WHAT IS LIFE?

LIFE CANNOT BE SEPARATED FROM FOUR FONDAMENTAL PROCESSES

- METABOLISM
- COMPARTMENTALIZATION
- MEMORY
- MANIPULATION

THE FIRST TWO HAVE THE SCALE OF SMALL MOLECULES, THE OTHER ONES CORRESPOND TO MACROMOLECULES

MEMORY AND MANIPULATION ARE LINKED BY A FUNDAMENTAL LAW THAT GIVES ITS RECURSIVE CHARACTER TO LIFE TRANSMISSION. THIS LAW IS THE GENETIC CODE

LIFE CONCERNS RELATIONSHIPS BETWEEN OBJECTS RATHER THAN OBJECTS (THE DELPHIAN BOAT)

MICROSCOPIC

MESOSCOPIC
A THEORY OF THE ORIGIN OF LIFE MUST EXPLAIN:

- HOW COMPARTMENTS ARE MADE
- HOW ARE CONSTRUCTED THE FIRST REPLICATING MOLECULES
- HOW IS GENERATED THE CORRESPONDENCE RULE BETWEEN MEMORY AND MANIPULATION

A PRIMITIVE METABOLISM PROVIDES A SOLUTION
J'AI LA PRÉTENTION DE DÉMONTRER AVEC RIGUEUR QUE DANS TOUTES LES EXPÉRIENCES OU L'ON A CRU RECONNAÎTRE L’EXISTENCE DE GÉNÉRATIONS SPONTANÉES, CHEZ LES ÊTRES LES PLUS INFÉRIEURS, OU LE DÉBAT SE TROUVE AUJOURD'HUI RELÉGUÉ, L'OBSERVATEUR A ÉTÉ VICTIME D'ILLUSIONS OU DE CAUSES D'ERREUR QU'IL N'A PAS APERÇUES OU QU'IL N'A PAS SU ÉVITER.

LOUIS PASTEUR
ARGUMENTS THAT ATTEMPT TO EXTRAPOLATE FROM MODERN BIOCHEMISTRY BACK TO THE ORIGIN OF LIFE ARE FUTILE

S. BENNER

THE METHOD USED IS THAT OF A RECONSTRUCTION OF PRECURSOR PATHWAYS BY RETRODICTION FROM EXTANT PATHWAYS

G. WÄCHTERSHÄUSER
IN THE USUAL MODEL OF A PREBIOTIC "SOUP" A VAST NUMBER OF VARIANTS OF A SET OF SMALL MOLECULES IS PRODUCED. BUT FAR FROM BEING A FEATURE FAVORABLE TO THE THEORY THIS ACTS AS A POISON WHICH FREEZES THE FUTURE OF THE BROTH.

IN A MODEL OF A PRIMITIVE METABOLISM, ONE MUST TAKE INTO ACCOUNT A SELECTIVE MECHANISM. THIS IMPLIES:
— THE EXISTENCE OF AN UPPER LIMIT IN THE NUMBER OF SPECIES PRODUCED AT A GIVEN TIME.
— FOR EACH SPECIES A MEASURE OF ITS FITNESS.
— THAT THE PROGENY OF THE BEST ADAPTED SPECIES INCREASES WITH TIME.
— THAT AS LONG AS A SPECIES IS NOT ON THE VERGE OF DISAPPEARING IT PRODUCES A SET OF SIBLINGS SOME OF WHICH ARE SLIGHTLY BETTER ADAPTED THAN THEIR PARENTS.
FREEMAN DYSON PROPOSED THAT LIFE BEGAN TWICE, TO ACCOUNT FOR THE TWO SPACE SCALES OF BIOMOLECULES.

BERNAL, GRANICK, CAIRNS-SMITH, WÄCHTERSHÄUSER, ... HAVE STRESSED THE INADEQUACY OF A PRIMITIVE PREBIOTIC SOUP, AND HAVE PUT FORWARD THE LIKELINESS OF THE INVOLVEMENT OF MINERAL SURFACES IN THE GENESIS OF BIOMOLECULES.

