When Have We First Seen the Genome? When did it disappear?

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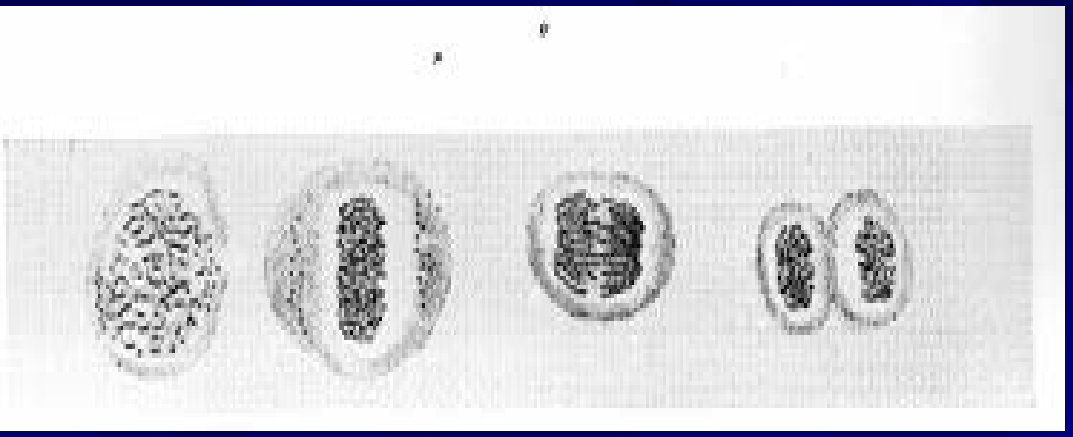
What does the genome look like?



- “Image Based Science”
- A “natural history” of the relations between images and concepts in one particular – but very important – historical case.

Image Based Science

- Science can operate concept-less; images can play a role similar to that of concepts. In particular “figures” can provide public, historically continuous, schemes or frameworks. Images are social & technological, intensional (image-of) and ritualized objects.
- “Biology” (in the relevant sense), ca. 1880-1930s, but probably also today, was significantly (if not primarily) an “image based science”.
- Different sciences, in particular physics and biology handle images differently.
- Biology, being “theory-less” and model-based, and with a strong functional bias, often reifies components of images, and treats them functionally. (Not as approximations.)
- What is not visible, in the figures, *not (merely?) the microscope*, is marginalized as non-functional.
- Images serve as both “observations” and as implicit models, creating an observation-model or description-model duality.

“the microscope **need not** be thought of as a window, but is most certainly an engine creating new optical phenomena… the image could be **either** a copy of a real thing not visible to the naked eye or a mere public hallucination. I suggest that it is moreover accurate and in fact more illuminating to keep **neutrality** in this respect and just think of images themselves as public hallucinations” (BvF, 2008, p. 109)

Images-Of-Images-Of

1. *Graven Images*: Images that are in fact things. Paintings and photos.
2. *Private Images*: Purely subjective images: dreams, after-images, hallucinations. Personal, not shared, not publicly accessible. “As if” one is seeing or hearing.
3. ***Public hallucinations***: In between (1) and (2): A whole gallery of images that are not things, but are also not purely subjective, because they can be captured on photographs: reflections in the water, mirror images, mirages, rainbows. *Van Fraassen (2008)*
4. **Productive rather than mimetic.**

- I think this line of work is of critical importance for all philosophy of science. I think BvF's recent work is a must read, and recent work on measurement and models, as constructive enterprises, highly evocative.
- But my aim today is slightly different. Not realism vs. empiricism, etc. but about concepts, and especially concepts *for describing* observations. ***Representational concepts.***
  - Images-Of-Images-Of
  - Natural history of the dynamics of image based science(s)

