Unit 1: Mechanistic Cell Biology

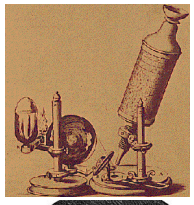
1. The Emergence of Cell Theory

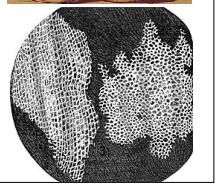
The Challenges of New Observational Tools

- New research tools, like the microscope, have to be invented and validated
- What we call the microscope resulted from the discovery that lenses, singly and in combination, can increase human ability to see
  - But they also create distortions, raising questions of whether what is seen with them exists
- As important as the development of new instruments is, equally important has been the challenge to figure out what they are showing us. Just seeing is not enough!

Robert Hooke-1665

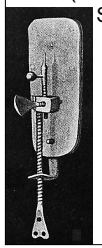
- Examined thin slices of cork and discovered:
  - "Yet it was not unlike a Honey-comb in these particulars...these pores, or cells, ... consisted of a great many little Boxes.... Nor is this kind of texture peculiar to Cork only; for upon examination with my Microscope, I have found that the pith of an Elder, or almost any other Tree, the inner pulp or pith of ... several other Vegetables ... have much such a kind of Schematisme, as I have lately shown [in] that of Cork."
- Hooke called them “cellulae” (Latin word for “little rooms”).
- He construed walls as the defining property of cells

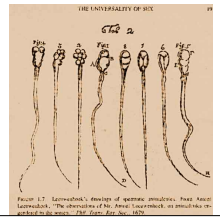


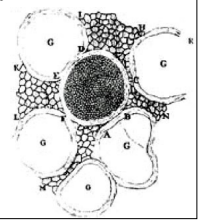


Antony van Leeuwenhoek

- Developed his own single-lens microscopes for use on fabrics (his day job was running a drapery business in Delft)
- He was the first to observe details of animal structure (muscle banding) as well as single-celled organisms (bacteria, sperm)
- Sent results to the new Royal Society







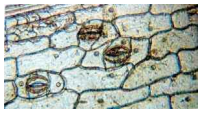
To Good to be True

- By the early 19th century numerous microscopists started reporting very smooth, regular, round structures within plant and animal tissue
- Lorenz Oken: articulated a grand theory
  - "all organic beings originate from and consist of vesicles or cells. These vesicles . . . are the infusorial mass or protoplasma whence all larger organisms fashion themselves or are evolved. Their production is therefore nothing else than a regular agglomeration of Infusoria—not, of course, of species already elaborated or perfect, but of mucous vesicles or points in general, which first form themselves by their union or combination into particular species."
- But what he saw are now thought to be artifacts produced by his microscopes

Limitations on early microscopes

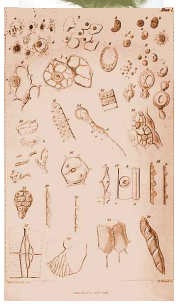
- Spherical aberration: failure of light rays to fall all in one plane when focused through a lens
- Chromatic aberration: dispersive action of lenses in breaking white light into primary colors
- Technical Advances
  - William Hyde Wollaston (1812): two plano-convex lenses, placed at a prescribed distance apart—counters spherical aberration
  - John Hershel (1821): aplanatic combination of lenses
  - Joseph Jackson Lister (1824-1830): combined lenses of crown glass with others of flint glass, so adjusted that the refractive errors of each were corrected or compensated for by the other

Robert Brown



- In 1827, utilizing a very simple microscope, observed active particles (Brownian motion)
- In 1831, observed an opaque spot in plant (Orchid) cells which he named the *nucleus* (Latin for kernel)

Matthias Schleiden: 1838



- In his study of plant tissue, took the nucleus, which he named the *cytoplast*, to be the most important structure in what he observed as cells
  - Inferred it was the unit from which the rest was formed
  - Treated it the defining mark of cells
  - Argued that despite the fact that cells had different appearances, they were all the same as a result of having a nucleus

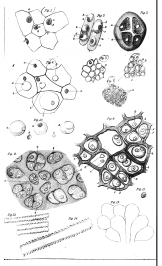
Clicker Question

What was the main point Schwann wanted to get across in Microscopical Researches?

