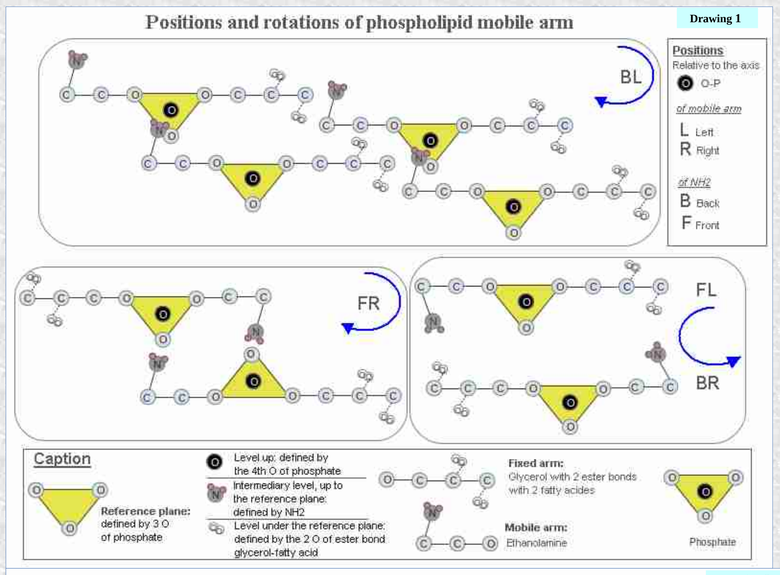
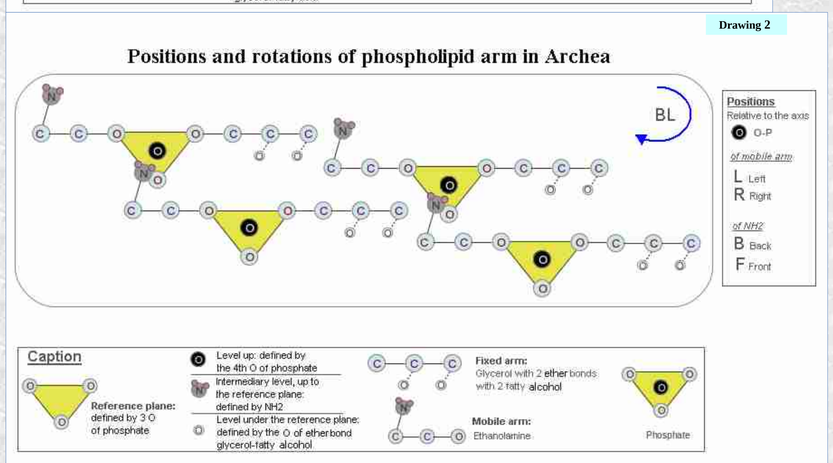
Drawing 1



Drawing 2



Drawing 1 & 2

Hypothesis of the mechanical origin of chirality in the phospholipids. here is treated the positioning of ethanolamine relatively to the phosphate. Its displacement towards the phosphate to establish hydrogen bonding causes a rotation. This hypothesis states that the clockwise rotation and positioning in single file of the phospholipid molecules, (RG box), results in bringing closer the two leaflets of the liposome, increasing its cohesion. In this configuration the serine chirality would be L, because its carboxyl can not be put under the reference plane defined by the phosphate (see caption in the drawing) and then would be near the carboxyl of two fatty acid molecules neighbors.

- **Positioning ethanolamine NH2 in the phospholipid molecule to obtain the greatest possible liposome cohesion.**

If you look toward the two free phosphate oxygens (see drawing 1), NH2 can occupy four possible positions: front-left (FL), left-back (BL), front-right (FR), right-back (BR). The BL is the only position to give a concatenation, with clockwise rotation, to a large number of PLD molecules.

Indeed, the 2 BR and FL positions rotate in the counterclockwise direction to reach the P. The other two positions rotate clockwise, but the FR position can put together only with a single other PLD, as NH2 and the two free oxygens of P are on the same side and neutralizes each other. On the other hand the position BL may concatenate PLD molecules while maintaining closer the two leaflets of the liposome by clockwise rotation.

