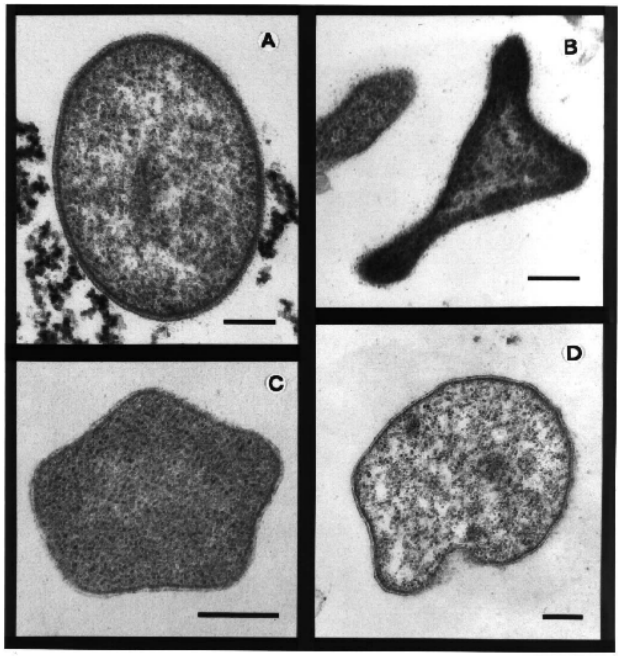
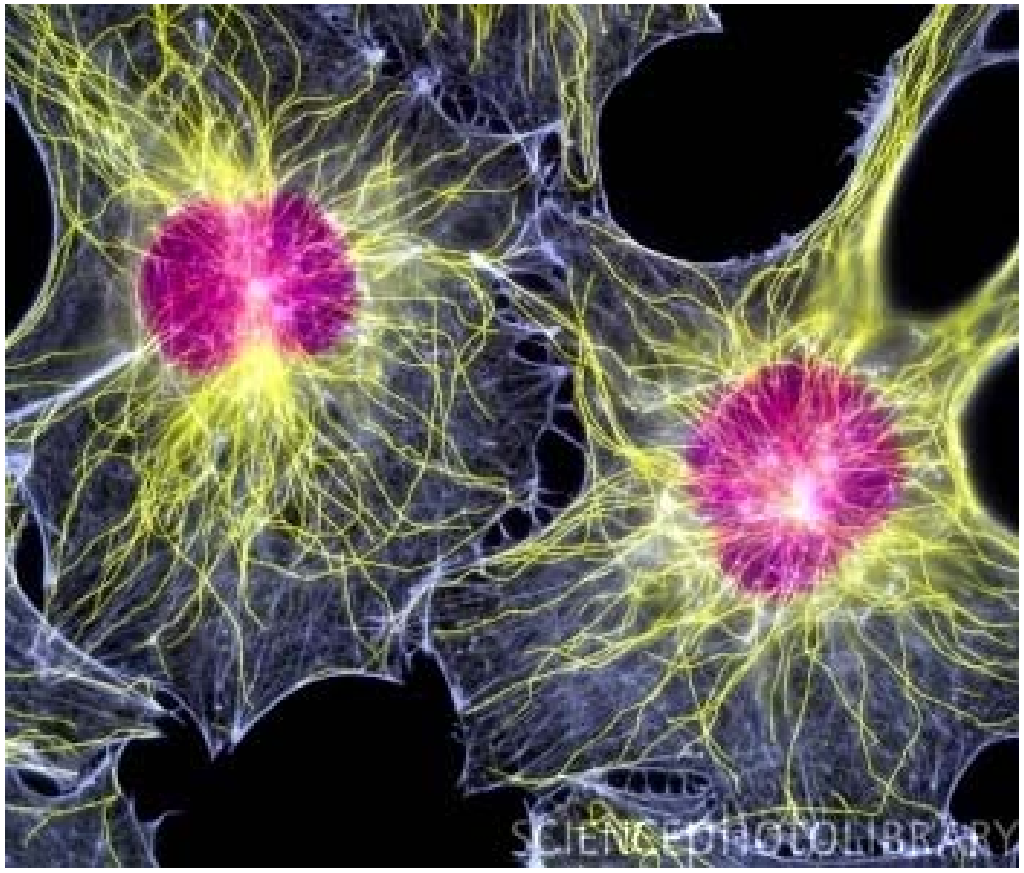
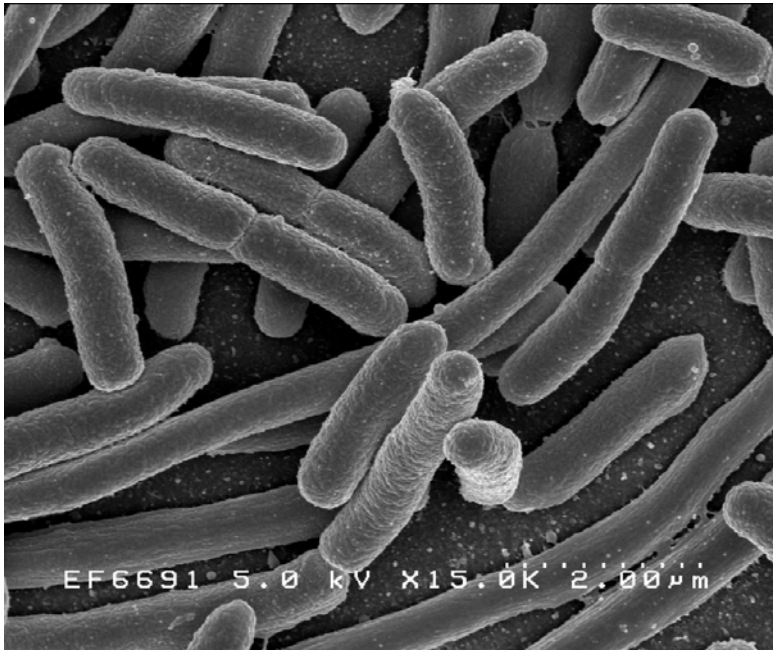
Sesión: **Abordajes experimentales al estudio del origen**

Dr. Ricardo Cabrera
(ricabrer@uchile.cl)
Departamento de Biología – Facultad de Ciencias
Universidad de Chile

