

Molecular Biology Through Discovery
Companion to Wrinch (1936) *On the Molecular Structure of Chromosomes*
Protoplasma 25:550-569

I. Introduction

By now you will already have acquainted yourself with the current conception of "gene", either from prior experience or from the Investigation *What is a Gene*. The gene should feel completely tangible, something you could look at and manipulate if need be. But if you hold firm to this view of the gene, you will have a difficult time appreciating why seemingly intelligent people in the mid 20th century could not grasp what is so plain to us and conceived of theories concerning DNA and protein that would appear to us impossible on the face of it.

On the other hand, if you let go of your mental gene (just for a moment,... it will come back), you may gain considerable benefits:

1. You will be able to look over the shoulders of those who pieced together the characteristics of genes and proteins and appreciate their patterns of thought. These patterns might serve you well in matters where you *don't* have good preconceived notions.
2. You will gain facility in a practice central to the scientific process: seeking out contradictory explanations of a phenomenon and holding them at arm's length, side by side.

Considering the ideas current in 1936 may put you in that frame of mind, and that is the purpose of offering you the article by Dorothy Wrinch.

Like many important figures in the history of molecular biology, Dorothy Wrinch came to the subject from outside of biology. She was the first female to receive a doctor of science degree from Oxford, studying symbolic logic with Bertrand Russell, a seminal figure in logic and mathematics. By the mid 1930's, Wrinch was well established in pure and applied mathematics. At the age of 35, she turned her attention to biology for the first time. The article of concern to us, a review of what was known concerning the physical nature of chromosomes, was amongst her initial efforts in biology.*



Dorothy Wrinch

Our interest in the article is to assess how the gene was viewed 16 years before Watson and Crick's model. Any model of a gene must explain: (1) How is the gene a repository for genetic information? and (2) How is genetic information propagated from one generation to the next?

II. Initial survey of article

With that in mind, find the article (if you haven't already), and take a look at it.

One thing you will notice immediately is that it is 20 pages long! I'm not sure I want to wade through that much unless I have a good idea from the outset that the gain-to-pain ratio will be

* Note to those going on to a career in research: A common strategy by graduate students is to write a review article on the field that is to be their focus of study. This leads to multiple beneficial outcomes. First, you gain a panoramic view of your field. Second, you become known to your field through the publication, even though your own research has not ripened sufficiently to be published.

high. A look at the table of contents ("...cytology", "...cytogenetic...") and a quick skim of the first few pages ("...embryology...", "...mitosis...") leads me to doubt this.

However, the table of contents also shows a very provocative section: *The Nature of the Gene*. Great! Let's go there.

OK, you're there, right? Somewhat surprisingly, perhaps, you find just a single paragraph! Another thing that jumps out immediately is that this is not a research article

SQ1. How do you know that this is not a research article? What is it instead?

(Not sure what a research article is? Check *Course at a Glance*, *Strategies*, and beyond)

One paragraph... we can handle that. Diving in...

SQ2. How do you interpret the first sentence?

I confess, I had a good deal of trouble with it, except for the last phrase, which convinced me that it wasn't worth bothering with. The third sentence and beyond seems more potentially rewarding.

SQ3. How do you interpret the remainder of the paragraph?

She seems to presume that we know what a micelle is, and if we did, no doubt the paragraph would be more comprehensible. Maybe this was explained earlier? Fortunately, you're looking at a PDF document and you can use Acrobat Reader's excellent search facility... no, not the pathetic Ctrl-F but rather Shift-Ctrl-F (you may have a binoculars icon on your Reader toolbar).

SQ4. Using Reader's contextual search facility, look for earlier instances of the word 'micelle'. Is an explanation provided?

SQ5. Do whatever is necessary to learn what 'micelle' means. Your conclusion?

Hah! As it happens, you already know what 'micelle' means. You just may not have associated that word with its meaning. Ordinarily I wouldn't spend time looking up words. I'd just blip over them and hope that their meaning, if important, would emerge as I went along. But 'micelle' is so central to this paragraph and, looking at the table of contents, central to the article as a whole, I decided there was no way around this one.

SQ6. Armed now with your knowledge of what a micelle is, do you now understand Wrinch's view of what a gene is?