AMONG THE MANY REACTIONS THAT OCCUR AT THE SURFACE OF MINERALS, THOSE INVOLVING GROUP-TRANSFER ON A SMALL FAMILY OF UNIVERSAL CARRIER MOLECULES IS PLACED IN THE LIMELIGHT. THE CORRESPONDING PROCESS CAN BE TERMED HOMEOTOPIC TRANSFORMATION.
ANOTHER ASPECT OF METABOLISM MUST BE TAKEN INTO
CONSIDERATION: IT MUST FAVOR SYNTHESIS OF
MACROMOLECULES IN WATER.

IN 3-DIMENSIONS THE INCREASE OF ENTROPY DISFAVOURS
POLYMERIZATION, BUT IN 2-DIMENSIONS, IF A WATER
MOLECULE IS LIBERATED DURING POLYMERIZATION,
FORMATION OF MACROMOLECULES IS FAVOURED.
CHARGED MOLECULES INTERACTING WITH SURFACES CAN PERMIT BUILDING UP OF A SELECTIVE PROCESS.

MANY AUTHORS HAVE IN THE PAST PROPOSED HYPOTHESES TO TAKE IT INTO ACCOUNT:

- 1951 BERNAL CLAYS
- 1957 GRANICK Fe$_2$O$_3$ + FeO + S
- 1975 CAIRNS-SMITH & HARTMAN CLAYS
- 1988 WÄCHTERSHÄUSER FeS (PYRITE)
BEFORE CONSIDERING THE GENETIC CODE AND DNA ONE MUST ACCOUNT FOR THE CORRESPONDING SYNTHESIS INSIDE A COMPARTMENTALIZED ORGANELLE.

=> SYNTHESIS OF LIPIDS
SYNTHESIS OF COENZYMES
SYNTHESIS OF NUCLEOTIDES
WHAT IS EASY:

SYNTHESIS OF SOME AMINO-ACIDS
(ASSUMING NITROGEN REDUCTION)

SYNTHESIS OF MOLECULES WITH A THREE CARBON ATOM BACKBONE
WHAT IS DIFFICULT:

SYNTHESIS OF BASIC AMINO-ACIDS

SYNTHESIS OF COENZYMES

SYNTHESIS OF LIPIDS

SYNTHESIS OF NUCLEOTIDES (ESPECIALLY PYRIMIDINE NUCLEOTIDES)
PATHWAYS UTILIZING UNEXPECTED PHOSPHATE RESIDUES:

SERINE (SERINE~PHOSPHATE)
PYRIDOXAL PHOSPHATE
ISOPRENYL ~ PYROPHOSPHATE
4-PHOSPHOPANTETHEINE
THIAMINE ~ PYROPHOSPHATE

CONTAINING NUCLEOTIDES:

CYTIDYLATE (LIPIDS)
ADENYLATE, GUANYLATE, URIDYLATE (SUGARS)
COENZYMES (NAD, CoA...)
tRNA OUTSIDE TRANSLATION

FORMATION OF A PEPTIDIC LINK
- Gly~ARNtGly  murein
- Phe~ARNtPhe  N-terminal
- Leu~ARNtLeu  N-terminal
- Arg~ARNtArg  Ubiquitine

HOMEOTOPY
- Met~ARNtFMet  →  FMet~ARNtFMet
- Glu~ARNtGln  →  GlnARNtGln
- Ser~ARNtSeCys  →  SeCys~ARNtSeCys

DIVERSE
- Lys~ARNtLys  Lipides
- Glu~ARNtGlu  Aminolevulinate

OTHER
- Base modification
AMINO-ACIDS IN THE SYNTHESIS OF NUCLEOTIDES AND COENZYMES