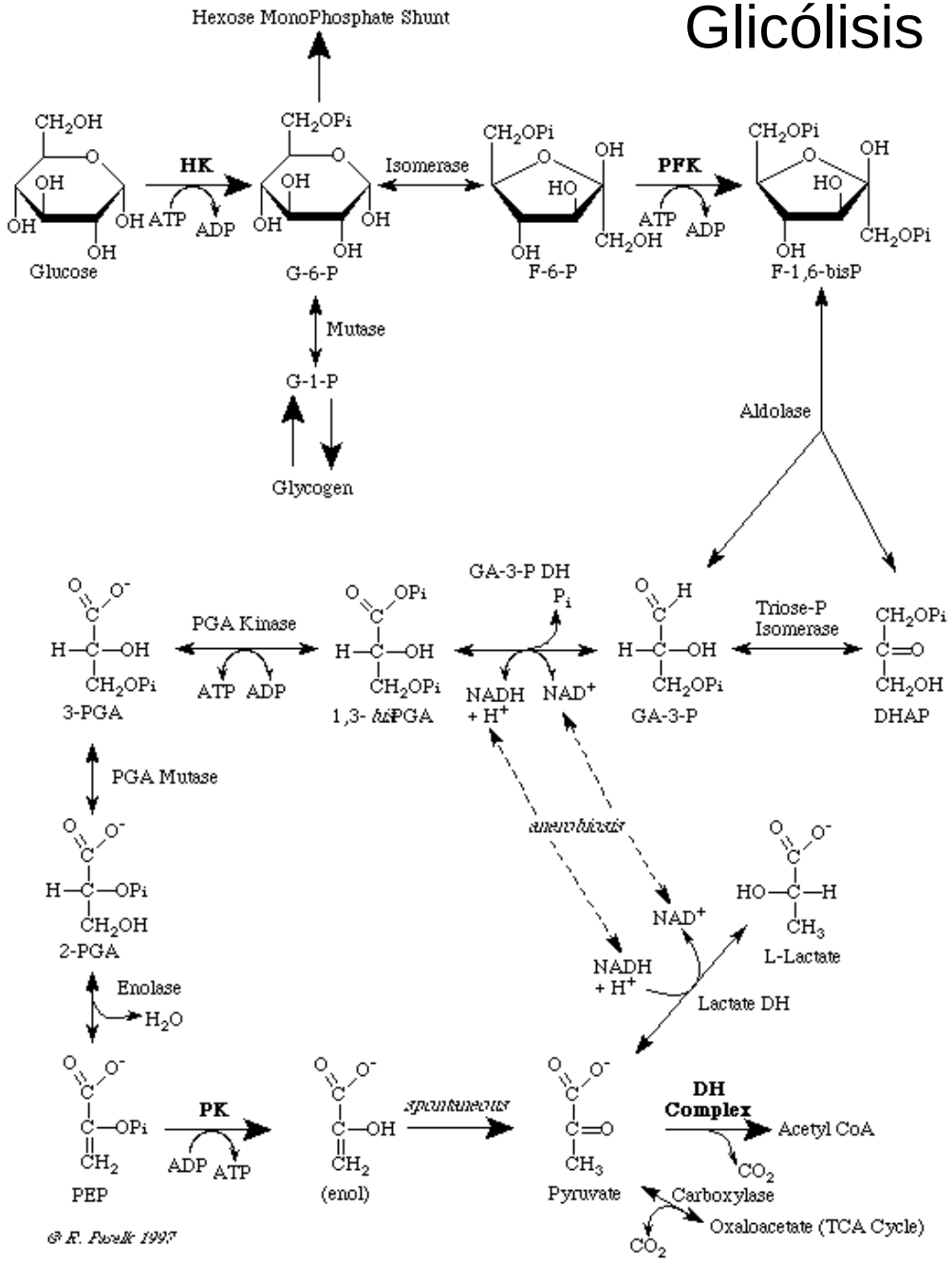
Organización celular y automantención



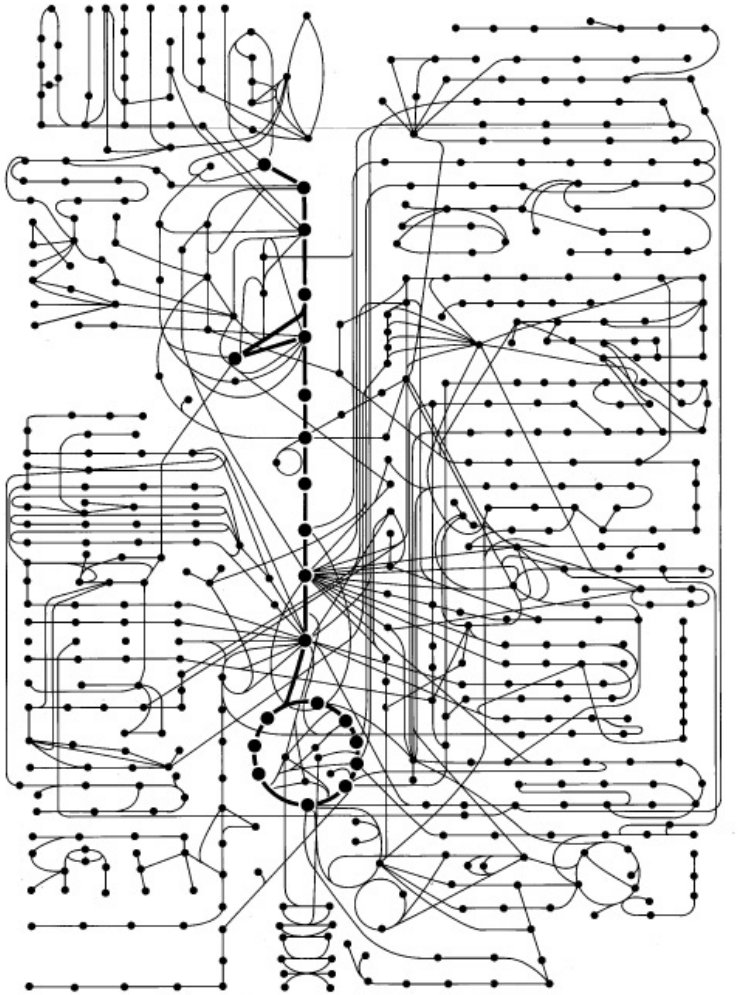


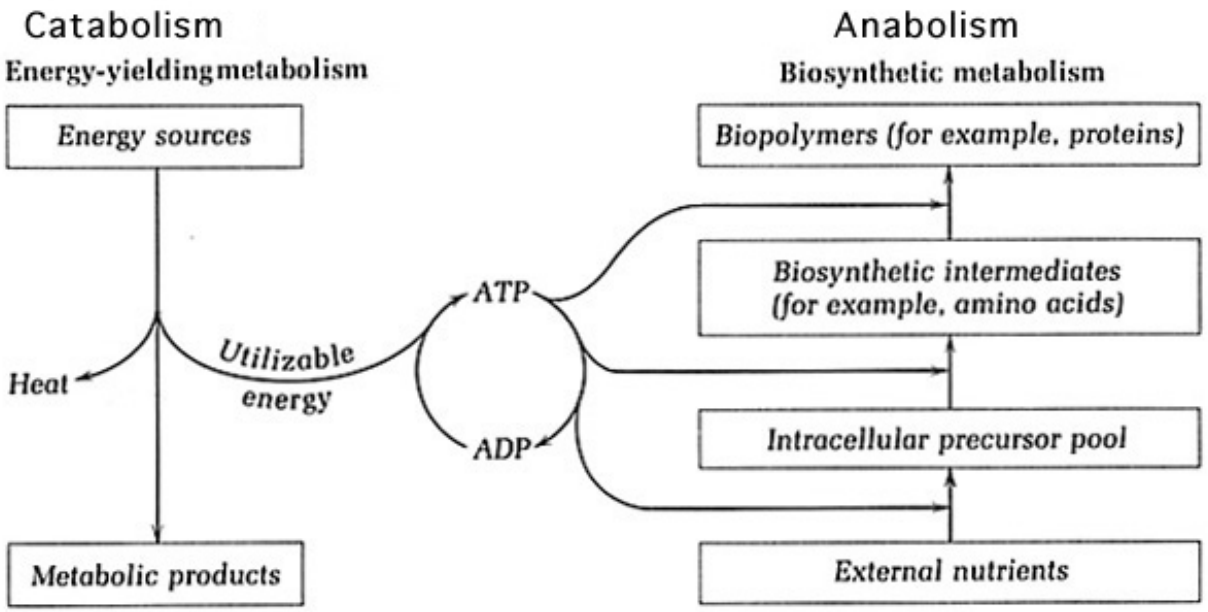


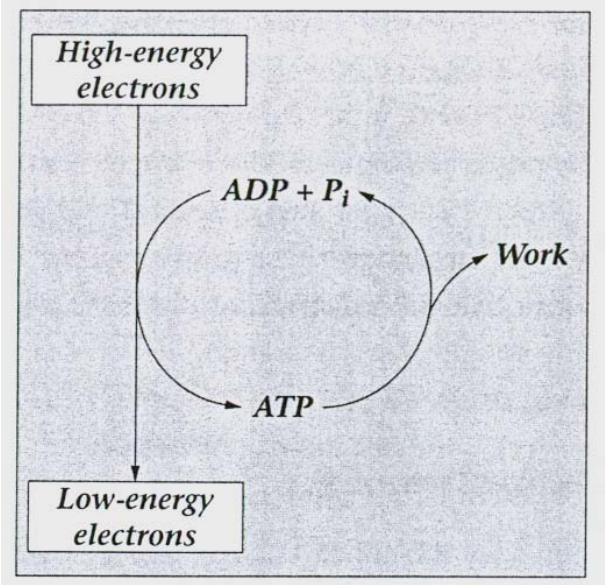
