Comparative biochemistry of cells: The extent, origin and control of biochemical variability.

I Known biochemical structures.

A Comparative aspects of cellular organization

1 The nuclear apparatus

a. Chemistry of plant and animal nuclei

Morphology, cytochemistry

Chromosomal structure and organization

Metabolic role and activities

Structural associations with cytoplasm

b. Protozoa and algae

c. Do bacteria have nuclei?

1. Chromosomal organization genetic evidence

2. "Nuclear" organization--electron microscopy, cytochem.

3. Relations to protoplast membrane

2 Cytoplasmic organization--animals vs plants vs microbes.

a. Mitochondria

1. Mitochondrial evolution--cytology, distribution.

2. Mitochondrial integration--functional--structure.

3. Mitochondrial roles.

4. Do bacteria have mitochondria?

5. Protoplast membrane--distribution, structure composition, role relation to mitochondria.

B Endoplasmic reticulum

1 Structure in animal and plant cells

2 Existence in unicellular organisms?

3 Secretion

4 Relation to cell surface, pinocytosis

C Ribosomal structure and function

1 Distribution of free ribosomes.

a. Origin

D Photosynthetic apparatus

1 Distribution

2 Structure

3 Origin, multiplication, inheritance

E Other structures

1 Golgi apparatus

F Cell sap

1 Osmotic properties, pH, composition

2 Role, organization ?, origin

G Cell membranes and walls

1 General structure and role:

a. Animal vs plant vs unicellular organisms

b. Bacteria vs protozoa, algae vs yeast and fungi

2 Distribution, role and biosynthesis of sialic and muramic acids

3 Selective toxicity of antibiotics with special references to cell walls

4 Mono- and dideoxyhexoses--distribution and origin

5 Biosynthesis of cell walls and capsules--structures, control

H Virus structure

1 Comparative aspects and principles of organization

2 Relations of structure to problems of penetrating host

3 Genetic structure

4 Are viruses derivative or primary organisms? (origin of viruses and nucleoproteins)

I Cell specialization

1 Chemical aspects of differentiation

J Aging and cytopathology

1 Selective advantages

K Selective advantages of existing structures

II Known biochemical activities

A Systems of energy metabolism

1 Anaerobic metabolism

a. Electron transfer--anaerobic dehydrogenases

1. Pyridine nucleotides

2. Folic acid derivatives

3. Transhydrogenation

4. Glutathione and other reductases

5. Mechanisms of H transfer and implications for evolution of organisation

6. Enzyme specificity and the organization of active sites

7. Isozymes

b. Flavoproteins

1. DPN or TPN--cytochrome c reductases

2. Cytochrome reducing dehydrogenases--variability

3. Diaphorases and lipoate dehydrogenases

4. Metal flavoproteins and

5. Autooxidyable flavoproteins and peroxide production

b. Cytochemistry

c. Peroxidatic decomposition

1. Organic mechanisms

2. Catalase

3. Peroxidase variability

4. Cytochrome c peroxidases

2 Cu enzymes and O_2 transferases

a. Ascorbic acid systems

b. Polyphenol oxidases

1. Aspects of melanin production

c. Hemocyanins

d. O_2 transferases

3 Terminal oxidation by Fe enzymes

a. Cytochromes--cytochromes in anaerobes b.