A. That the microscope is the most useful instrument for studying biology
B. That although they appear to be different, the basic units of plant tissues are all the same--cells
C. That although they appear to be different, the basic units of animal tissues are all the same--cells
D. That new cells form from old ones through a process of cell division

Theodor Schwann

- Problem in extending the account of cells to animals:
  - the units observed with the microscope are highly variable
- Schwann focused on the similarities of some animal cells (ovum, epidermis) to plant cells
  - Following Schleiden, he came to emphasize the nucleus, which he found in embryonic tissues
- Main strategy:
  - show that despite the variability, animal cells all originate in the same manner and so are all the same kind of thing.



Clicker Question

For both Schleiden and Schwann, an defining feature of cells is how they are formed. What is their basic account:

A. Cells form through a process of divison of existing cells
B. The process of cell division is preceded by the division of chromosomes
C. Cells form by first depositing the cytoblast/ nucleus and then different material around it
D. The cytoplasm forms first, and the cytoblast/ nucleus only later forms within it

Cell Theory

- Schwann's claim: cells are the fundamental units of living organisms
  - "Each cell is, within certain limits, an Individual, an independent Whole. The vital phenomena of one are repeated, entirely or in part, in all the rest."
- "There is one universal principle of development for the elementary parts, of organisms, however different, and this principle is the formation of cells"
  - Key reasoning strategy: All cells develop in the same way and hence are fundamentally the same despite observed differences

Schwann's Project

- Demonstrate that animal tissues develop in the same manner as plants
  - "I compared the cells of cartilage and of the chorda dorsalis with vegetable cells, and found the most complete accordance. The discovery, upon which my inquiry was based, immediately lay in the perception of the principle contained in the proposition, that two elementary particles, physiologically different, may be developed in the same manner. For it follows, from the foregoing, that if we maintain the accordance of two kinds of cells in this sense, we are compelled to assume the same principle of development for all elementary particles, however dissimilar they may be . . ."

Schleiden's (1838) Account of Growth in Plants

- "He found, that in the formation of vegetable cells, small, sharply-defined granules are first generated in a granulous substance, and around them the cell nuclei (cytoblasts) are formed, which appear like granulous coagulations around the granules. The cytoblasts grow for a certain time, and then a minute transparent vesicle rises upon them, the young cell, so that in the first instance, it is placed upon the cytoblast, like a watch-glass upon a watch. It then becomes expanded by growth."

Analogy with Crystals

- Already in the Preface Schwann announces:
  - "The principal result of this investigation is, that one common principle of development forms the basis for every separate elementary particle of all organised bodies, just as all crystals, notwithstanding the diversity of their figures, are formed according to similar laws"
- What role does the analogy to crystal formation play in Schwann's thinking?

Analogy with Crystals Developed

- "The only other difference in the formation of cells is, that the separate layers do not consist of the same chemical substance, while a common crystal is always composed of one material. In instituting a comparison, therefore, between the formation of cells and crystallization, the above-mentioned differences in form, structure, and mode of growth fall altogetner to the ground. If crystals were formed from the same substance as cells, they would probably, in *these* respects, be subject to the same conditions as the cells."

Discussion Question

Assuming that cells behaved in Schwann's microscopes as they do today (that is, they form via division, not crystallization processes), what explains Schwann seeing a process of crystallization?

A. Schwann was fairly careless with his microsope and really didn't pay much attention to what was there.
B. The attractiveness of a mechanical analogy (crystallization) led him to interpret what he saw in a different way than we do.
C. Given the microscopes of the time, what could actually be seen was ambiguous and could easily be interpreted as crystallization.
D. Other

Schwann's "Cell-Theory"

- "The elementary parts of all tissues are formed of cells in an analogous, though very diversified manner, so that it may be asserted, *that there is one universal principle of development for the elementary parts of organisms, however different, and that this principle is the formation of cells. . . .* the fundamental phenomenon attending the exertion of productive power in organic nature is accordingly as: *a structureless substance is present in the first instance, which lies either around or in the interior of cells already existing; and cells are formed in it in accord with certain laws, which cells become developed in various ways into the elementary parts of organisms"* (p. 165)

Cells and Physiology

- Cells not just anatomic units, but structures that correspond to function:
  - "This variety in the elementary parts seemed to hold some relation to their more diversified physiological function in animals, so that it might be established as a principle, that every diversity in the physiological signification of an organ requires a difference in its elementary particles; and, on the contrary, the similarity of two elementary particles seemed to justify the conclusion that they were physiologically similar" (p. 162).