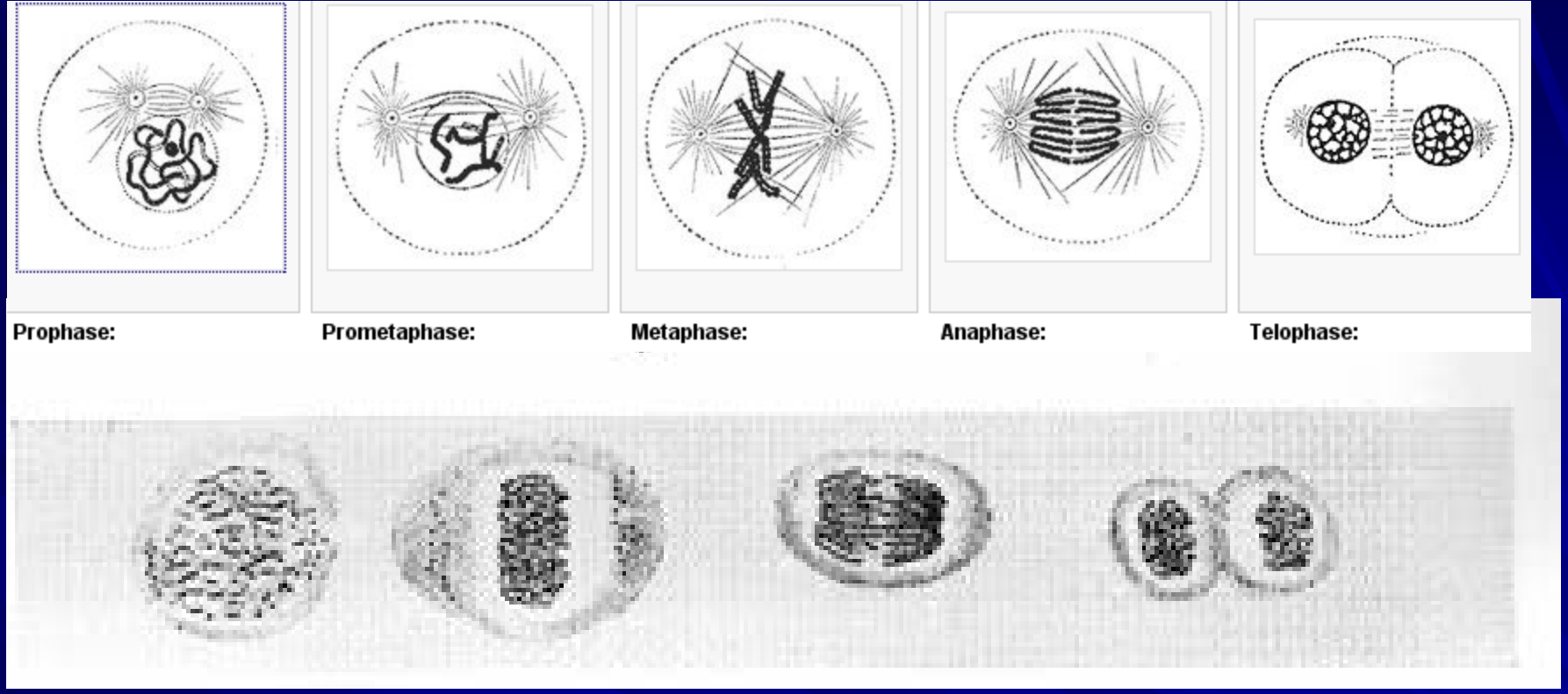
Dynamics of Image-Based-Science

- 1. Can scientific (representational) concepts that are meant to refer to empirical entities be ahead of empirical possibilities, yet still be coherent and scientifically productive? **I suggest that early observations on cell division and fertilization, in the 1880s, gave rise to empirically grounded and theoretically useful concepts (ca. 1920) that were however ahead of what was actually observed.**

- 2. How did changes in the genome concept reflect changes in microscopy and later the sequencing of DNA? **I suggest that as observation improved the genome concept became less, rather than more, empirically grounded in what is actually observed.**

What does the genome look like?