Glicólisis



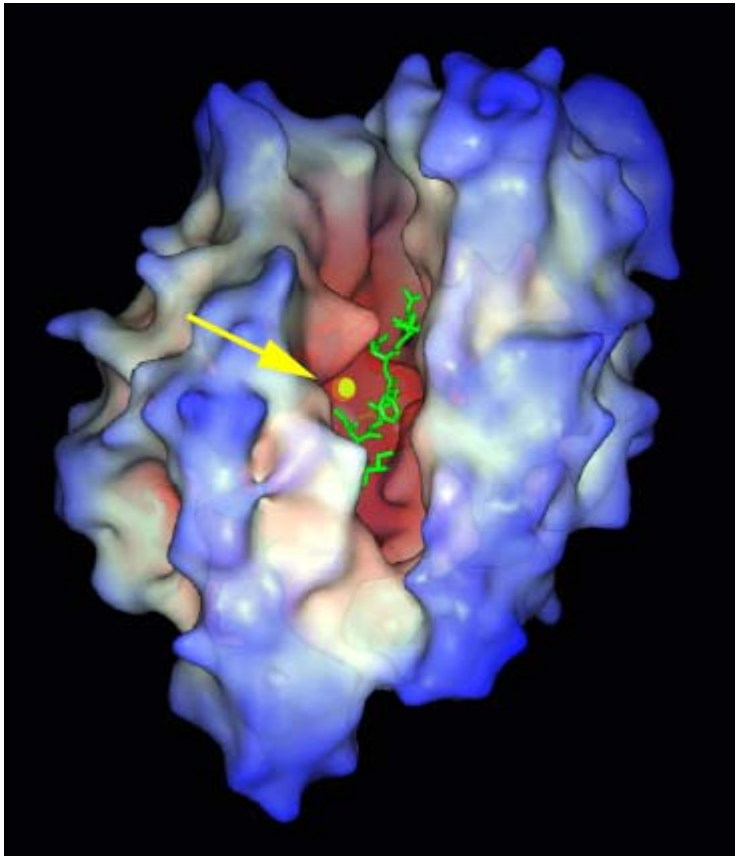
Vías metabólicas

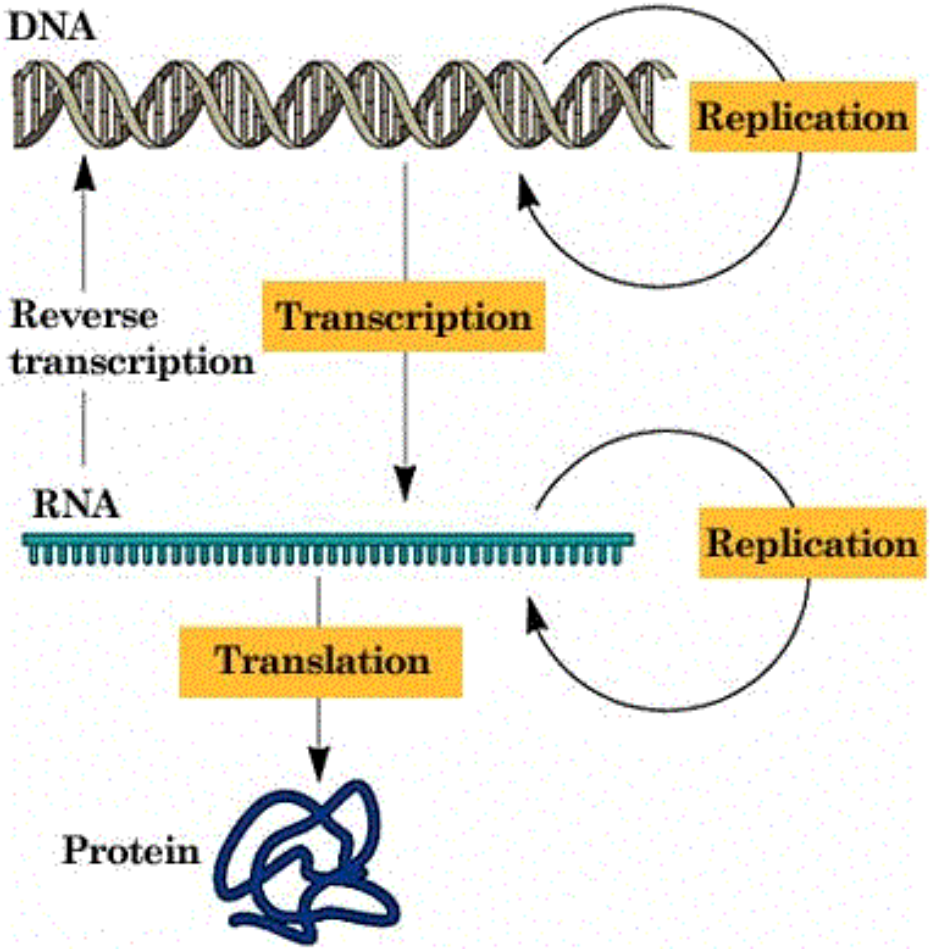


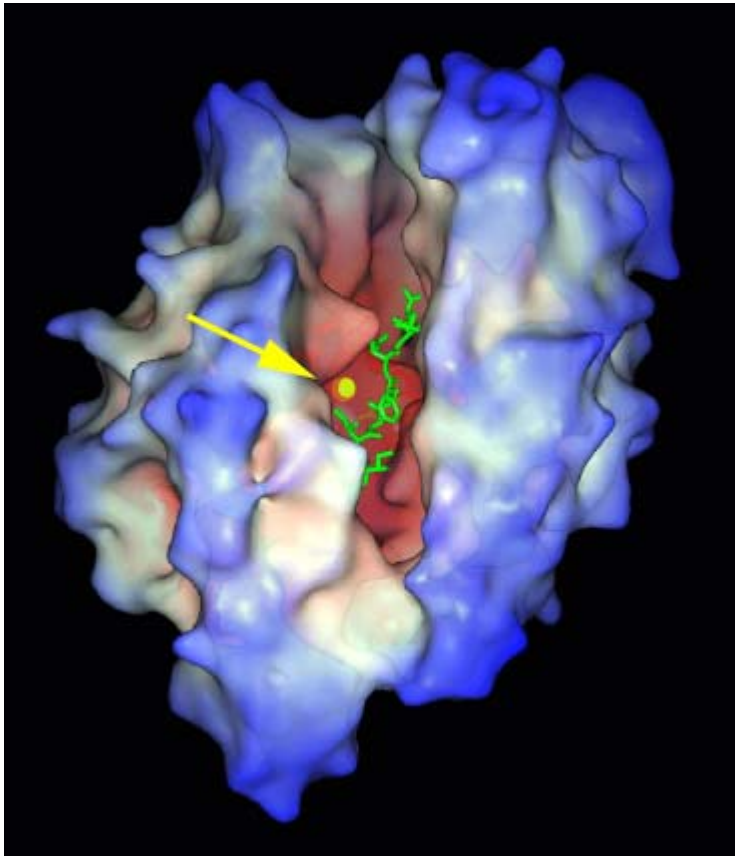

Catabolism
Energy-yielding metabolism
Energy sources
Heat
Utilizable energy
ATP
ADP
Metabolic products
Anabolism
Biosynthetic metabolism
Biopolymers (for example, proteins)
Biosynthetic intermediates (for example, amino acids)
Intracellular precursor pool
External nutrients