- **The chirality of serine is L.**

The carbon of the carboxylic function of serine positions by electron repulsion. In fact if you draw the layout of several PLD neighbors (in top view, see drawing 1-RG), we see that the PLD of a row fit together in the adjacent row and the carbon of the amine (NH2) is in the same level and aligned along an oblique line, with the carbons bearing the esters of glycerols.

If we position the carboxyl group of serine under the plane defined by P (which would give the D-serine), then it will find itself surrounded by four oxygen atoms of two ester bonds belonging to two molecules of successive PLD. There will then, in a confined space, six oxygens for a single hydrogen for hydrogen-bond, in the best cases depending on the pH. As the two carboxylic functions of the two fatty acids are fixed, following the overall coherence of the liposome, that of serine, mobile, is expelled by electron repulsion automatically above the plane defined by the P. Then we have L-serine.

In the case of archaea is no longer electron repulsion that occurs, but the steric hindrance. The carbon of the carboxylic function of serine would be inserted between the heads of fatty acids, which move the 2 PLD of the adjacent row, greatly increasing steric hindrance. But the steric hindrance should be minimal for these prokaryotes, as will see also for the chirality of glycerol-P of the fixed arm.

- **Prebiotic glycerol-phosphate chirality.**

In Archaea, with the ether bond of fatty acids to minimize the steric hindrance, the 2 ether bonds may be on the same side as the two free oxygen atoms of P, to fill the vacant space beneath the half-reference plane defined by P (see Drawing 2). As the position of the serine relative to P is imposed mechanically, as we saw above, the amine (NH2) and oxygen from the first ether bond are, at once, each in a different half-plane, the chirality of the glycerol-P is then levorotatory such as serine, since they are superimposed by rotation. Is an L-glycerol-3P if the terminal alcohol was above glycerol as the carbon of serine CO2H is above the membrane. Or to reduce steric hindrance, the terminal alcohol glycerol must be below its carbons. It is then a D-glycerol-3P or L-glycerol-1P, which is found in archaea.

With the ester bond, the electron repulsion between it and the free oxygens of P automatically positions aliphatic chain closest to the P on the same side as the amine of serine, on the other side of the half-plane defined by the P (see Drawing 1-RG). And by steric hindrance and repulsion with the first, second aliphatic chain is on the side of the half-plane containing the P and under the carbons of glycerol for the same reasons of steric hindrance for archaea. Hence the L-glycerol-3P (sn-glycerol-3P) of bacteria or D-glycerol-1P (see KEGG [1] for synonyms).

P r e s e n t a t i o n o f t h e a r t i c l e

The phospholipid molecule (PLD): *see shaded boxes above for the demonstration from article.*

- The hydrophilic head of a phospholipid has two arms, the fixed one that contains glycerol esterified with two fatty acids, and the mobile one which carries cation (serine, ethanolamine, choline) or glycerol, which are attracted by the phosphate anion a neighbor LDP. In this article I demonstrate that chirality of the fixed arm is determined by the steric hindrance of the ester bonds (L-glycerol-3P) for bacteria and the ether bonds (D-glycerol-3P) for Archaea (see drawing 1 and 2).
- I also demonstrate that the chirality of the movable arm carrying the glycerol or serine is of the type levorotatory (L), bringing the two layers of the liposome when the arm moves to the anion P, thus increasing the mechanical cohesion of the liposome (see drawing 1).

