

When Did the Genome Disappear?

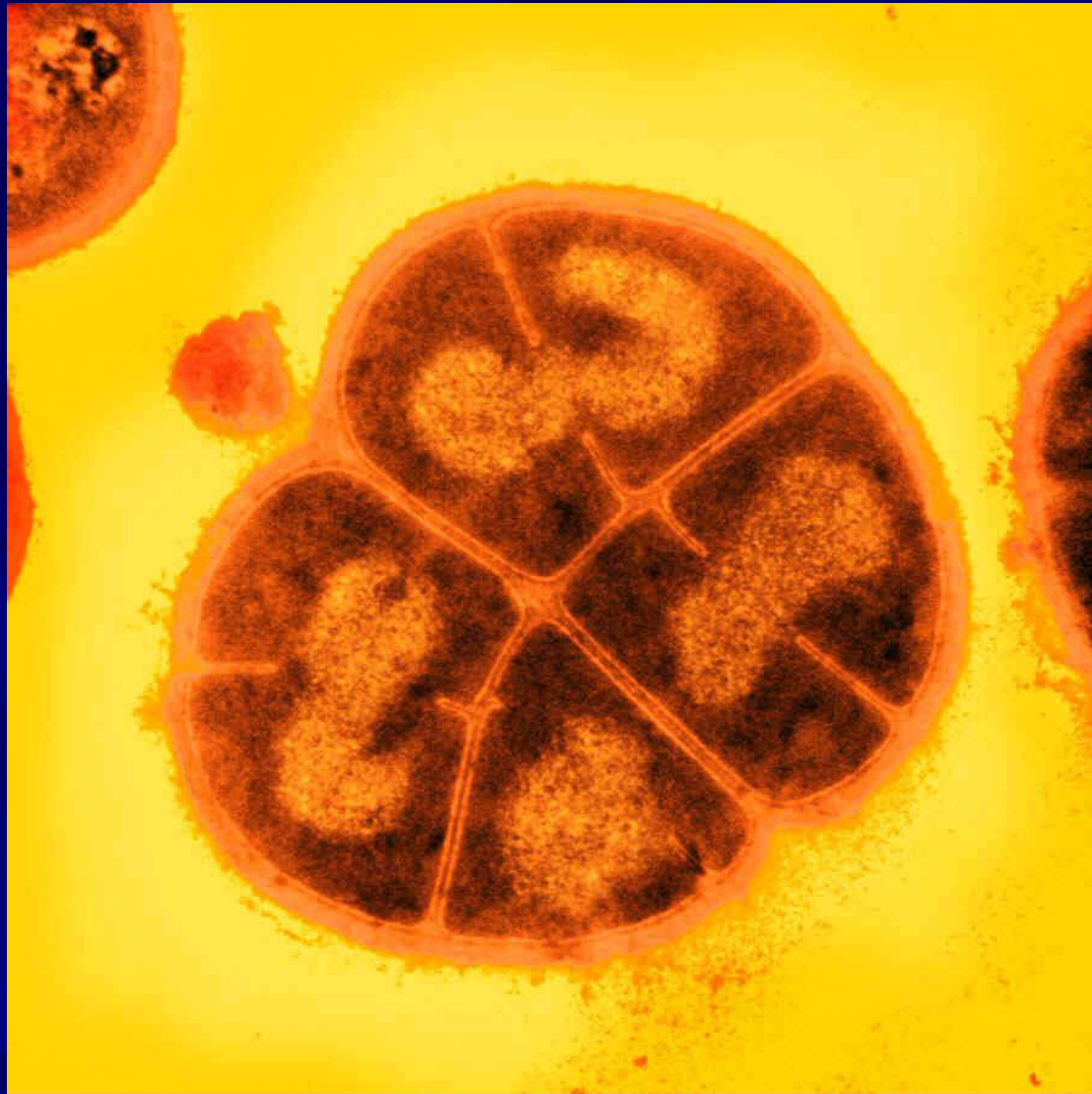


Ehud Lamm

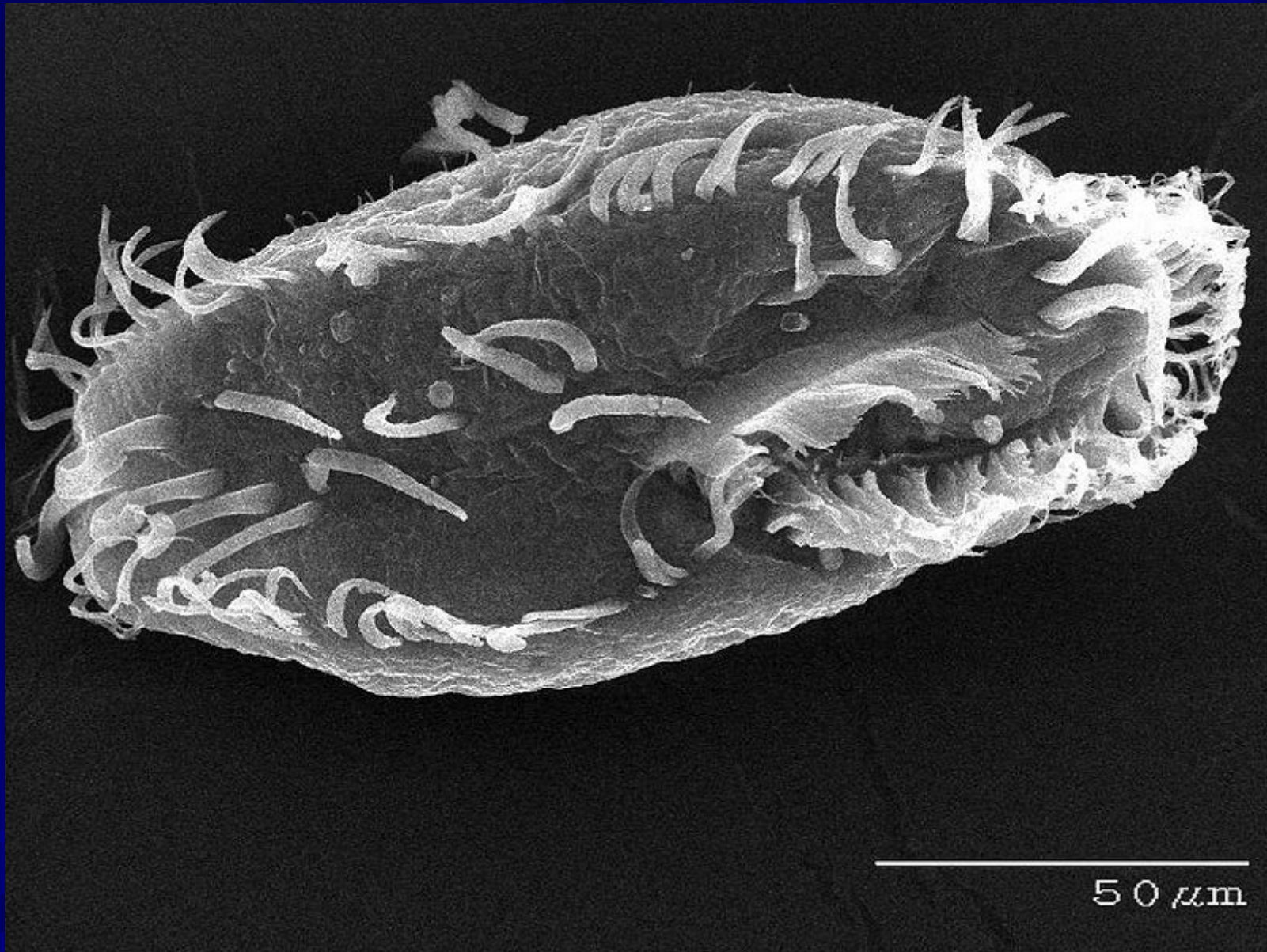
<http://www.ehudlamm.com>

**The Cohn Institute for the History and Philosophy of Science and Ideas
Tel-Aviv University**

NIH – August 2017



D. radiodurans



Oxytricha trifallax

B

XLV.