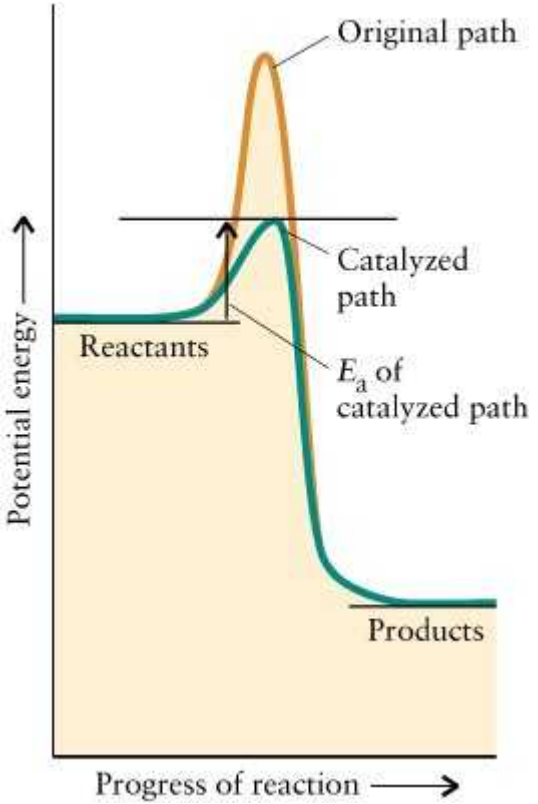

High-energy electrons
ADP + P_i
Work
ATP
Low-energy electrons

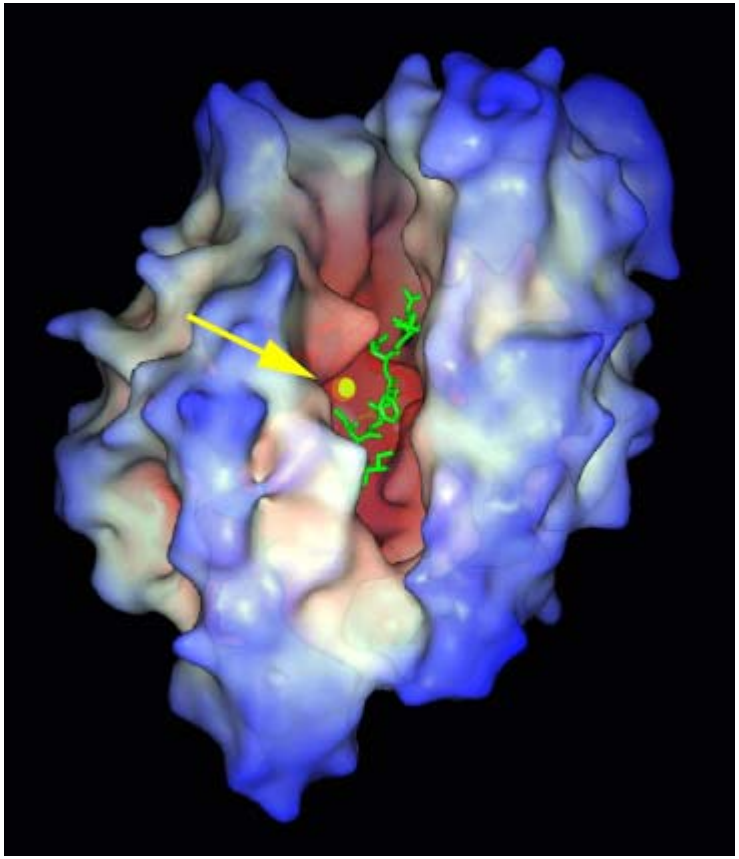
Organización celular y automantención



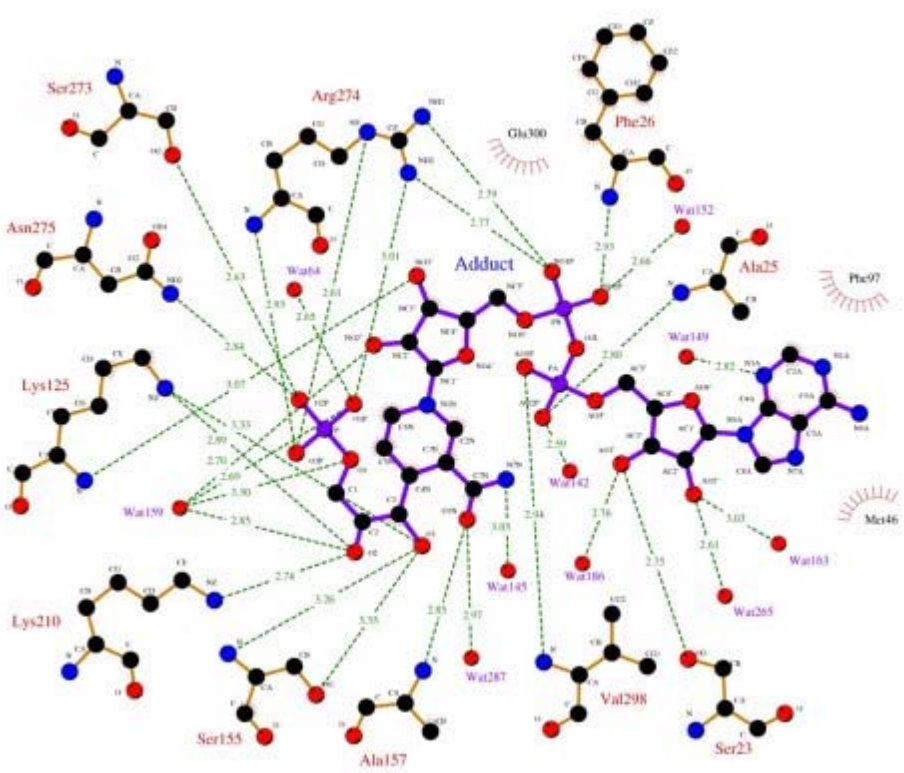




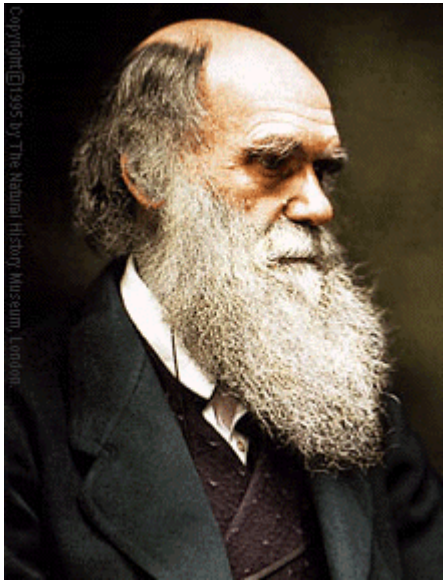

Original path
Catalyzed path
Reactants
E_a of catalyzed path
Products
Potential energy
Progress of reaction



b


Ser273
Arg274
Glu300
Phe26
Asn275
Wat152
Wat64
Adduct
Ala25
Phe97
Wat149
Lys125
Wat142
Met46
Wat159
Wat163
Wat186
Wat145
Wat265
Lys210
Wat287
Val298
Ser155
Ala157
Ser23

Charles Darwin

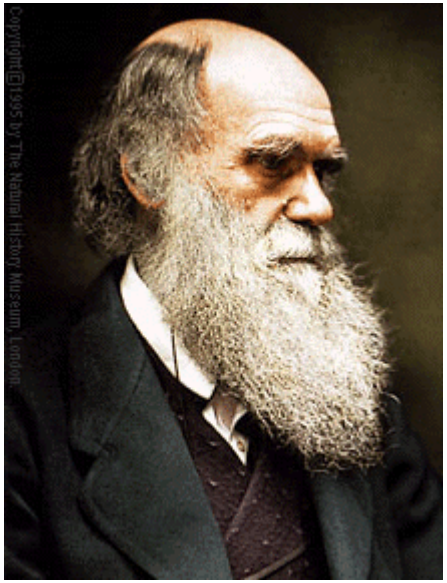


It is often said that all the conditions for the first production of a living organism are present, which could ever have been present. But if (and Oh! what a big if!) we could conceive in some warm little pond, with all sorts of ammonia and phosphoric salts, light, heat, electricity, etc., present, that a protein compound was chemically formed ready to undergo still more complex changes, at the present day such matter would be instantly devoured or absorbed, which would not have been the case before living creatures were formed.

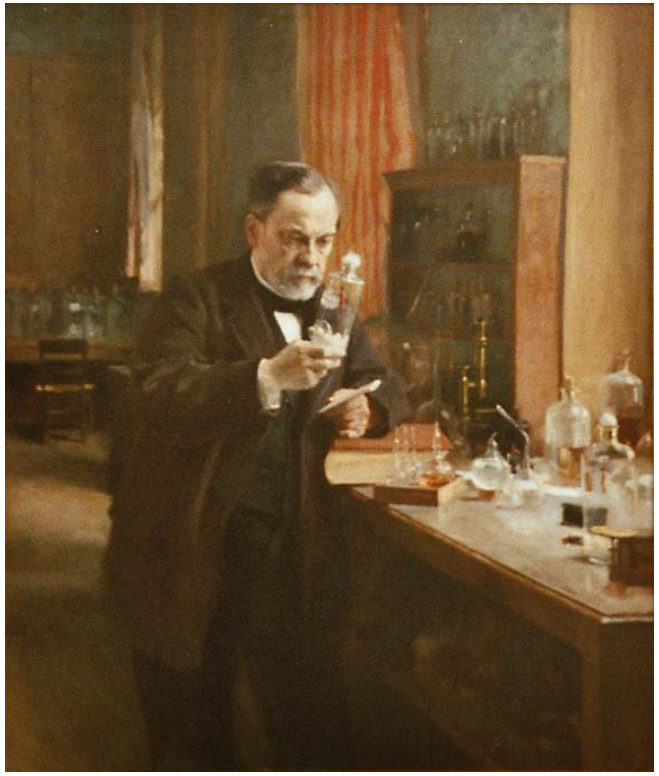
De acuerdo con la Teoría Celular todas las células provienen de otras células.