● Synthesis of hydrophilic head:

In prebiotic:

- Presumably for the mobile arm esterification could be done after positioning. I also thought that ethanolamine should be prebiotic molecule to be esterified in the first because of its simplicity and requiring no necessary positioning a chiral carbon.
- By cons, for the fixed arm, difficulty in obtaining glycerol in the prebiotic oil, the fact that we must create two ester bonds on the same glycerol and to the large number of conformations to be treated if we were to go through a phosphate intermediate glycerol led me to issue the following hypothesis: "The DHA phosphate should be hydrogenated and esterified in place", poly-anionic surface will facilitate hydrogenation and keto-enol tautomerism of DHA will fit 2 fatty acids neighbors arranged head to tail (sharing two hydrogen bonds) to create the conformation of glycerol with minimal hindrance. In this case the L-glycerol-3P, from a possible hydrogenation of glyceraldehyde-3P will be fixed, while the D-glycerol-3P will be excluded, according to my above cited demonstration of chirality of glycerol-P.

In biotic: *see Figures 1 and 2 below.*

• The fixed arm:

The D-glyceraldehyde is not trapped by the membrane and serves homochirality sugars; Enzymes that bind glycerol are membrane (ie the reaction occurs on the surface) or they hydrogenate the DHA-P before esterification (reaction EC. 111.94, reversible as if it was modeled on the isomerization DHA-P <= > L-glyceraldehyde-3P) or there is a first esterification and subsequent hydrogenation (EC. 111.54, irreversible) followed by the second esterification. Esterifications are irreversible. So, in prebiotic, the hypothesis of DHA-P hydrogenated seems strengthened.

✔ *Case of L-glyceraldehyde-3P*: This molecule does not appear to exist in metabolism. Yet a specific enzyme of its hydrogenation was isolated and L-glycerol-3P is fixed to the membrane at 81% (Kalyananda M.K. et al 1987.) The authors raise the question of the origin of the glyceraldehyde. It is as if the free DHA did not exist for the given thermodynamic equilibrium.

• The mobile arm:

Surprisingly ethanolamine I thought the simplest molecule and easier to install proves undesirable. In prokaryotes it does not exist in free form, otherwise there is only one enzyme to break it into NH3 and acetaldehyde (EC. 4317). Then attachment phosphate does not directly, while outside the membrane (non-membrane enzymes EC. 271.32 and EC. 271.82), free phosphate and free choline or ethanolamine, can be linked (in eukaryotes only). In fact there are two processes involved in fixing the mobile arm.

✔ *Energy process*: the mobile arm-fixed arm bond is a similar nucleic acid phosphodiester bond. While ester bonds we saw so far are simple bonds. The second bond is more energy, it is preceded by a phosphate bond in which the CDP requires a second enzyme to replace. Where the intervention of the CTP.

✔ *The conformational process*: Three conformations are manageable.

✗ **Position the cation** (or for OH glycerol): This is related to the steric hindrance of the arm. Requires that the arm is cumbersome (in volume and charge) so that it can position itself. This is the case of serine, choline and glycerol-P (differentiation between D and L). This is not the case either ethanolamine or glycerol. Ethanolamine is obtained from serine already positioned, by decarboxylation (EC. 278.29), glycerol is obtained by dephosphorylation (EC. 313.27) of glycerol-3P previously installed (EC. 2785).

✗ **Position the nucleic base**, necessary intermediate phosphodiester bond: this position is similar to trapping amino acids with their zwitterion. Indeed it is the CDP, with its NH2 and its sugar, that is most similar to an amino acid, from nucleic acid bases. Purines and uracil are not suitable because of their size or their lack of NH2 (uracil). The dCDP plays the same role and measured a ratio of 0.88 between the 2 nucleic acids (DE Vance 2008). The role of positioning the CDP is clearly separated from its energizing role (EC. EC.2788, 277.41) where the phosphate of the fixed arm is no longer free to rotate around the phosphoester bond.

✗ **Position the tetrahedron P of fixed arm** that can still rotate around its bond with glycerol. This positioning is not clear but we guess with (EC.313.27) which eliminates. But also with the phosphatidyl-CDP where the second P blocks the first P.

● Prebiotic homochirality and initialization of metabolism

- **Homochirality:**

✔ The sugars are derived from D-glyceraldehyde-3P is not fixed by the membrane. Hence their homochirality.