Schwann's "Theory of the Cells"

- Presents this as more speculative than the claims that all organisms are made of cells and that they form through crystallization.
- Cell as the basic unit of life:
  - "The cells, therefore, not only attract materials from out of the cytoblastema, but they must have the faculty of producing chemical changes in its constituent particles. Besides which, all the parts of the cell itself may be chemically altered during the process of its vegetation. The unknown cause of all these phenomena, which we comprise under the term ***metabolic phenomena of the cells***, we will denominate the ***metabolic power***."

Clicker Question

What is a crucial claim of Schwann's "theory of the cell"?

A. That cells are controlled by vital processes very different from those found in inorganic nature
B. That cell activities are teleological in character--serving to accomplish ends
C. Cells operate according to "blind" laws of nature and distinctive features of cells are due to what chemical (matter) is present
D. Despite appearances, cells always arise by division of existing cells

Teleological vs. Physical Views

- Purposeful behavior is different than what is found in inorganic nature (Schwann rejects this)
  - "that which arranges and combines the molecules is a power acting with a definite purpose. A power of this kind would be essentially different from all the powers of inorganic nature" (pp. 186-7).
- Physical alternative (Schwann's view)
  - "The other view is, that the fundamental power of organised bodies agree essentially with those of inorganic nature, that they work altogether blindly according to laws of necessity and irrespective of any purpose, that they are powers which are as much established with the existence of matter as the physical powers are" (p. 187).

Vitalism: Power in the Whole vs. Mechanism: Causes in the Parts

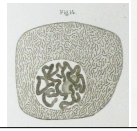
- On one view "the cause of the growth of the elementary parts resides in the totality of the organism. The other mode of explanation is, that growth does not ensue from a power resident in the entire organism, but that each separate elementary part is possessed of an independent power, an independent life, so to speak; in other words, **the molecules in each separate elementary part are so combined as to set free a power by which it is capable of attracting new molecules and so increasing**, and the whole organism subsists only by means of the reciprocal action of the single elementary parts."

Cell Division

- While Schleiden and Schwann were presenting a view of cell formation on analogy with crystals, other investigators (e.g., Hugo von Mohl) observed what they described as cell division
- Until further advances in microscopy, especially the introduction of stains in the 1860s and 1870s, it was not possible to settle this dispute through observation
- Rather, what mattered was the conceptual framework in which cells were understood
  - For Schleiden and Schwann, defending a mechanical conception of life was central and crystallization was an accepted mechanical process
- Other theorists, however, had different concerns
- Rudoph Virchow was a pathologist
  - For him, continuity of disease was a central concern
  - He opposed spontaneous generation, a view then widely held, since it would break continuity
  - In 1855 put forward the claim "Omnis cellula e cellula"

Discovering Mechanisms of Cell Division (1870s-1880s)

- With improved microscopes and stains, more detailed observations were possible, especially of the nucleus
- Robert Remak
  - Division of nucleus precedes cell division
- Edouard van Beneden
  - Characterized structures in the nucleus as bâtonnets (little rods)
  - Reported that they moved apart in the process of division
- Hermann Fol
  - Described spindle and astral rays
  - Proposed analogy with lines of force in magnets
- Walther Flemming
  - Described mitosis
  - *Omnis nucleus e nucleo*
  - Named chromatin



Turning Attention to the Substance within Cells

- Hugo von Mohl: plant cells contain “an opaque, viscous fluid, having granules intermingled in it”
  - Recalled earlier observations of the movement of cell contents
  - Nucleus lies within the fluid, not bound to the cell wall
  - Named the fluid: protoplasm
- Dujardin (1835): sarcode: "I propose to give this name to what other observers have called a living jelly - this glutinous, transparent substance, insoluble in water, contracting into globular masses, attaching itself to dissecting needles and allowing itself to be drawn out like mucus; lastly, occurring in all the lower animals interposed between the other elements of structure."

Shift of Focus from Cells to Protoplasm

- Cohn: “But all these properties are possessed also by protoplasm, that substance of the plant cell which must be regarded as the chief site of almost all vital activity, but especially of all manifestations of movement inside the cell.... Hence it follows with all the certainty that can generally be attached to an empirical inference in this province, that the protoplasm of the botanists and the contractile substance and sarcode of the zoologist, if not identical, must then indeed be in a high degree similar formations.”
- Max Schultz (1860): cell “a small mass of protoplasm endowed with the attributes of life.”