Durante gran parte de la historia la creencia general era que muchas formas de vida se generaban continuamente en un proceso denominado “generación espontánea”, a partir de materia inorgánica y orgánica

Charles Darwin
The Origins… (1859)

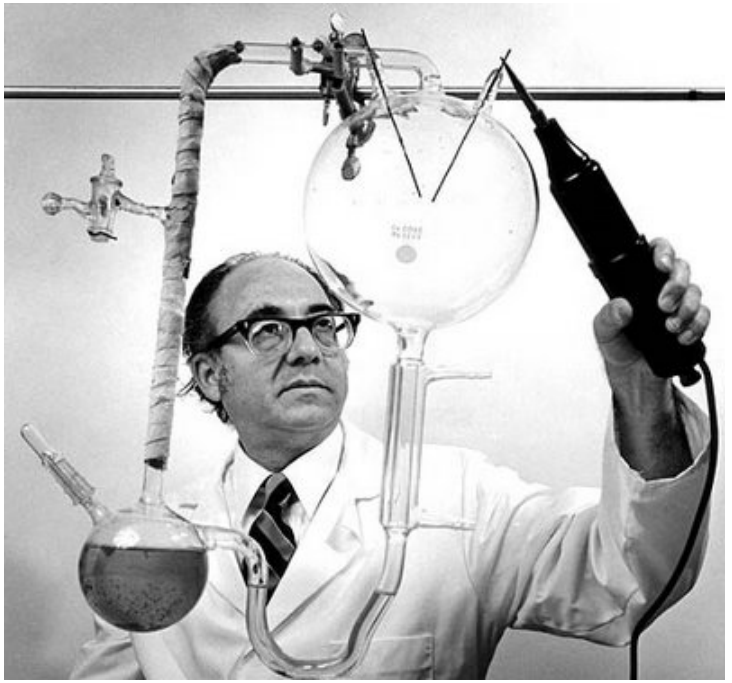


Louis Pasteur
(1862)



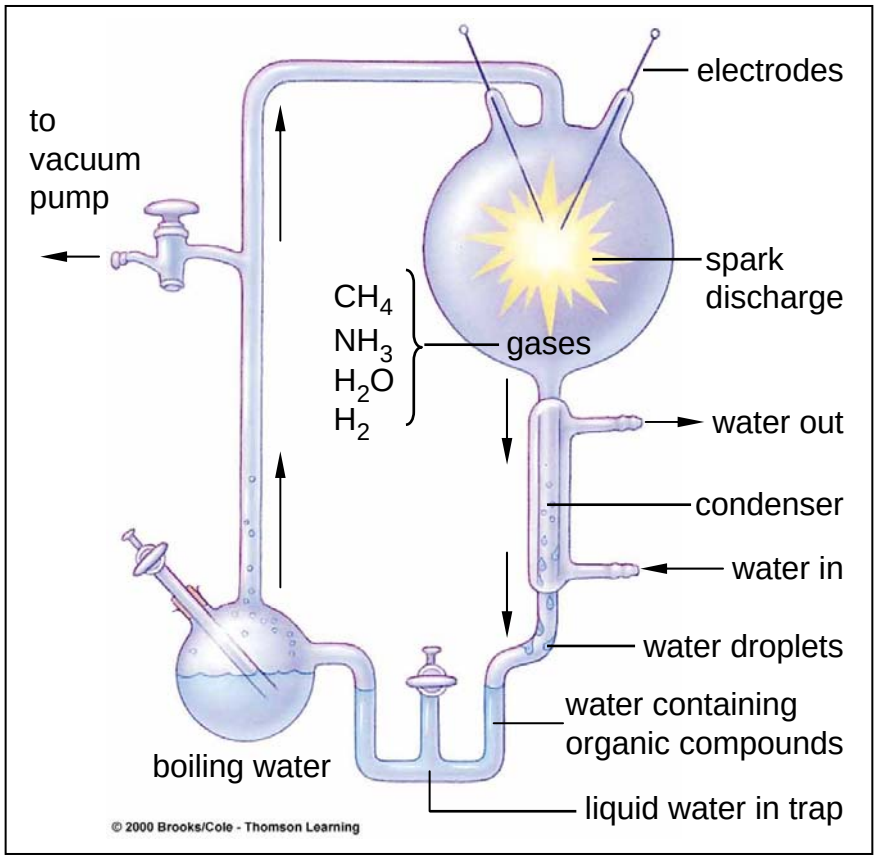
Alexander Ivanovich Oparín
1924

Stanley Miller
1953



Propuesta de un escenario plausible
Concepto de evolución química

Walther Löb, 1913, publicó haber encontrado Gly en condiciones semejantes, mientras estudiaba la electroquímica de gases en relación con la fijación de N_2 y CO_2 en plantas



En una atmósfera reductora, es posible sintetizar aminoácidos y bases nitrogenadas a partir de moléculas más simples. Estos resultados no son obtenidos en condiciones neutras u oxidantes.

"No geological or geochemical evidence collected in the last 30 years favors a strongly reducing primitive atmosphere…Only the success of the laboratory experiments recommends it."

—R.A. Kerr

"Origin of life: new ingredients suggested."

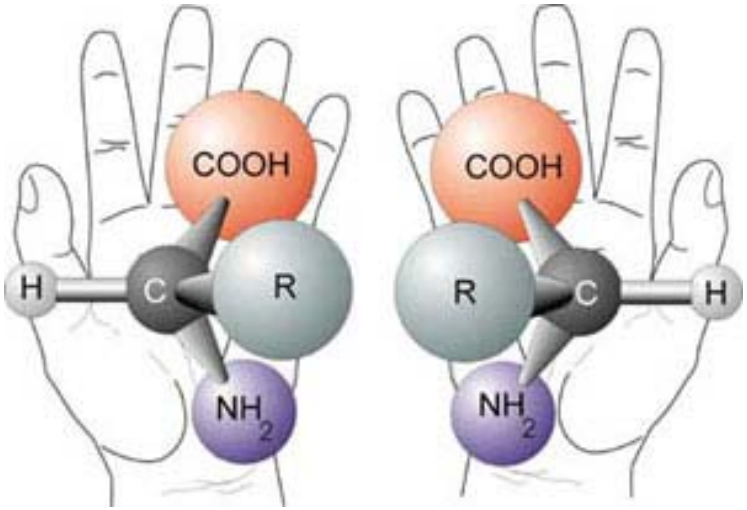
Science 210(4465), 42 (October 3, 1980).