✔ For the amino acids (aas), in the context of mechanical cohesion, it has shown that the chirality of serine. Can be attributed homochirality of aas to the theory of prebiotic chemo-osmosis over the theory of mechanical cohesion. Thus the movement of the mobile arm of hydrophilic heads lead the L-aas but not D-aas. Thus will be formed in the membrane, the pseudo-alpha helices of L-aas, with right helicity, which are the source of ion channels and membrane proteins (prebiotic chemo-osmosis).

Only the synthesis of mobile arm, although it requires a single esterification, appears inaccessible because the esterification of the second phosphodiester bond is very energetic and it does not have the effect of surface such as the fixed arm. Both processes can jointly accelerate the esterification:

✗ The synthesis of the fixed arms creates more or less large polyanionic surfaces of phosphate (PO4 -,-PO4H) which play the same role as the carboxylic anions for fastening the fixed arm, but much less efficiently because less extensive.

✗ Sequestration of amino acids: The L-aas with their zwitterion may participate in the mechanical cohesion as serine. This is what I call the sequestration of aas. It is different from trapping aas by the hydrophilic heads, already formed, we saw in prebiotic chemo-osmosis. It consists in an L-aa in place of serine, when this is possible in particular for the 1st implemented hydrophilic heads, in spaces without mobile arm.

- **Initialization metabolism.**

✔ *Synergy between mechanical cohesion and L-aas*:

The scenario I describe here uses the synergy between L-aas and mechanical cohesion. Two virtuous circles then establish:

✗ The increase in the number of hydrophilic heads of the same chirality increases the cohesion of the vesicle, cohesion which in turn promotes the binding and sequestration of molecules of the same chirality.

✗ The concentration of L-aas by sequestration creates groupings aas catalyzing more effectively synthesize hydrophilic heads but also the 1st metabolic pathways.

✔ *Table steps of the scenario* (Table 1) :Seen here "recall Article prebiotic oil" for the synthesis of prebiotic soup, and the scenario under Table 1. Full references are in the articles.

✗ The scenario begins with the synthesis of the hydrophilic heads under the theory of the mechanical cohesion (steps 1 and 2) and continues assuming certain coenzymes can be sequestered such first aas (steps 3 to 7). Allowing groups of L-aas on the wall to synthesize new L-aas and new coenzymes.

✗ Initialization of metabolism is assumed to occur in aqueous vesicles of the oil phase. It can continue into liposomes which the membrane is not necessarily completely covered by hydrophilic heads. There we find processes of chemo-osmosis prebiotic that will replace exhausted molecules through passive diffusion and exchange through the membrane protein molecules.

In the liposome 2 prebiotic metabolisms that complement are then put in place:

- Membrane metabolism from the outer leaflet underlied by chemo-osmosis that trap external L-aas and mineral coenzymes to make membrane proteins.
- The metabolism of the wall of the inner leaflet in contact with the internal environment. This metabolism sequester early L-aas and the simplest coenzymes on the wall. It also stores the phosphate in covalent bonds. It is based on simple reactions like formose reactions using small molecules that penetrate by passive diffusion.

✗ The scenario reaches the synthesis of fatty acids. Which then allows fission reproduction of liposomes. When molecular evolution will lead to DNA replication, in certain liposomes, it may then be synchronized with the reproduction of these liposomes.

Table 1. **Mechanical cohesion and the steps of initializing the prebiotic metabolism.**

Légende : aa for amino acids; ***ADEGS*** symboles of aa ; PE phospholipids ; DGA, LGA, DHA : D-L glyceraldehyde and glycerone; Bases for nucleic bases.