Ueber die chemische Zusammensetzung der Eiterzellen ¹⁾).

Von Dr. F. Miescher aus Basel.

Die Chemie des Eiters ist bis vor Kurzem fast nur von den Gesichtspunkten aus studirt worden, die für die Untersuchung von pathologischen Tränenmassen massgebend waren. In neuerer Zeit hat man sich mit der Erforschung der Eigenschaften des Protoplasma auch an die Eiterzellen gewandt. Insbesondere musste sich aber seit den bekannten Untersuchungen über die Herkunft der Eiterzellen der Gedanke aufdrängen, dass hier das nächstliegende Material sei zum Studium dieser Zellenspezies, die als constante Grösse nunmehr an so vielen Orten wird eingeführt werden müssen; ein Material, nicht tadelfrei, mit Vorsicht zu verwerthen, aber das einzige leicht zu beschaffende und deshalb zum vorläufigen Ausgangspunkt geeignet.

In diesem Sinne habe ich versucht, über die eigentlich gewebsbildenden Stoffe in den Eiterzellen zu einiger Orientierung zu gelangen. Die ganze Reihe der Extractivstoffe, in sofern sie ihrer Menge und Beschaffenheit nach nicht als wesentliche Gewebsbildner zu betrachten sind, habe ich bei Seite gelassen. Das Material zur Untersuchung wurde mir durch dankenswerthe Vermittlung der Herren Assistenzärzte Dr. Bever und Dr. Koch aus der Tübinger chirurgischen Klinik geliefert. Die Verbände, weitaus überwiegend von Operationswunden herrührend, wurden gesammelt, täglich auf das Laboratorium

1) Die Untersuchungen, welche Hr. Miescher in dieser Abhandlung schildert, sind im Tübinger Schlosslaboratorium von Herbst 1868 bis Herbst 1869 ausgeführt und mir kurz darauf zur Veröffentlichung in diesem Hefte übergeben, dessen Erscheinen durch mehre unvorhergesehene Umstände sehr verzögert ist.

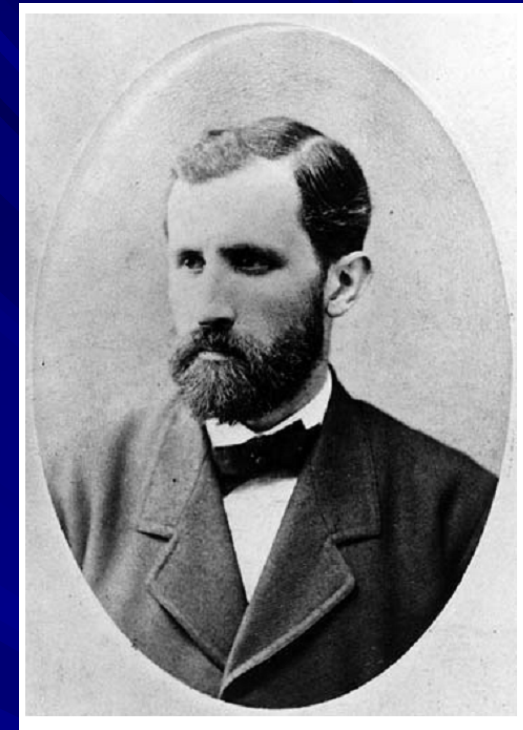
Hoppe-Seyler.

Hoppe-Seyler, *med. chem. Unters.*

39

C

Darstellung, welche den Ngehalt niederdrücken musste. — Auf Grund bloss qualitativer Versuche würde man an eine Verbindung von Lecithin mit einem Eiweissstoff oder Eiweissabkömmling denken, etwa wie man sich das Vitellin oder Ichthin vorgestellt hat. Aber 5,8% PO₄ und 14% N in einer und derselben Substanz lassen sofort diese Annahme dahinfallen. Wir haben vielmehr hier Körper *sui generis*, mit keiner jetzt bekannten Gruppe vergleichbar. Etwaige vielleicht berechtigte Zweifel an der vollkommenen Reinheit meines Präparats ändern an dieser Thatsache nichts. Dass der Phosphor wirklich an die organische Substanz gebunden ist, davon habe ich mich an zwei Versuchen überzeugt, der eine an 0,28, der andere an 0,38 gr. trockener Sub-