TABLE 1-4 Yields from Sparking a Mixture of CH_4, NH_3, H_2O, and H_2

Compound	Yield (%)
Glycine[a]	2.1
Glycolic acid	1.9
Sarcosine	0.25
Alanine[a]	1.7
Lactic acid	1.6
N-Methylalanine	0.07
α-Amino-*n*-butyric acid	0.34
α-Aminoisobutyric acid	0.007
α-Hydroxybutyric acid	0.34
β-Alanine	0.76
Succinic acid	0.27
Aspartic acid[a]	0.024
Glutamic acid[a]	0.051
Iminodiacetic acid	0.37
Iminoaceticpropionic acid	0.13
Formic acid	4.0
Acetic acid	0.51
Propionic acid	0.66
Urea	0.034
N-Methylurea	0.051

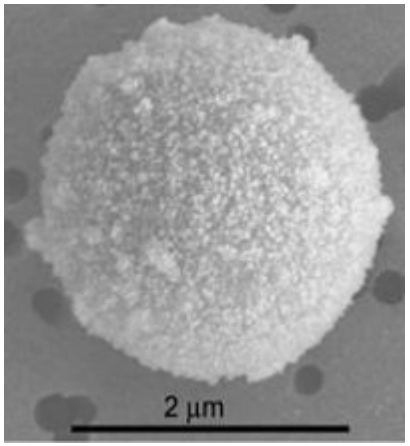
[a] Amino acid constituent of proteins.

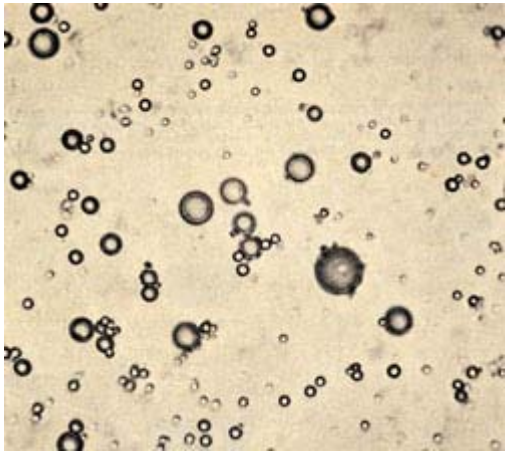
Source: Miller, S.J. and Orgel, L.E., *The Origins of Life on Earth, p.* 85, Prentice-Hall (1974).


COOH
H
C
R
NH2
COOH
R
C
H
NH2

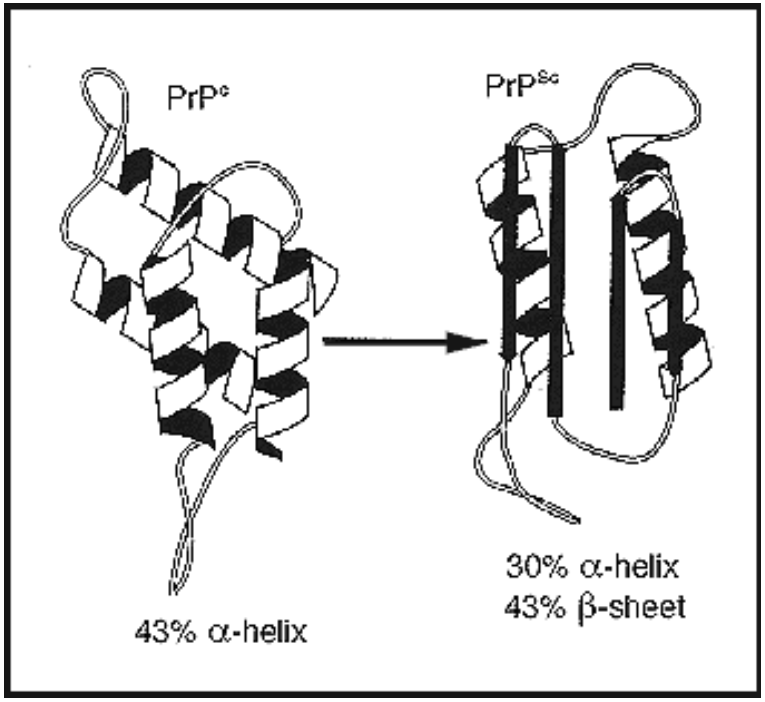
ORGANIC COMPOUNDS IN THE MURCHISON CHONDRITE

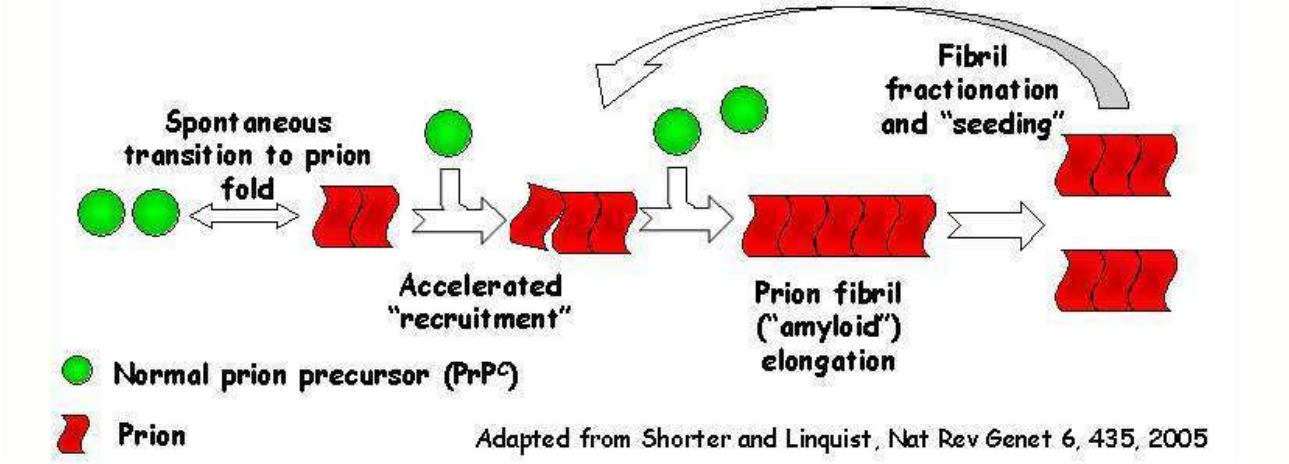
Class	Concentration (ppm)	Compounds Identified
Monocarboxylic Acids	>300	20
Polar Hydrocarbons	100-120	10+
Amino Acids	60	74
Amides	55-70	49+
Aliphatic Hydrocarbons	>35	140
Dicarboxylic Acids	>30	38
Aldehydes & Ketones	27	9
Aromatic Hydrocarbons	>15-28	87+
Hydroxy Acids	15	51
Alcohols	11	8
Amines	8	10
Basic N-Heterocycles	7	32
Purines and Pyrimidines	1	5
Sulfonic Acids	71	8
Phosphonic Acids	2	4