	Fixation	Sequestered	Products	Accumulation	Removal	Utilization	aa present	Comments; enzymes analogy with groups of L-aa sequestered ; from the KEGG website.
0	**Vesicle. Prebiotic Energetics** : Formose. Hydrothermale Synthesis of aa : *ADEGS*.							Aqueous vesicule in oil, wall with fatty acids .
1	DHA LGA L-Ser		Hydrophilic heads PS	DGA D-Ser cohesion	LGA	H2	*ADEGS*	prebiotic catalytic Hydrogenation, without enzymes, of DHA and LGA and not of DGA. Accumulation of D-ser and homochirality of sugars is due to fixing the LGA.
2		L-aa	groupes L-aa	D-aa	initial free L-Ser	*ADEGS*	*ADEGS*	Differenciation between the surface (L-aa) and the aquous inside (D-aa).
3		B6	L-Ser *NQCTWY ADEG* PE PtdGro Ptd2Gro	Cohesion 2-oxo-acids	initial free aa	H2S NH3 indol phenol acetaldehyde	*NQCTWY ADEGS*	**B6 and homogeneous grouping of amino acids catalyze better the reactions** of 1 step without ATP, using NH3. Interconversions between aa accumulate oxo-acids that with DHA and DGA, they prepare the intermediate metabolism of carboxylic acids.
4			dR-1P dATP			DGA-3P + acetaldehyde Adenine		Reactions without coenzymes : 4124, 5427 produce **D-dRibose-1P**. Then with Adenine : 2421,271.76,2743,2746 produce **dATP**.
5	CTP	Cytosine	Cytosine + dR-1P	Cohesion		Cytosine dR-1P dATP		Equivalent of 2421 do not exist for cytosine ; groups of L-aa could catalyze the synthesis of dCTP in-situ.
6		B1	ATP CTP NAD B6 SAM FAD FMN Biotine *FHKPIVM* PC	Cohesion	H2 initial B6 initial	Bases nicotinate DHA+DGA dATP	*FHKPIVM NQCTWY ADEGS*	**B1** consists of m1 and m2, m1 can be sequestered. The synthesis of B1 can be done in-situ as for dCTP. With B1, 412.13, 313.11, 2211, 5131, 5316 and from DHA+DGA is obtained R-5P that with dATP can be done **PRPP** (2761) and **R-1P** (5427). A + R-1P + PRPP + **PPP** → **ATP** : 2421, 2428, 2743, 2741. C + R-1P + ATP → **CTP** : 2422, 271.48, 274.14, 2746. N + PRPP + ATP +NH3 → **NAD** : 242.11, 2771, 6351. D-Ribulose-5P (5131) + DGA-3P + L-Gln → Pyridoxal-P (**B6**) : 4.-.-.-, YaaD, Pyridoxal biosynthesis lyase pdxS; 2.6.-.-, YaaE, Glutamine amidotransferase subunit pdxT.
7		THF	**CoA** fatty acids *LR*		DHA DGA from formose, Phosphate		*LR FHKPIVM NQCTWY ADEGS*	**THF** consists of m3 and m4 that can be sequestered. Pyruvate + B1 + NAD + THF + ATP + L-Asp + L-Cys → **CoA** : 2216, 11.86, 4219, 212.11, 111.169, 411.11, 6321, 271.33, 6325, 411.36, 2773, 271.24.

The steps of initializing the prebiotic metabolism, Table 1:

We will now place the script initialization of prebiotic metabolism starting with the synthesis of hydrophilic heads generating mechanical cohesion and differentiation between the wall rich in sequestered L-aa and the liquid inside rich in D-aa.

Then comes the sequestration of B6 which would act as a coenzyme for groups of L-aa of the wall. I introduced the first in B6 by analogy, because in the biotic metabolism, activates countless reactions between aa, and between aa and NH3. Thereby increasing tenfold the virtuous cycle of catalysis.

Step 0.

These are the starting materials in the aqueous vesicle in the oil phase. Every molecule is susceptible to be present. However for concentrations I refer to experiments at high temperature (150°C) and high pressures (300 bar).