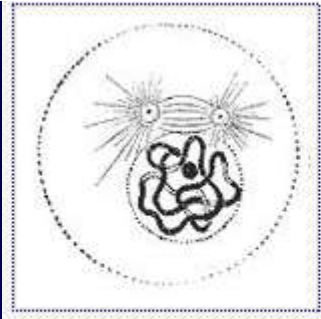


Johann Friedrich Miescher (1844–1895)

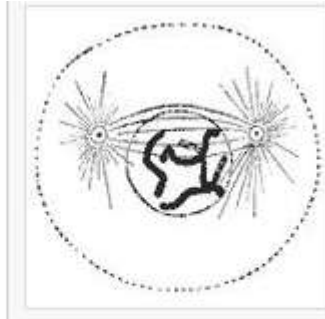
Dahm, *Hum Genet* (2008) 122:565–581

Weissmann's speculations are struggling with half-chemical terms, which are on the one hand unclear, on the other hand they refer to an older state of chemistry. **If, as very possible, one molecule of protein contains 40 asymmetric Carbon atoms, this gives 2^{40} , this means approximately one billion isomers. And this is only one kind of isomers, and the isomers of nitrogen and the unsaturated valences are not considered. Therefore, to deliver the plurality that is demanded from the theory of heredity, my theory is better suited than any other theory.** Through it all transitions from the unnoticeable to the vastest differences become imaginable, however, a thorough scrutinization of this question is in order.

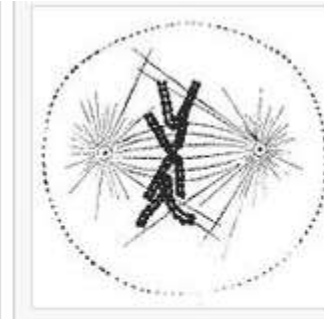
(Miescher to Wilhelm His, Basel, 13. Oct. 1893. P122)



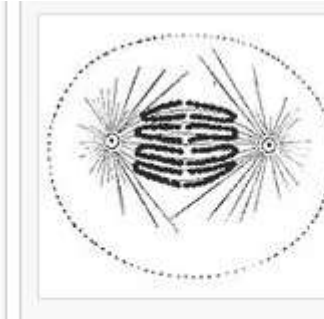
Prophase:



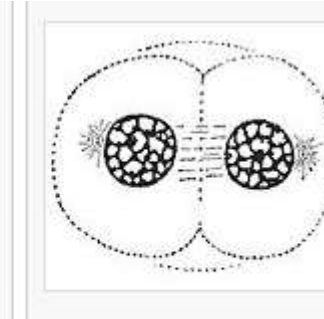
Prometaphase:



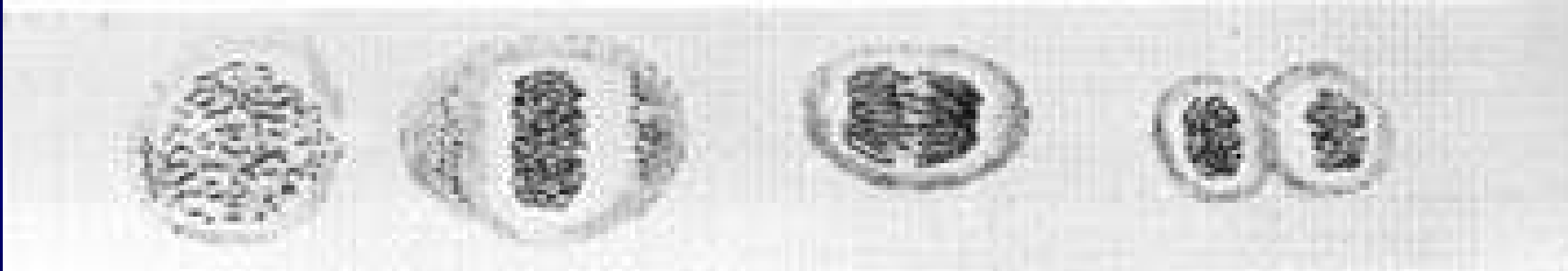
Metaphase:



Anaphase:



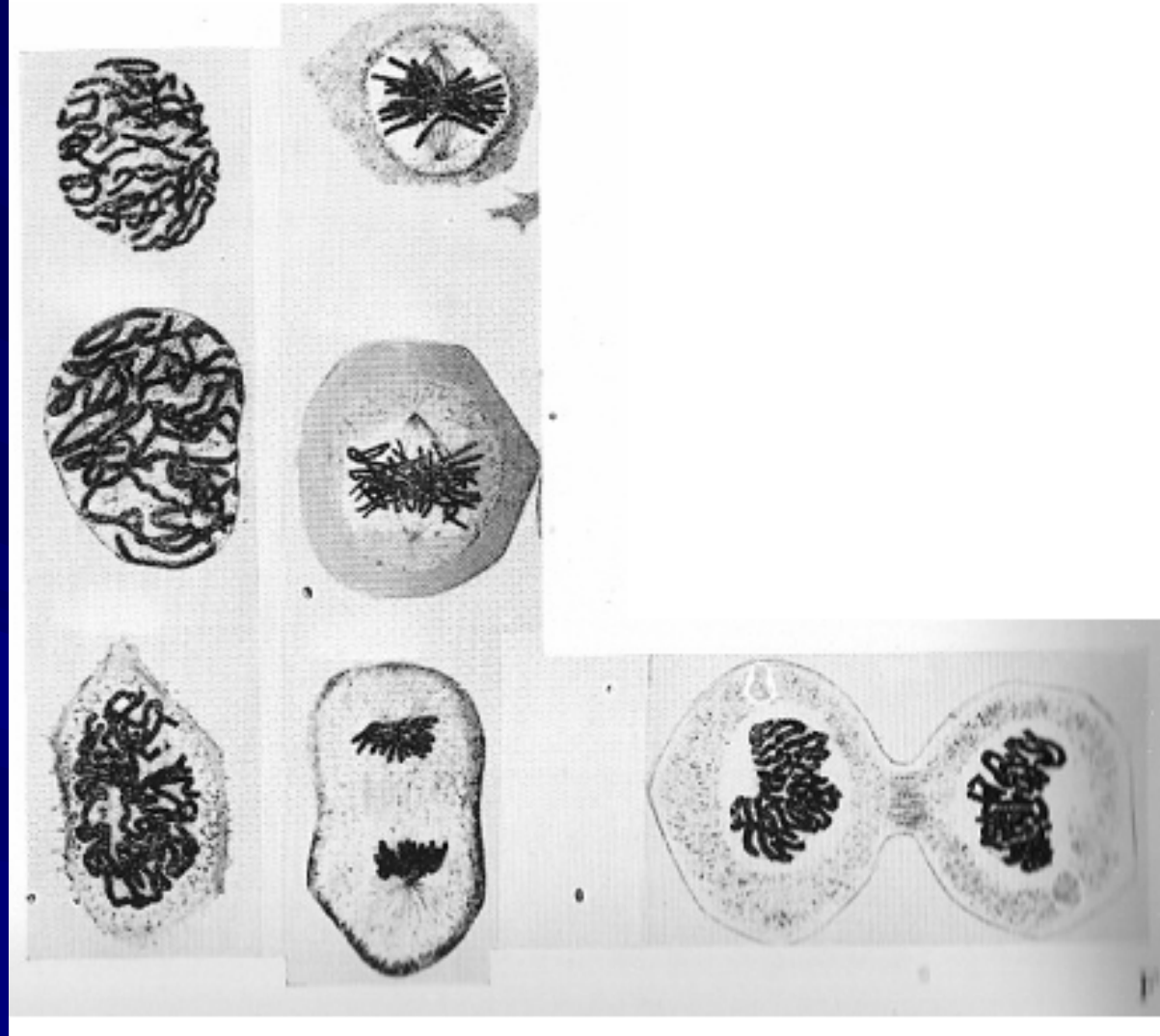
Telophase:



Figures from Flemming (1882) of the division of a living cartilage cell from a Salamander larva.