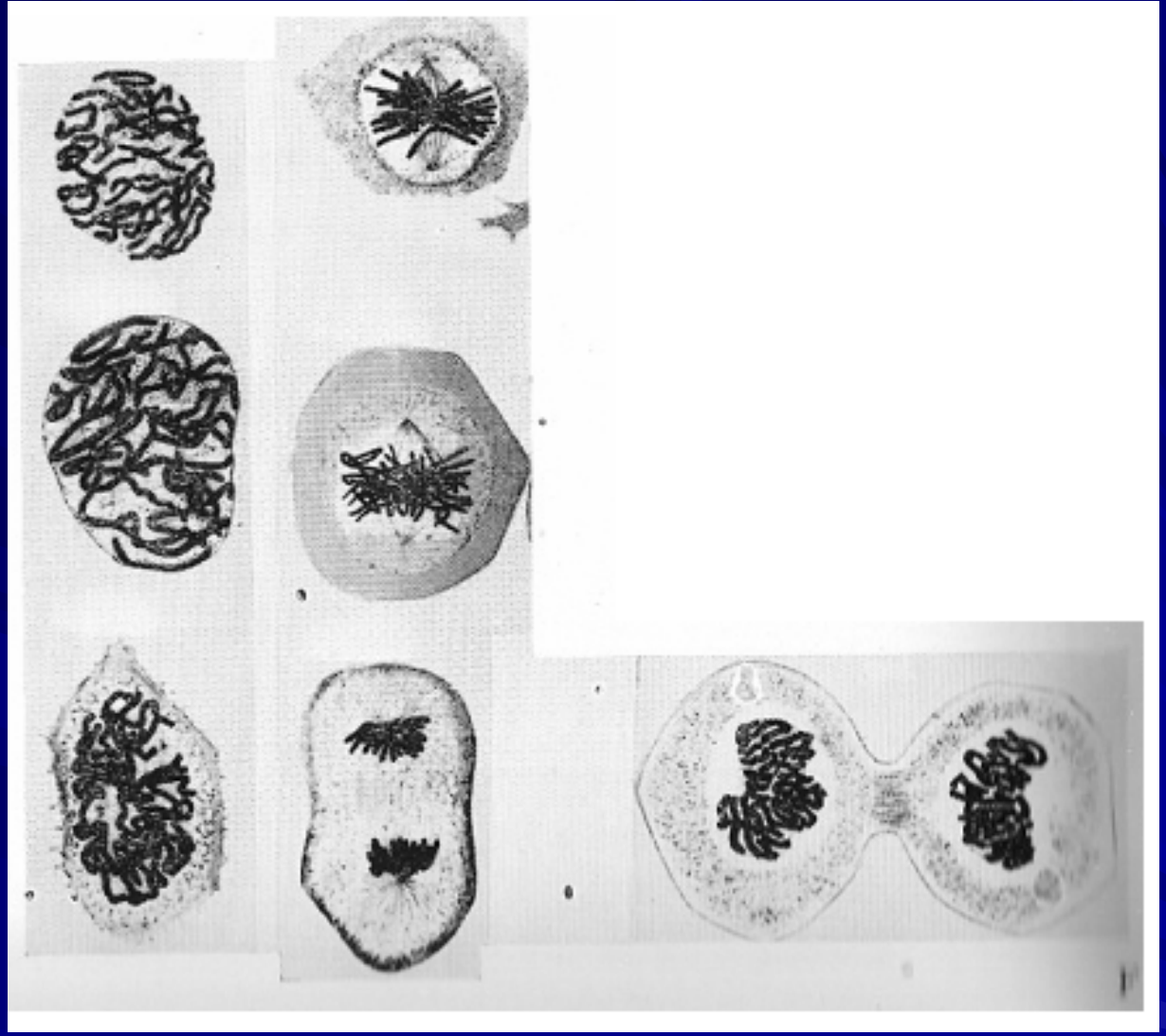
from fadenknäuel to genome



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)