- H2 H2S CO2 N2, then NH3 : gases of hydrothermal vents (Charlou 2002, Proskurowski 2008).
- Phosphates and polyphosphates of seabed (Arrhenius 1997).
- alkanes, fatty acids, alcohols and aldehydes from Fischer-Tropsch process which acetaldehyde (Rushdi 2001, McCollom 1999, 2006).
- dihydroxyacetone glyceraldehyde glyoxal by hydroformylation or formose reaction at 120 bars and 140°C .
- amino acids ADEGS produced in hydrothermales experiments with nitrogene molecules .
- Precursors of coenzymes and aromatic rings in very small amounts of prebiotic pocket of oil (hypothesis): nucleic bases, AGCUT; pyridoxamine, the two nuclei of thiamine, the two nuclei of folate and nicotinate for NAD.

Step 1.

Synthesis of hydrophilic head following the analysis of the previous paragraphs. Fixing on the wall of L-ser, DHA and LGA, and accumulation of D-ser DGA in water. Origin of homochirality of sugars via DGA. Virtuous cycle (synthesis of heads) / (mechanical cohesion).

Step 2.

- Sequestration of L-aa by the wall and concentration of D-aa in water. L-ser is gradually disappearing from the water with the decrease in the hydrothermal synthesis of aa with time.
- Combination of L-aa on the wall to form pseudo-enzymes. They are perhaps not very effective, but multiple combinations, more or less ephemeral, are possible. Over the surface of hydrophilic heads grew more groups could be strong and numerous, they will be more cooperative in catalysis and in their grouping itself. This is the virtuous cycle of catalysis subtended by the mechanical cohesion.

Step 3.

- The accumulation of DGA and D-ser displaces very slowly the equilibriums towards L-ser.
- Sequestration of B6 accelerates the isomerization of D-ser to L-ser, the deamination of D-ser to pyruvate (EC 431.18) and its amination to L-ser (EC 431.17).
- Under the action of B6, synthesis of new aa: From pyruvate, NH3 and indole (Trp) or phenol (Tyr). Thiolysis of hydrophilic heads with H2S (Cys). Condensation of Gly and acetaldehyde forming Thr. Amination of Glu to Gln and Asp to Asn (see KEGG for the analogy with enzymes).
- Under the action of B6, decarboxylation of PS serine to give PE (EC 411.65). Ethanolamine produced very little in the hydrothermal synthesis of aa, has been fixed in place of serine but much more difficultly as we have seen previously. There are mechanical cohesion strengthening by PE because it has no reactive heads.
- Under the action of B6, Thr deamination to give 2-oxo-butanoate (EC 4125) further required for the synthesis of Ile Val Leu.
- Transaminations between aa (ADEGS more new CNQTWY) for the production of L-Ser, which accumulates 2-oxo-acids.
- DGA, DHA, 2-oxo-acids, NH3, H2S, ADEGS and CNQTWY are prebiotic intermediary metabolism.
- All these new products through B6 are obtained in a single reaction.

Step 4.

- Synthesis, without coenzyme, of the first deoxy-pentose in two reactions (EC 4124, 5427) which the second is autocatalytic (formation of ribose bisphosphate): DGA-3P + acetaldehyde = D-dRibose-1P.
- Synthesis of deoxy-adenosine without coenzyme (EC 2421), then 2 phosphorylation with P and PPP give the dADP (EC 3135, 2743).
- The passage to dATP require ATP in the biotic metabolism (EC 2746). I assume, in prebiotic metabolism, that is entirely possible that dATP is formed very slowly by self-catalysis (confusing dATP and ATP in EC 2746) or in the presence of polyphosphates such as two reactions that precede it. Besides, this is an esterification and I founded my theory of prebiotic molecular evolution on esterification (see Section 5.1.2).

Step 5.

- This step may seem theoretically superfluous , but step 6 below requires thiamine and 7 reactions to arrive at the ribose-1P. Now we have seen that the sequestration of thiamin, folate and dCTP need an in-situ condensation of two parts to form each coenzyme. The dCTP should appear before the CTP.
- In the biotic metabolism, there is no equivalent of (EC 2421) for dCTP as in step 4. Now the passage by the CTP or dCTP for fixing the movable arm (EC 277.41), regardless of the arms, seem crucial. Also the formation in situ of dCTP in the presence of groups of sequestered L-aa, rapidly bring high mechanical cohesion. The dCTP acts as a coenzyme since dCTP, after hydrolysis can be regenerated by phosphorylation of dCMP.