c. Cytochrome c-cytochrome oxidase

d. Other autoxidizable cytochromes

4 Biology of oxidation-reduction

a. Analysis of pathways

1. Enzymology

2. Spectrophotometry

3. Inhibitors

b. Distribution of systems within cells

1. Bacteria vs other cells

2. Distribution on organelles

a. Nuclei and soluble fraction

b. Mitochondria

c. Microsomes

d. Protoplast membranes

3. Integration--reaction chains and utilizable energy

4. Derivation of energy--oxidative phosphorylation

c. Anaerobes

1. Are modern anaerobes primitive organisms?

a. Mechanism of Stickland reaction

b. Distribution of cytochromes

c. Efficiency

2. Anaerobic and aerobic parasites

3. Fermentative processes

d. Oxygen utilization in biosynthesis

e. Relations in division and differentiation

1. Role of TPNH

2. Role of -SH compounds

3. Sporulation

4. Insect development

5. Nutritional controls

6. Genetic controls

7. Environmental controls

B. Systems of atmospheric carbon and nitrogen utilization

1 Phototrophy

a. Photosynthesis--carbon cycle

1. Higher plants and algae

a. Carbon cycle--within cell

b. Photocleavage of water

1. Mechanisms--energy transfer

2. Related oxidation-reductions

3. Functional organization of chloroplast

2. Bacterial photosynthesis

b. Photoassimilation

c. Chlorophylls

d. Carotenoids

e. Biosynthesis of pigments--control, significance for evolution

2 Nitrogen fixation

a. Nitrogen cycle--evolutionary consideration

b. Organisms fixing N

1. Microbial)
) properties of fixation
2. Symbiotic)

c. Enzymatic mechanisms: anaerobic and aerobic
photosynthetic

d. Hydrogenase

e. Nitrification

f. Denitrification

C. Systems of carbohydrate metabolism

1 Energetics

a. Chemical currency

1. ATP and other triphosphates

2. Phosphagens

3. Acetyl-thiamine pyrophosphate

4. Thioesters

5. Carboxyanhydrides, amides

2 Embden-Meyerhof-Parnas scheme--variability

a. Enzymes

b. Reoxidation of DPN--insects, tumors

c. Other hexoses, aminohexoses, uronic acids

3 Oxidative phosphogluconate pathway

4 Hexose phosphate cycle

5 Pentose and tetrose metabolism

6 UDP mechanisms. Origin of ascorbates

7 Nonphosphorylative routes and others

8 Analysis of routes used--variability

9 Control of alternative paths--pathology

D. Pyruvate degradation

1 Diversity in conversion of pyruvate to C_2 fragments

2 Origin and degradation of lactate--glyoxalase, etc.

3 Carboxylase

a. Thiamine mechanisms

b. Acetaldehyde and ethanol metabolism.

4 Acetoin production and metabolism--mechanisms

5 Oxidation of pyruvate

a. Bacteria vs animal cells--routes to acetyl-CoA and acetate

b. Biosynthesis and functions of CoA and intermediates

c. Phosphoroclastic reactions

E. Utilization of acetate

1 Fatty acid biosynthesis and metabolism

a. Bacteria vs animals--activation mechanisms

b. Origin of cyclopropane, mono- and multi-unsaturated acids

c. Degradation

2 Carotenoid and other terpenoid biosynthesis

3 Sterol biosynthesis and degradation

a. Distribution and O_2 requirement

b. Comparative structures

c. Origin of oxygenated derivatives

d. Hormonal role

4 Lipid biosynthesis

a. Variability of structures--distribution

b. Biosynthesis

c. Degradation

d. Integration with other substances, e.g. protein

5 Detoxification, acetyl amino acids in metabolism

F. Citric acid cycle

1 Variability in enzymes, reactions, organization

2 Variability in function--energy vs fragments (amino acids)--estimation

3 Glyoxylate cycle

4 Four carbon acid metabolism and CO_2 fixation

a. Variability in mechanism

b. Distribution and control

c. Proprionate cycle

d. Other possibilities--Thunberg condensation

5 Other products--glutaconate, maleic, citramalic, etc.

G Amino acid metabolism

1 Structures

2 Reactions

3 Distribution

4 Metabolic origin

5 Degradation and interconversions

6 Nature and control of enzymes of the pathways

7 Interrelations with other areas of metabolism--nicotinamide, etc.

H Tetrapyrrole biosynthesis

1 Catalytic functions of iron--a.structural relation to porphyrins

b. Absorption, transfer, and insertion of Fe

2 Cellular distribution and concentration of tetrapyroles

a. Environmental effects

b. Developmental effects

c. Genetic control

3 Distribution and structure of tetrapyvoles, chlorophyll, porphyrins and linear tetrapyvoles.

4 Relations of structure to enzymatic activities

5 Early intermediates to Mg protoporphyrin IX

6 Mg protophorphyrin ------ chlorophylls

7 Mg protophorphyrin ------ heme

8 Evolutionary considerations

I Water balance and nitrogen excretion

1. Amino acid degradation

2. NH_3 detoxification

3. Purine and pyrimidine degradation and excretion

J Purine and pyrimidine biosynthesis

K Nucleic acid metabolism

1 Polyribonucleotide biosynthesis--variability, structure, specificity, primers

2 Polyribonucleotide degradation--variability

3 Scavenger mechanisms

4 DNA biosynthesis and degradation

5 Roles of nucleic acid in genetic continuity and expression

a. Duplication--mechanism

b. Control of protein synthesis

L Protein metabolism

1 Mechanism of biosynthesis

a. Amino acid activation and transfer

b. Templates, coding mechanisms

c. Cyclic peptides, cell walls

d. Control of

2 Mechanisms of degradation

M Polysaccharide metabolism

1 Mechanisms of biosynthesis

a. Monosaccharide activation

b. Primers and specificity

c. Sulfates, phosphates

1. Activation

d. Integration with other substances, e.g. proteins

e. Control of

2 Mechanisms of degradation

N Survival value of existing metabolic systems

III Environmental effects on biochemical structure and metabolic systems

A Structure) as function of temperature, pH, ionic strength, osmotic
) pressure, atmospheric composition, pressure, humidity,
B Metabolism) light (radiation)

IV Possible chemical systems of biological structure and function

A Known mechanisms which would permit survival of an organism on

1 Mars

2 Venus

3 The Moon

B As yet undetected mechanisms