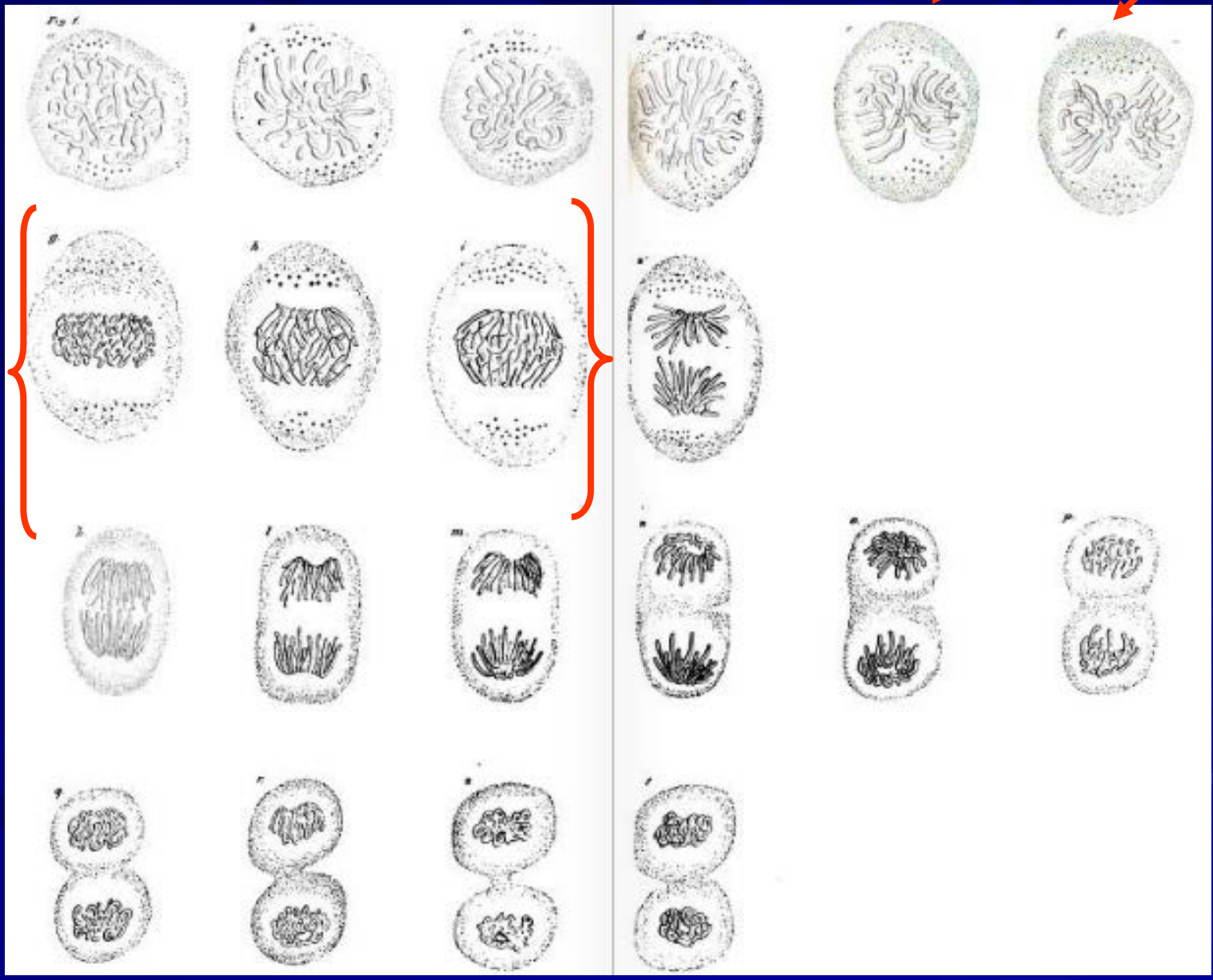
Figures from Flemming (1882) of dividing epithelial cells from the same source. Fixed and stained.