Step 6.

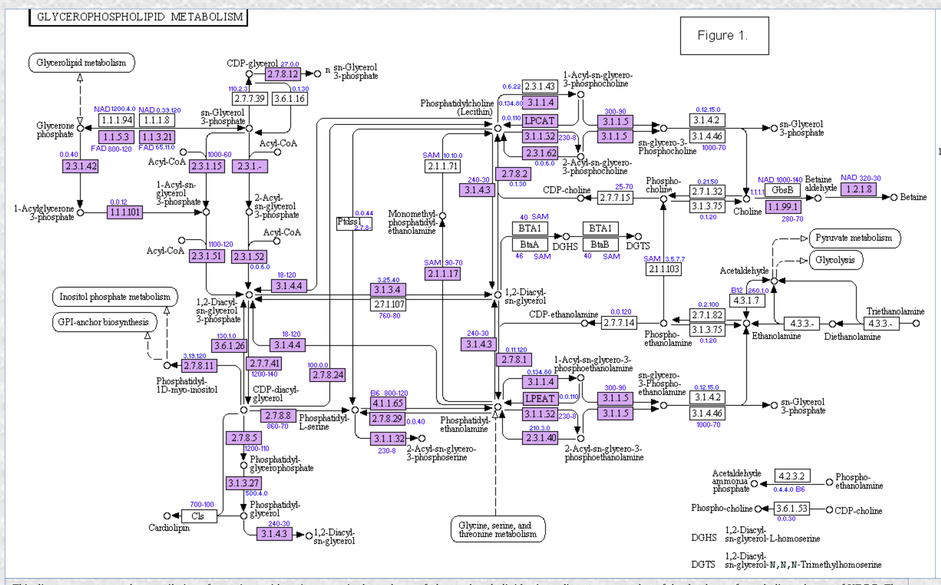
- In-situ synthesis of B1 (see drawing molecules below).
- It is the accumulation of DGA in the first stage of the scenario that will promote, by displacement of thermodynamic equilibrium, its condensation with DHA, both in phosphorylated form: DGA + DHA-3P-P (EC 412.13).
- ATP: There is six reactions and the participation of B1 and dATP, only coenzymes, to arrive at the central molecule PRPP then isomerization to reach the Ribose-1P required for the synthesis of ATP from the adenine and PPP.
- The synthesis of CTP requires ATP.
- The synthesis of NAD requires ATP and nicotinic acid.
- The synthesis of S-adenosylmethionine (SAM), flavins (FAD and FMN) and biotin requires only prebiotics coenzymes already created.
- The pyridoxal-5P (B6) begins with an intermediate in the synthesis of D-ribose-1P, D-ribulose-5P: D-ribulose-5P-3P + DGA + L-Gln (EC 5131).
- Cohesion will develop at high speed with the CTP. Replacing the prebiotic hydrogenation (H2) by the hydrogenation by the NAD and B6 is synthesized de novo.
- 7 new aa can be synthesized which histidine we have seen, important for the active sites of proteins: FHKPIVM.
- The synthesis of methionine allows the synthesis of SAM and hence the production of PC.

Step 7.

- In-situ synthesis of folate (THF) (see drawing molecules below).
- Synthesis of coenzyme A, the last 2 aa LR and fatty acids.