PURINES          Q  G (S)  Q  D (S)
PYRIMIDINES      D

GLUTATHION       E  C  G
4-PHOSPHOPANTETHEINE  V  A  C
NICOTINAMIDE     D (Q)
PYRIDOXAMINE     S (Q)
PYRROLQUINOLONE QUINONE  E  Y (PEPTIDE)
ETC...
ORIGIN OF tRNA SYNTHETASES

IF HOMEO TOPIC TRANSFORMATION IS AT THE ROOT
OF METABOLISM ON tRNA MOLECULES, tRNA SYNTHETASES
MUST DERIVE FROM AMINO ACID BIOSYNTHESIS:
GATTI & TZAGOLOFF HAVE FOUND THAT ASPARTYL-
tRNA SYNTHETASE IS RELATED TO ASPARAGINE
SYNTHETASE, AND DI GIULIO (1993) HAS SHOWN
THAT GLUTAMINE tRNA SYNTHETASE IS RELATED TO
GLUTAMINE AMIDO-TRANSFERASES
GRANICK (1957), YCAS (1974) AND JENSEN (1976) PROPOSED THAT ENZYME SPECIFICITY EVOLVED FROM RECRUITMENT OF PREEXISTING PROTEINS THAT CATALYSE SIMILAR REACTIONS.

THIS HAS BEEN OFTEN VERIFIED

- pabB trpE
- pabA trpG guaA

- thrC dsdA ilvA trpB
- metB metC
- cysK trpB

- pdxB serA
- umk thrA lysC gltK carK

GONCHAROFF & NICHOLS 1984
KAPLAN & NICHOLS 1983
ZALKIN et al. 1985

PARSOT 1986, 1987
PARSOT et al. 1988
LÉVY & DANCHIN 1988

SCHOENLEIN et al. 1989
SERINA et al. 1995
A PRESENT-DAY ILLUSTRATION OF RECURSIVE HOMEOOTOPY IS REPRESENTED BY THE GENERATION OF PEPTIDIC ANTIBIOTICS OR BY THE SYNTHESIS OF FATTY ACIDS.

IT IS FASCINATING TO REMARK THAT THE GENES NECESSARY FOR BOTH TYPES OF SYNTHESES CODE FOR VERY SIMILAR ENZYMES AND THUS STEM FROM A COMMON ANCESTOR.

ANOTHER REMARKABLE FEATURE IS THE FORMATION OF PEPTIDES CATALYZED BY A PHOSPHORYLATED PEPTIDE (PHOSPHOPANTETHEINE) FOLLOWING A PROCESS INDEPENDENT OF TRANSLATION.

AS A CONSEQUENCE, PEPTIDES OR REACTIONS USING PEPTIDES SHOULD BE TAKEN INTO CONSIDERATION FOR THE SYNTHESIS OF COENZYMES AS WELL AS OF NUCLEOTIDES (AS IT IS INDEED OBSERVED IN PRESENT DAY METABOLISM).

AS AN EXAMPLE, ONE SHOULD REMARK THE PRESENCE OF PEPTIDES LEADING TO INTRA-MOLECULAR REARRANGEMENTS, SUCH AS BACTERIOCINS WHICH PRODUCE LANTHIONINE AND THE LIKE FROM AMINO ACIDS SUCH AS SERINE AND CYSTEINE.
A TWO-DIMENSION STRUCTURE FAVORS POLYMERISATION THROUGH ELIMINATION OF A WATER MOLECULE IN THE MEDIUM IN THE PRESENCE OF AN ELEMENTARY SET OF AMINO-ACIDS THIS PERMITS SYNTHESIS OF FERREDOXINS (WHICH INCORPORATE AN IRON-SULFUR NUCLEUS).

NITROGEN FIXATION IS A PREREQUISITE IT REQUIRES Fe-Mo-Co:

FERREDOXIN
MOLYBDENE AND MAY HAVE BEEN ASSOCIATED TO MOLYBDOPTERIN AS A COFACTOR
Molybdopterin