“systolicher” Stern

sternformen

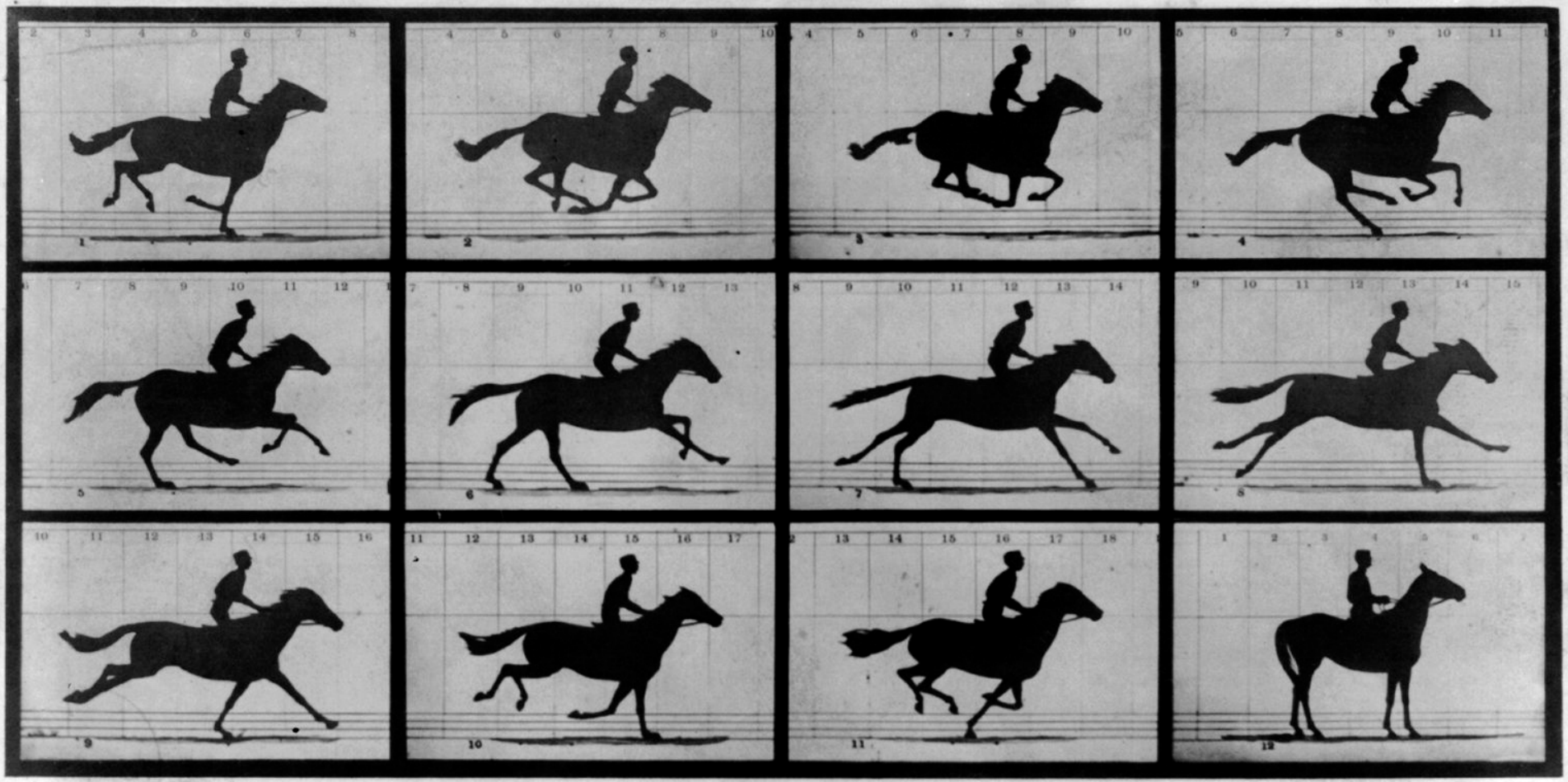
fadenknäuel

metakynesis



Observation-Model Duality

- Descriptive (observational) vocabulary
  - “fadenknauel”, “sternformen”
  - Time-series (stages of process of image making)
  - Typically raises empirical questions (e.g., individuation of chromosomes)
  - Describe which organism, which stains etc. were used (Images-of-Images-Of)
- Model
  - 2D (not 3D)
  - Lines (in image)->Linear (*necessary qua image)*
  - Stages (in images)->stages of a process
  - Optical resolution -> level of functional explanation (*necessary qua image)*
  - What’s not in the image is not needed for functional explanation
  - Typically raises functional questions (e.g., heredity)
  - Focus on “universal” (cross-species) properties: Cell Division etc. (Images-Of-Images-Of)



Copyright, 1878, by MUYBRIDGE.

MORSE'S Gallery, 417 Montgomery St., San Francisco.

THE HORSE IN MOTION.

Illustrated by

MUYBRIDGE.

AUTOMATIC ELECTRO-PHOTOGRAPH.

"SALLIE GARDNER," owned by LELAND STANFORD; running at a 1.40 gait over the Palo Alto track, 19th June, 1878.

The negatives of these photographs were made at intervals of twenty-seven inches of distance, and about the twenty-fifth part of a second of time; they illustrate consecutive positions assumed in each twenty-seven inches of progress during a single stride of the mare. The vertical lines were twenty-seven inches apart; the horizontal lines represent elevations of four inches each. The exposure of each negative was less than the two-thousandth part of a second.

1878

Historical hypothesis I

- What is seen here is are images "of the genome".
  - (this is a semantic quagmire)
- This genome is a *dynamic system* and hence mechanism, and potentially comprising "molecular machines"
  - though the observation is *in vitro.*

Rationality of IBS

- What where they looking *AT*? What are these images of *OF?*
  - Concepts like “genome” have to be retrospective, hence the semantics of scientific discourse pre-concept is image-based.

- The coherency, continuity, rationality of pre-conceptual phase is either at the level of concepts such as “kern”, “stern” etc. or the images. The latter option seems more convincing to me.