“CHROMATIN”

(by 1884 the inh. of chromosomes; 1885 chromatin hypothesized as basis of inheritance)



Figures from Flemming (1882) of dividing epithelial cells from the same source. Fixed and stained.

“systolischer” Stern

sternformen

fadenknäuel

metakinesis



Noteworthy views

Decade	Scientist	Genome as...
1930s	Darlington	Genetic System: Integrated with mating system, determiner of variation, ecological
1940s	Goldschmidt	Hierarchically organized Genome evolution affected by drift
	Dobzhansky	Intra-chromosomal systems (e.g. inversions) that are the result of selection
1960s	Nanney	Sequence as library, epigenetic reading instructions
1970s	McClintock	Reactive (goal-directed)





Decade	Scientist	Genome as . . .
1980	<i>Doolittle & Sapienza</i> <i>Orgel & Crick</i>	Selfish Genetic Elements (SGEs)
1990s	Shapiro	Read/Write system; 'Natural Genetic Engineering'
2000–	Allis	Histone code
	Grewal	Chromatin as platform for propagating epigenetic marks
	Lynch Koonin Gregory	The 'New Populationist View'

Which quote is earlier?

“GENES within the nucleus are relatively unchanging, permanent hereditary units: they comprise the nuclear genotype. The chromosomes which bear them, on the other hand, **change considerably in behaviour and appearance**. In this respect the nucleus presents a phenotypic aspect. This nuclear phenotype changes not only during cell division: throughout the life history of any organism it is subject to the control **and interaction of the genotype and the environment.**”

“... as recently as three decades ago, it was difficult for many traditional geneticists to change their view of genes and chromosomes as static entities, often likened to “beads on a string.” The discovery of transposition was important **in providing a new concept of genomes as fluid and dynamic entities.** It represented a true paradigm shift whose importance in the history of science has probably not had time to be fully appreciated.”

Defining the concept

Darlington 1932: “[Genome], a chromosome set, q.v. Winkler, 1916.”

(the square brackets indicate the term is not used in the text)

Advances in Cytology

Genotype: “the kind or type of the hereditary properties of an organism. Johannsen”.

Advances in Cytology

Darlington and Mather 1949:
“Chromosome Set, especially as
considered genetically. Winkler
1916.”

The Elements of Genetics

*The term genome was in fact introduced by
Winkler (1920). Darlington gives the wrong
reference in both of the books I quote here.*

Genotype: “1. The kind or type of the hereditary properties of an individual. Johannsen 1909. 2. The hereditary materials considered as a unit.”

The Elements of Genetics

Dawkins 1982: “The entire collection of genes possessed by one organism.”

(Gene is defined noncommittally as “a unit of heredity”).

The Extended Phenotype: The Gene as the Unit of Selection

Genotype: “The genetic constitution of an organism at a particular locus or set of loci. Sometimes used more loosely as the whole genetic counterpart to phenotype.”

The Extended Phenotype: The Gene as the Unit of Selection

In modern molecular biology and genetics, the genome is the entirety of an organism's hereditary information. It is encoded either in DNA or, for many types of virus, in RNA. The genome includes both the genes and the non-coding sequences of the DNA/RNA.

Wikipedia (29/2/2012)

An organism's complete set of DNA is called its genome. Virtually every single cell in the body contains a complete copy of the approximately 3 billion DNA base pairs, or letters, that make up the human genome.

www.Genome.gov

<http://www.genome.gov/18016863>

What happened to the genome-first perspective?

