Crewell-Simon Lecture

Introductory remarks.

"Some branch of physics of general interest."

What in molecular biology?

explaining anything biological in terms of physics or chemistry.

mainly gene-protein and their synthesis but also muscle, nerve, etc.

Two roots:
1. Structural
   - Astbury, Bernal.

2. Combination of
   - biophysics, biochemistry, genetics, etc.
   - logical arguments

What is physics? "Physics can explain everything, chemistry and biology must be included."

What do physicists actually know? Some crystallography, a little physical chemistry, hardly any organic chemistry.
DNA $\rightarrow$ RNA $\rightarrow$ Protein

Nucleic Acid
poly nucleotide chain
nucleotide
phosphate sugar base

Protein
poly peptide chain
amino acid

4 bases
20 side chains

Genetic code
X-ray crystallography

Small molecules: to accurately bond distance, angles, and rules for hydrogen bonding, etc.

Polypeptide chain: amino acid sequence and size

Protein molecule: X-ray diffraction

Isomorphism, replacement method

Number of reflections in reciprocal lattice

(Also photographic method)

Geiger counter: linear detector

Automatic collection

Importance of computing

Electron density maps: interpret density

Plotting by computer

Final model of molecule

Nucleic acid

DNA fiber diffraction

Low resolution: saw axis (helical diffraction theory)

No many variables

Formula of DNA

General nature of solution

Structure of DNA

Example of a small molecule

A base pair in a crystal

Hydrogen bonds
electron microscope

electron can be deflected by elastic or magnetic lens. Specimen must be in a vacuum, thus dry, handicap for biological. limited penetration power.

resolution limited by wavelengths, b and small aperture, due to spherical aberration, but down to 5-10 A.

main other limitation is due to contrast.

main methods

1. shadowing technique, give c and impervious.

   classical technique: polysome

   modified technique: phase DNA

2. thin section: with special microtome (diamond knife)

   example: muscle, sarcomere, actin, myosin, ribonucleic, elements.

   some

   some cross-section

   some staining

   higher magnification log: TM V (+ model)

3. reject contrast: actin double helix

human, was, virus

problem of one side v both sides, Klea technique.
Radioactive tracers

Very useful are: means one can study materials that

in small amount. mainly $^{32}$P, $^{14}$C, $^{3}$H. - automatic.

difficult to illustrate, because of the detailed

biochemistry.

Example: tracer neutron analysis of DNA.

DNA replication by base pairing

can be done in test-tube. needs enzyme,

like 4 precursors and a template DNA.

method — 5

result — 5

 Autoradiography advantage of $^3$H because of short range

show DNA in a bacterial cell — 5

Claim picture. explain the scale — 5
Physical chemistry

briefly mention:

1. Electrophoresis: free paper, acrylamide gels.

Example: many abnormal human hbs

2. Chromatography: paper, in exchange, etc., sephadex.


Example of density gradient: Meselson-Stahl exp.

Leading principle:

explain problem of DNA replication. S

Use of heavy isotope N to give density difference. Show result S

Explain "duplex"

fit in another idea of one long molecule with a specificity point.
Influence of people

Those who stayed outside

- Schrödinger: "What is life?"
  the first 3/4 book
  its influence.
  Samuels' idea of coding.

Those who came in

1. the crystallographers: Arthur, Bragg, Bragg.
   2nd generation: Pons, Kendrew - chemists!

2. those who do genetics of biochemistry,
   Max Delbrück: his school, his outlook.
   Seymour Benzer.

Quite a number of others, mainly genetics bias.
   Sally Gilbert and biochemistry.
Idea

Two examples only:

1. Symmetry: e.g. regular helix \( \alpha \)-helix \( S \)
   - TMV rod virus
   - Virohedron: 60 subunits
   - Almost-symmetric structures
   - Coiled coils \( S \)
   - Actual virus structures

2. Logic in genetics.
   - Mutants of a special type
     + ad
   - The base plus mutant
   - conclude how a triplet code
   - Mutly is a multiple of three.
Influence of physics

can be grouped under several headings:

(1) discipline, e.g. (protein) crystallography.

(2) instrument, e.g. electron microscope and techniques: ultracentrifuge, radioactivation traces.

(3) idea, e.g. simplicity: symmetry.

(4) people: either those who stayed as physicists or those who gave up physics and entered molecular biology.
Sums up.

where would molecular biology be without physics?

preceded physics (but not chemistry) see v. beadon's

no crysallography

e/m

radioactive trace,

heavy isotopes.

and no physicists in biology,

now of molecular biology copied everything

but where is no chemistry at all,

or no physical chemistry.

or no genetics.

Sure then could be another lecture!