Caveats

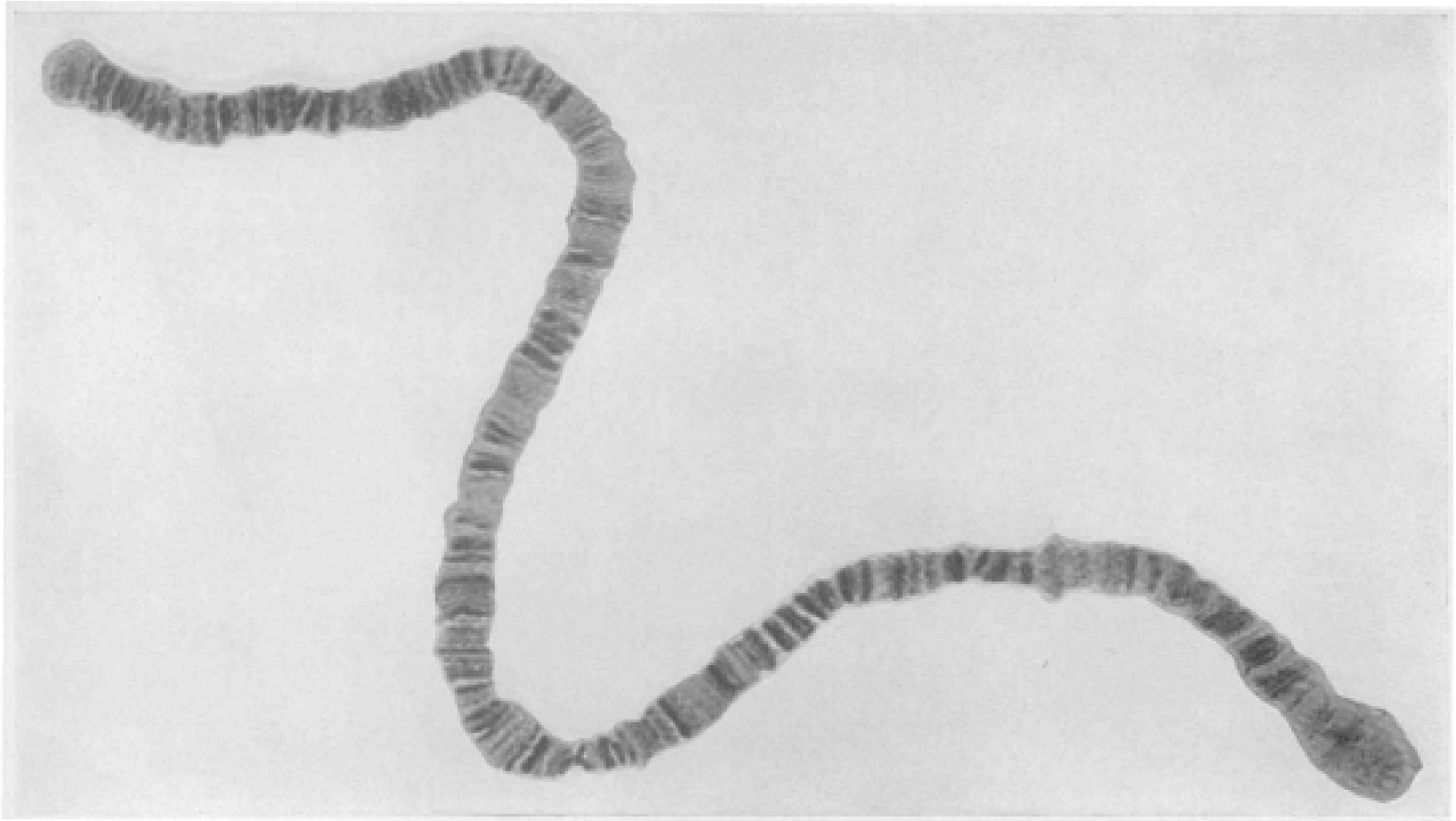
- It was not known that the thing viewed was the seat of inheritance (hence not a “gene-om”). At the earliest this was discovered in 1894, but the debate continued into the 1920s.
- Flemming himself was among those who thought that heredity resides in the cytoplasm.
- The connection to Mendelism that now seems so obvious in the image, and justifies seeing it as an image of the genome, was missing prior to the discovery of Mendel in 1900.
- It was quite possible to attempt to account for the behavior in a “Newtonian” manner (mechanistically rather that mechanismically)

Alternative explanations

- Not the “genome”, but the “chromatin”. Not work in genetics (which relies on other kinds of observations), but in cytology. Later (much later) will be *identified with* the genome (and later this identification will be relaxed somewhat, as we will see). But still two “levels” of study and this remains true today.
- “Two” phenomena are being studied, so two sets of observations (even if one image?). A good theory/explanation will account for both; They turn out to be the same, which was a great (and future) discovery (“the chromosome theory of inheritance”).

Mostly correct, but… the question remains what are the figures **images-of**. If not of the genome than of what? This is not a question of theory-ladenness.