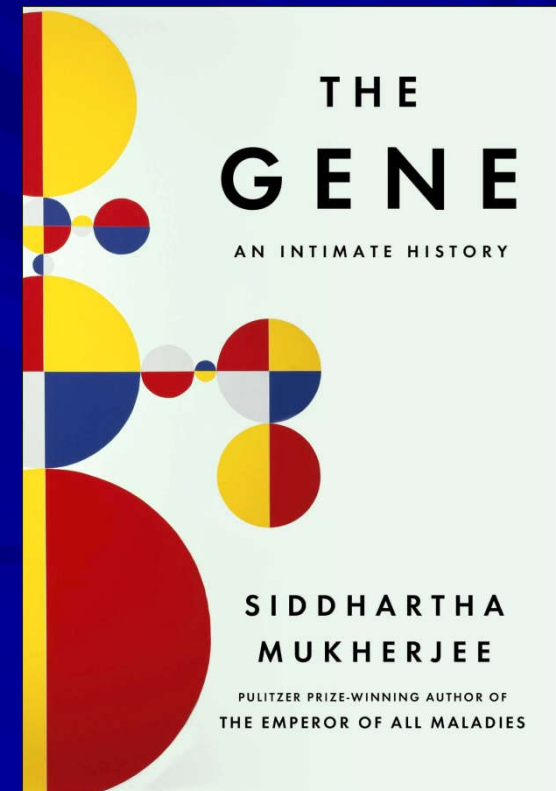
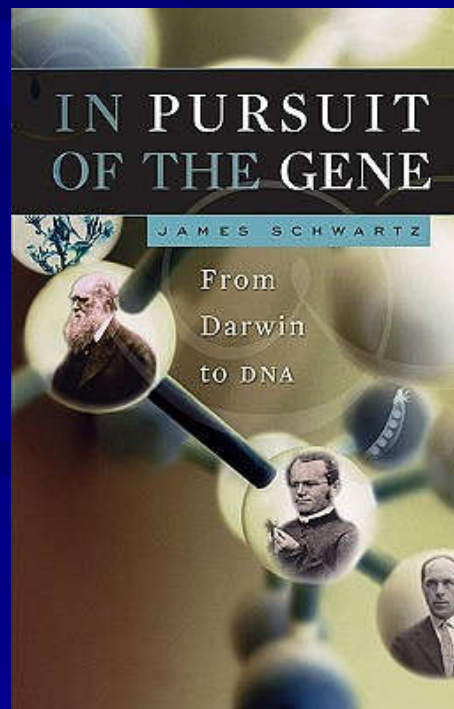
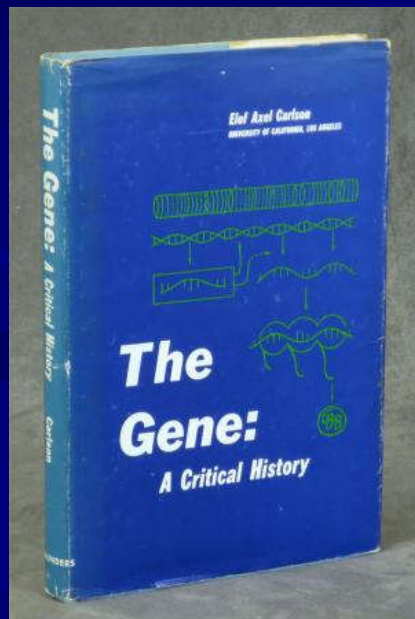
- Genes became the focus of evolutionary analysis, and when later DNA was discovered to be the bearer of genes, gene coding DNA rather than its surrounding scaffolding became the focus of evolutionary explanation.

- As developmental biology and genetics became separate endeavours, the evolutionary significance of the developmental dynamics of the genome fell through the cracks.

