

BIOCHEMICAL ASPECTS OF EVOLUTION (14 chapitres, 6 cours, 12 heures)

Athel Cornish-Bowden, UCL, 2, 3, 5, 9, 10, 11 Mars 2010, 14h-16h

Salle ISV, Place Croix du Sud 4-5, Bât Carnoy B0, Louvain-la-Neuve

1. Introduction

Unity of biochemistry: "Il n'y a, philosophiquement parlant, qu'un seul animal, modifié par quelques retranchements ou par de simples changements dans la proportion des parties », Geoffroy Saint-Hilaire, 1807; « From the elephant to the butyric acid bacterium -- it is all the same", Albert Jan Kluyver, 1926.

Thinking in different dimensions: why are enzymes so big?

Information content of amino acid sequences: to what extent can they be regarded as random or haphazard?

2. The Biochemical Basis Of Evolution

Why do genes change at all? Wouldn't it be better (from the point of view of the gene itself) if it stayed completely the same from generation to generation?

Base pairing in DNA: How rigid are the pairing rules?

Errors and error-correction

Fixation of mutations

Mitochondrial Eve and Y-chromosome Adam: Were they a couple, or even contemporaneous? How long ago did they live?

Dimensions again: The allometric law

Natural selection: What happens when a breeder breeds for strength or speed?

Gene duplication, chromosome duplication: Chromosomal abnormalities in the human population.

3. Adaptation, Accidents

The Panglossian view: All changes are adaptations

Examples of putative adaptations

Sperm whale and horse myoglobin

Horse-liver alcohol dehydrogenase

Vitamin A in polar-bear liver

Non-coding DNA

Six codons for arginine, two for aspartate

The "universal" genetic code: How universal? How difficult to change it?

4. Cellular Metabolism

Why so complicated?

How did it arrive to its present state?

Classification into pathways: How arbitrary is this? Could we do it differently?

Enrique Meléndez-Hevia and the pentose phosphate pathway

5. Combinatorial Games And Metabolism

The farmer, fox, geese and oats: a well-known puzzle for children

A classic problem in cryptography: how can a secret message be usefully transmitted to someone who doesn't have the key?

Evolution as a biased random walk: bacterial chemotaxis as an analogy

Moving prisoners between cell blocks

The organization of the pentose phosphate cycle appears to be optimal: Is it really, or did the result just follow a problem with arbitrary designed to give an already chosen answer? Is the result obvious?

The Calvin cycle

Is the shortest route necessarily the best?

6. The Structure Of Glycogen

The problem of osmosis: How to store very large numbers of glucose molecules in the liver and muscles without provoking osmotic stress?

Osmotic effects in everyday life: Adding water to blood; boiling potatoes

Glycogen: The equivalent of 50 000 molecules of glucose in one beta-particle

Wrong structure shown in most textbooks

Optimality: How many chains on the surface available for attack? How many susceptible sites on the surface?

How many glucose units stored in the complete molecule? How large (in volume) is the complete particle?

7. Entropy Enthalpy Compensation

The need for some scepticism

Correlation between biological observations: (i) non-existent; (ii) suggestive; (iii) good; (iv) too good to be true

Correlation between entropy and enthalpy of activation

How are entropy and enthalpy typically measured? van t Hoff plots, Arrhenius plots, calorimetry

8. Control Of Fluxes And Concentrations

Homeostasis: maintaining constancy in the face of changing needs

Rate-controlling steps, key enzymes etc. Is glycolysis controlled by the activity of phosphofructokinase? If not, by what?

Feedback inhibition, allosteric effects, cooperativity

Flux control coefficients: Summation relationship, control is shared by all the enzymes in the system

How to understand the summation relationship so thoroughly that it becomes obvious

Flow in natural (unregulated) systems: river basins

Coupling between half reactions

9. Inheritance In Diploid Organisms

Dominance and recessivity: Basic ideas of Mendelian inheritance

Haploid, diploid, polyploid organisms

Heterozygote phenotypes: breeding peas, eye colour, phenylketonuria

Darwin's and Mendel's views contrasted

The "new synthesis"

Selecting for pea colour in a paint-mixing world

Dominance understood in the light of the summation property

Why don't we detect the slight difference between the dominant homozygote and the heterozygote?

Dominance in *Chlamydomonas reinhardtii*, a haploid organism that passes through occasional diploid generations

10. The Metabolic Economy

Mechanisms, feedback inhibition, allosteric interactions, cooperativity

Naive ideas about flux regulation

Enzyme inhibition: succinate dehydrogenase

Need for cooperativity

Haemoglobin and myoglobin compared

Examples of supply-driven processes: glucose uptake by the liver

A real example of metabolic regulation: the aspartate pathway in *Arabidopsis thaliana*

11. Failures Of Natural Selection

The effects of stoichiometric constraints: arthritis, or why large animals cannot obtain enough glycine for efficient maintenance of collagen

The effects of unnatural diet: human obesity and how it can be avoided

12. Origin Of Life: On Earth?

Time and resources available on earth

Size of the universe: not as big as people think

Probability arguments

Age of the universe: not as old as people think

Minimal organisms

Necessity for a protein sequence to be precisely correct: carbonic anhydrase, superoxide dismutase, histone IV, domain shuffling

Frequency of improbable events

Science, technology and bee dancing

13. Biochemical Basis Of Cancer

Aneuploidy: effect of changing many enzyme activities simultaneously, failure of metabolic control

Targets for anti-cancer drugs: why it's not a good idea to treat the thiamine (vitamin B1) deficiency typical of cancer patients.