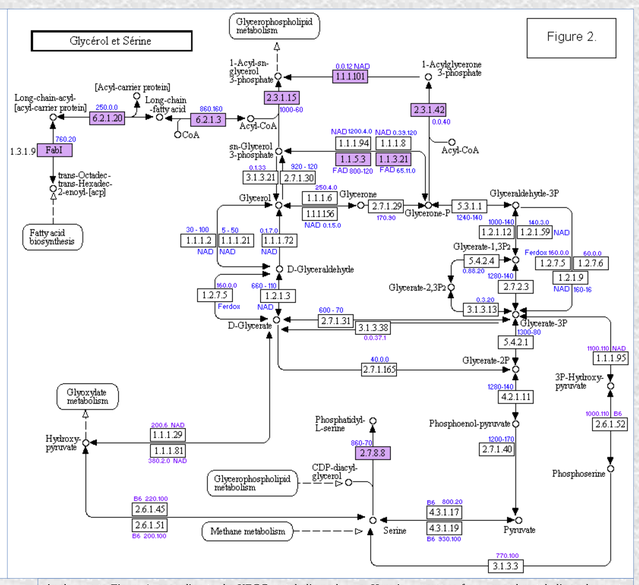
GLYCEROPHOSPHOLIPID METABOLISM

Figure 1.



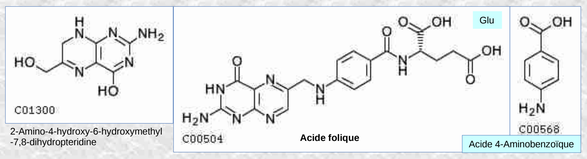
This diagram represents the compilation of organisms with a given gene in the pathway of glycerophospholipids: According to a screenshot of the database of metabolic pathways of KEGG. The colored rectangles correspond to membrane enzymes. KEGG.
The colored rectangles correspond to membrane enzymes. The compilation is a rough and personnel count of organisms listed in the database, and consists of two numbers, the first that of prokaryotes and the second that of eukaryotes.
When the number is weak, second count is do from lists of Brenda or RefSeq databases (from the links provided by KEGG) and is coupled with that from the list of KEGG. Example: 0.5.60 corresponds to 0 prokaryotes in the list of KEGG, 5 prokaryotes in Brenda and RefSeq, and 60 eukaryotes in KEGG. The drawings of arrows and the names of molecules are those of KEGG.

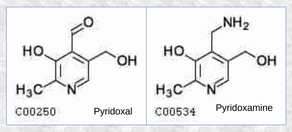
Figure 2.

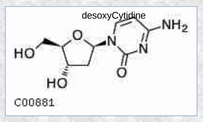


Analogous to Figure 1, according to the KEGG metabolic pathways. Here is a montage from several metabolic pathways to represent traffic between Serine, Glycerone, fatty acids and phospholipids:Fatty acid Biosynthesis, Fatty acid Metabolism, Glycerolipid Metabolism, Glycerophospholipid Metabolism and Glycolysis.

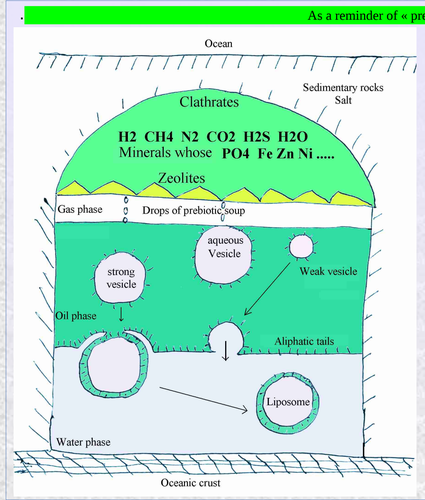
Search for enzyme in KEGG data base with code E.C. : http://www.genome.jp/dbget-bin/www_bfind?enzyme







As a reminder of « prebiotic petroleum »



Synthesis of prebiotic soup by diagenesis clathrates, and liposome formation

Clathrates et zeolites

Clathrates and zeolites have cell structures. They can be intimately mixed.

Here zeolites are drawn apart to show that they come from the oceanic crust.

Synthesis of prebiotic soup

The clathrates are converted to prebiotic soup under the action of diagenesis and catalysis by minerals and optionally by zeolites.
The remaining minerals and zeolites form a salt layer after disappearance of clathrates.

Liposome formation

Liposomes are formed, after migration of the vesicles to the water under the action of gravity, by invagination of the water/oil interface containing phospholipids and fatty acids of vesicles which have aborted.