- Something can be an image-of more than one thing (image-of-image-of).
- What it is an image-of depends partly on the observer (who decides what to include in the figures; how to arrange them; how to describe them), but mostly on the community of practice, so this can change (and bifuracate) over time. Depends on the scientific question being asked (and this is not a simple notion)
- Images are “public hallucinations” in this sense.
- You can be more or less of a realist about the different “senses” of the image.



"PORTRAIT" OF A SALIVARY GLAND CHROMOSOME

Frontispiece

Ever since the gene hypothesis was generally accepted, geneticists and cytologists have dreamed of the day when it would be possible to see the actual genes, instead of having to be satisfied with studying their "shadows," which were "reflected" in the morphological development of generations of organisms. Giant salivary gland chromosomes of the fruit fly (*Drosophila melanogaster*), whose study is the subject of the accompanying article, are proving to be a new genetic tool of the utmost importance. The chromosome illustrated here is the right arm of the third chromosome—the light and dark bands and areas represent a definite pattern, which can be identified in any third chromosome, this pattern having an astonishing uniformity, somewhat as the pattern of a spectrum is characteristic of a given kind of light. Just what these bands are, and just where the actual genes are located is still not determined, but some of them have been "bracketed" in very small regions—close to, if not actually on, some of the dark bands. (see Figure 4).

PAINTER,SALIVARY CHROMOSOMES AND THE ATTACK ON THE GENE .*J Hered*.1934 .

Where Are the Genes?

The methods have been described by which it has been possible to restrict the morphological position of gene loci to the area covered by one or even a part of one of the deeply staining bands on the X chromosome. **Where then are the genes? Are they represented by the deeply staining material or by some other part of that region of the chromosome?** To answer these questions we are led to a consideration of one of the oldest problems in cytology, namely, the ultimate structure of these cross bands and of the chromosomes. At this point I wish to state that while I have used the term "band" in all of my papers, I was very careful to state in my article in *Science* that these cross striations "appear to run around an achromatic matrix." **As to the ultimate nature of these "bands," I have not been, nor am I now, willing to commit myself finally.** (*ibid.*)

“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

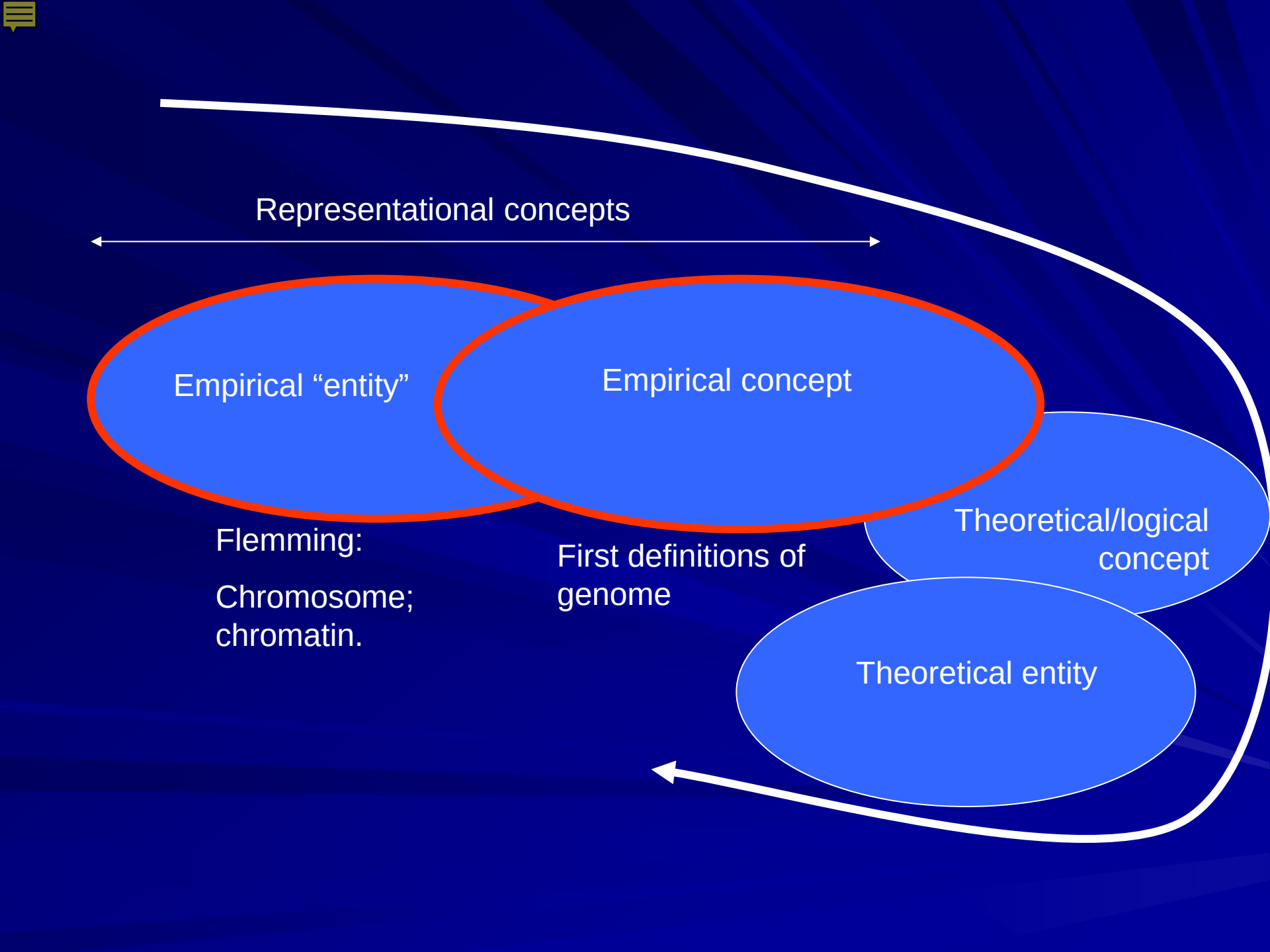
In modern molecular biology and genetics, the genome is the entirety of an organism's hereditary information. It is encoded either in DNA or, for many types of virus, in RNA. The genome includes both the genes and the non-coding sequences of the DNA/RNA.