14. Towards A Definition Of Life

Historical views: vitalism, Stéphane Leduc, D'Arcy Thompson, Erwin Schrödinger

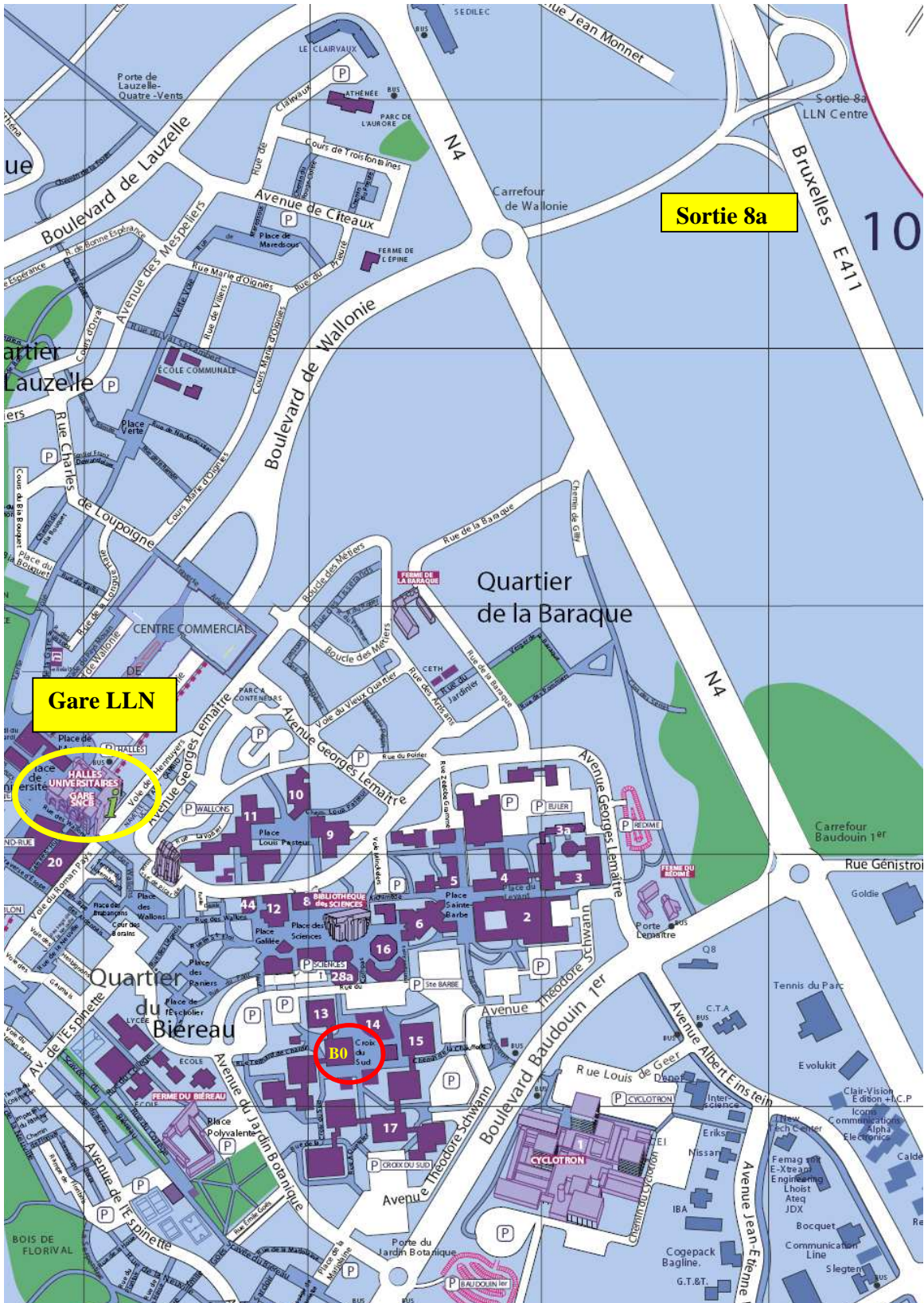
Current views: Robert Rosen ((M,R) systems), Tibor Gánti (the chemoton), Stuart Kauffman (autocatalytic sets), Humberto Maturana and Francisco Varela (autopoiesis)

Organizational invariance: an organism cannot depend on the outside world for the catalysts that it needs.

Closure to efficient causation

The meaning of catalysis

Artificial life



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