Sidney Fox





Adapted from Shorter and Linquist, Nat Rev Genet 6, 435, 2005

The Intervening Sequence RNA of *Tetrahymena* Is an Enzyme

ARTHUR J. ZAUG AND THOMAS R. CECH

A shortened form of the self-splicing ribosomal RNA (rRNA) intervening sequence of *Tetrahymena thermophila* acts as an enzyme in vitro. The enzyme catalyzes the cleavage and rejoining of oligonucleotide substrates in a sequence-dependent manner with $K_m = 42$ μM and $k_{cat} = 2$ min^{-1}. The reaction mechanism resembles that of rRNA precursor self-splicing. With pentacytidylic acid as the substrate, successive cleavage and rejoining reactions lead to the synthesis of polycytidylic acid. Thus, the RNA molecule can act as an RNA polymerase, differing from the protein enzyme in that it uses an internal rather than an external template. At *p*H 9, the same RNA enzyme has activity as a sequence-specific ribonuclease.

IN RNA SELF-SPLICING, THE FOLDED STRUCTURE OF AN RNA molecule mediates specific cleavage-ligation reactions (*1–5*). Self-splicing exemplifies intramolecular catalysis (*6*) in that the reactions are accelerated many orders of magnitude beyond the basal chemical rate (*7, 8*). The reactions are highly specific, as seen in the choice of a free guanosine nucleotide as a substrate in the self-splicing of the *Tetrahymena* ribsomal RNA precursor (pre-rRNA) and other RNA's containing group I intervening sequences (*1–3, 7*). Furthermore, the cleavage-ligation activity mediates a series of splicing, cyclization, and reverse cyclization reactions, suggesting that the active site is preserved in each reaction (*9, 10*). However, the RNA is cleaved and rejoined during self-splicing; because the RNA is not regenerated in its original form at the end of the reaction, it is not an enzyme. The RNA moiety of ribonuclease P, the enzyme responsible for cleaving transfer RNA (tRNA) precursors to generate the mature 5′ end of the tRNA, has been the only example of an RNA molecule that meets all criteria of an enzyme (*11–13*).

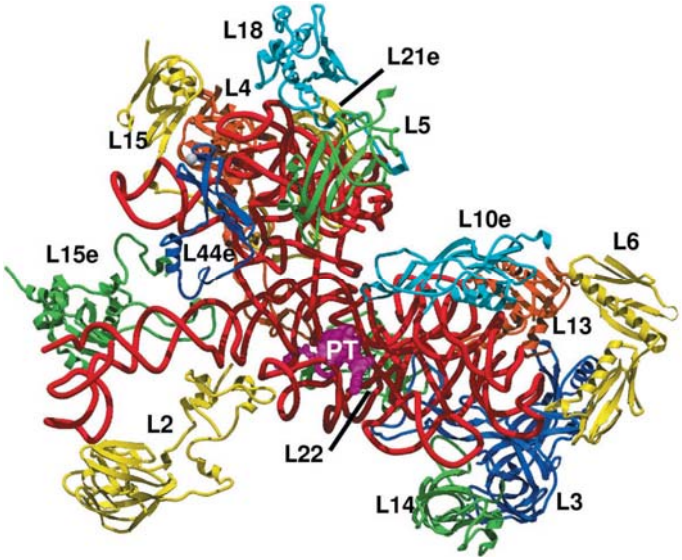
Following self-splicing of the *Tetrahymena* rRNA precursor, the excised IVS RNA (*14*) undergoes a series of RNA-mediated cyclization and site-specific hydrolysis reactions. The final product, the L − 19 IVS RNA, is a linear molecule that does not have the first 19 nucleotides of the original excised IVS RNA (*9*). We interpreted the lack of further reaction of the L − 19 species as an indication that all potential reaction sites on the molecule that could reach its active site (that is, intramolecular substrates) had been consumed; and we argued that the activity was probably unperturbed (*9*). We have now tested this by adding oligonucleotide substrates to the L − 19 IVS RNA. We find that each IVS RNA molecule can catalyze the cleavage and rejoining of many oligonucleotides. Thus, the L − 19 IVS RNA is a true enzyme. Although the enzyme can act on RNA molecules of large size and complex sequence, we have found that studies with simple oligoribonucleotides like pC_5 (pentacytidylic acid) have been most valuable in

Thomas R. Cech is a professor and Arthur J. Zaug is a research associate in the Department of Chemistry and Biochemistry, University of Colorado, Boulder, 80309-0215. Send correspondence to T.R.C.

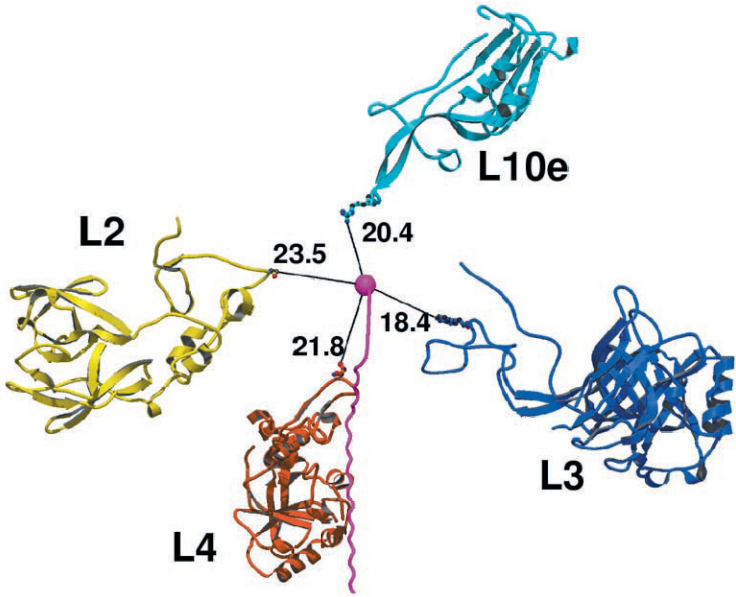
En 1982, Tom Cech y cols. Descubrieron que un intrón dentro de un RNA no procesado del protista *Tetrahymena thermophila puede catalizar su propio clivaje (denominado autosplicing)* para producir la forma madura del RNA.

Actividad catalítica en el ribosoma

- Sitio activo del ribosoma



- Si removemos la parte RNA, la proteína más cercana se encuentra a > 18 Å



Nissen P, Hansen J, Ban N, Moore PB, Steitz TA., Science 289, 920-930 (2000)