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


Representational concepts
Empirical “entity”
Empirical concept
Theoretical/logical concept
Theoretical entity
Flemming:
Chromosome; chromatin.
First definitions of genome

Epistemic Iteration

(Hasok Chang, Inventing Temperature, 2004)

- "Epistemic iteration is a process in which successive stages of knowledge, each building on the preceding one, are created in order to enhance the achievement of certain epistemic goals. … In each step, the later stage is based on the earlier stage, but cannot be deduced from it in any straightforward sense. Each link is based on the principle of respect and the imperative of progress, and the whole chain exhibits innovative progress within a continuous tradition."

  - Enrichment
  - Self-correction

Morals

- No need for “concepts”; the (named) images suffice.
  - The coherency & rationality of pre-conceptual phase is at the level of “images” not of descriptive vocabulary, e.g. “sternformen”
- The original concept was empirically adequate, the recent one isn’t.
- The point is not that the earlier tools are “closer” to “reality”, less theory laden (a naïve point, to be sure!), but rather that the concept is closer (historically) to the early representations. Their being “more realistic” is a straightforward result of how concepts are formed; their history.

So what happened here?

- The logical concept (“genotype”) was reified, and occupied the “genome” concept.
  - A different concept (“chromatin”) is needed for the physical/mechanistic system.
  - The “logical” concept is used as a designator of function, and as a result there is a pressure to demonstrate that the function is exhausted by the logical-genome (DNA sequence). This affects both the understanding of the entity and the function, bi-directionally.
- In Biology the “winning” concept is the logical one (genome=genotype). In physics the logical concept can persist, but is understood as an idealization or abstraction (a light ray is a “line” in Geometrical Optics).
  - **Hypothesis II: One reason behind this difference is that in Biology, function is used to individuate phenomena.**
- Thus, the dynamics of image-based science are different in different sciences.

- The genome concept now in widespread use in Biology is not faithful to empirical knowledge of the "genome" (in the original sense); the 1920 concept "covered" (more extensive) empirical knowledge and provided scope for empirical work (partly because of the use of the observational/image concept "chromosome"); now additional concepts are needed for similar work ("conceptual constriction").
  - A "good" concept covers pre-conceptual observations and opens avenues for new research.
- **Hypothesis III: The dynamics of image-based science is part of the explanation of the state of the genome concept.**

Concluding Remarks

- Biology as an Image-Based-Science
- The distinction between Images and “Figures” (Images-Of-Images-Of)
- I suggested that (canonical) images (“figures”) become implicit models of phenomena.
- Observation-Model Duality of Figures
- I presented a typology of “representational concepts” and the dynamics of I.B.S

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