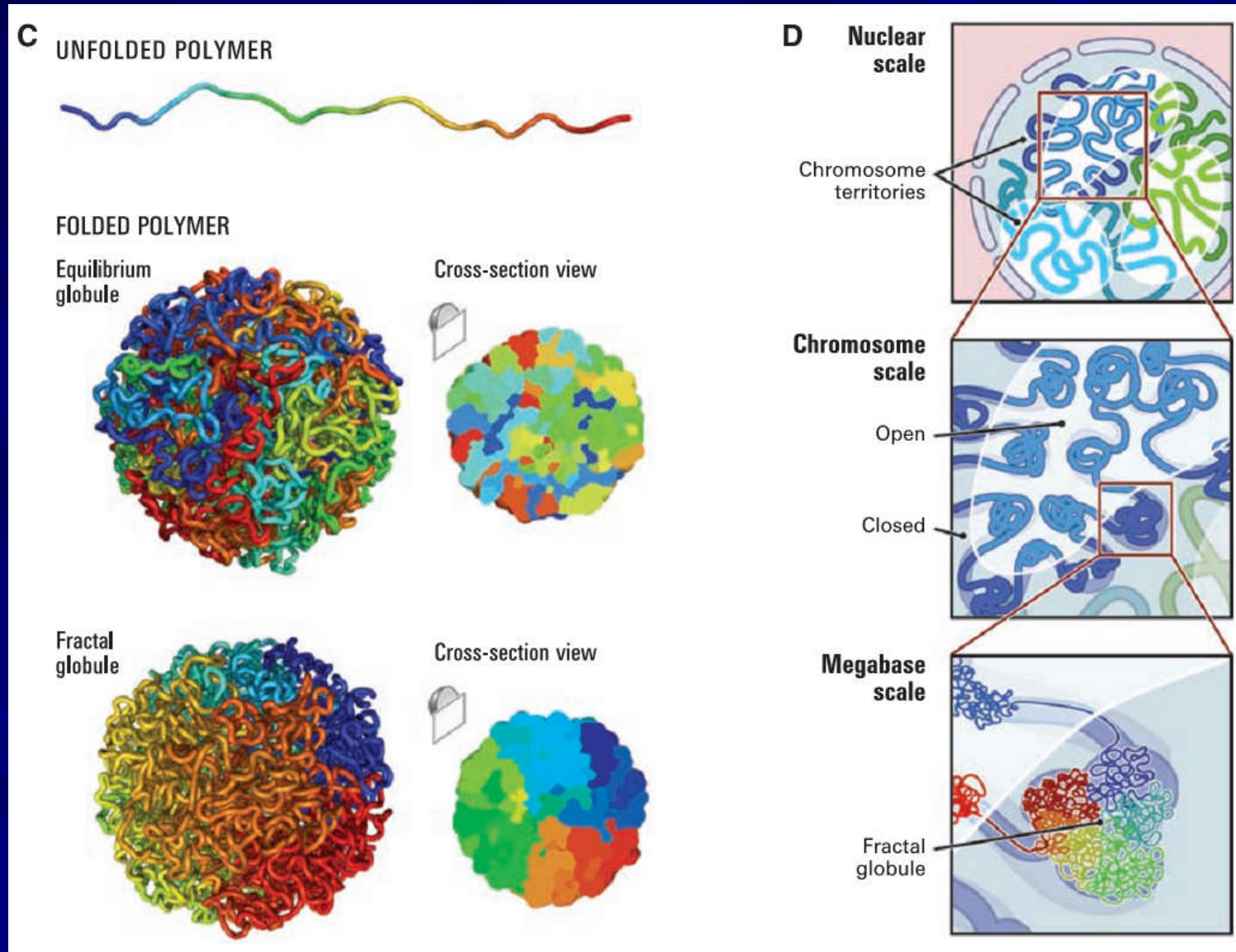
- Ideas such as Darlington's, McClintock's and Dobzhansky's implied that chromosomal organization offered advantages to species or populations, not individuals.

Three “culprits”

- Theory
- Technology
- The historical narrative



The Genome Reappears?



“In the future, attention undoubtedly will be centered on **the genome, with greater appreciation of its significance as a highly sensitive organ** of the cell that **monitors** genomic activities and **corrects** common errors, **senses** unusual and unexpected events, and **responds** to them, often by **restructuring** the genome.”

McClintock 1984, *The Significance of the Responses of the Genome to Challenge.*



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Thank You

■ Collaborators

- Prof. Oren Harman (BIU)
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