Not me. I'm beginning to think it might have been a mistake to jump right to section 10. But I still don't think I have to read the entire article.

III. Directed reading/hole plugging

Looking at the table of contents, I come to the belief that maybe I can get into the nature of the gene as a micelle by going to Section 6, *The Chromosome Micelle*. Go to that section and start reading it.

SQ7. Does Wrinch's claim concerning the constituents of chromosomes accord with our current knowledge?

The rest of this section talks about the structure of proteins. Since we're going to spend a considerable amount of time on this subject next week, I suggest that for now you just skim over it without much concern as to how much of it you understand, merely noting what topics she brings up. One thing of possible interest, in the last paragraph of this section (bottom of p.556), is "animal fibres", such as keratin.

SQ8. What is your mental image of fibrous proteins, such as keratin?

(If you don't have any, why not go out and get one?) One of our goals was to determine what views were prevalent in Wrinch's day regarding how genetic information is stored. The next section, Section 7, *Genetic Identity and Protein Pattern*, sounds possibly pertinent. Take a look.

SQ9. Wrinch makes a big deal about the 'linear specification' of both the genetic constitution of the chromosome and protein. What is meant here by 'linear specification'?

In the second paragraph of this section you are greeted by the welcome phrase "...we have pictured the chromosome micelle,..., as an aggregate of identical sequences of molecules in parallel." Picture? Great! Where is it?

SQ10. Can you find a picture in this article of the aggregate of which Wrinch speaks?

Yes you can, but you might have to look ahead a bit. Keep that figure in mind (and possibly in a separate window) as we continue reading Section 7, paragraph 2. She says that the micelle is distinctive longitudinally (top to bottom in the figure) by means of sequences of residues (the amino acid components of a specific protein) but is homogenous for all azimuths (practically speaking, she means from left to right in the figure). Earlier in the paragraph she suggested that the width (left to right) of this unit could be any value (depending on how many proteins were stacked side-by-side). The length would depend on the length of the protein.

SQ11. Length of what protein? The length of few proteins were known in 1936. Wrinch offered in Section 6 the example of one protein whose length was known, clupein. How long is clupein?

SQ12. How many different (nonidentical) proteins are shown in Fig. 3?

The next paragraph makes clear where Wrinch believes the information of a gene resides: in its "characteristic protein pattern". The second sentence hints at what she means by "protein pattern": the order of side chains (i.e. order of amino acids within the protein).

IV. Return to key section: Nature of the Gene

Now with all of this in hand, return to Section 10, *The Nature of the Gene*, where Wrinch describes her notion of the nature of the chromosome and its constituent genes. The (chromosome) micelle is described as an arrangement of units joined end to end, at intervals on the order of a hundred angstroms.

SQ13. Draw a picture of a portion of a chromosome as imagined by Wrinch, consisting of a few genes. Include dimensions (in angstroms).

V. How do genes and chromosomes replicate themselves?

The only loose end remaining is the second characteristic of the genetic material: it is duplicated and divides as the cell divides. Where does she explain this?

SQ14. Where do you find a discussion on the topic of division? Using Reader's contextual search facility, look for instances of 'divi' (so that you'll catch either 'divide' or 'division').

I found multiple instances in Section 12. In this paragraph, she presents two key ideas that together explain how a chromosome may replicate itself. First, she explains how the chromosome micelle might double in size while retaining the same order of genes, each gene consisting of identical proteins. This may sound like magic, but the idea is reasonable given what was known even then of fibrous proteins. Keratin fibers consist of keratin proteins that assemble to make a large homogenous aggregate. Similarly, collagen fibers are composed of a large number of identical collagen proteins. You don't find mixed collagen/keratin fibers.

SQ15. Where in Section 12 do you find a discussion on how the chromosome micelle grows in size?

The second idea concerns how the chromosome micelle divides. The idea she presents is also not unreasonable, as you can no doubt remember or readily imagine the experience of seeing a soap bubble (a micelle) splitting into smaller bubbles.

SQ16. What does Wrinch mean by "...this division is longitudinal..."? Must it be? Take your picture from SQ12 and indicate how the chromosome micelle might divide.

VI. Parting thoughts

SQ17. How specifically does Wrinch's view of genes compare to yours?

Wrinch made abundantly clear that there was little evidence that could be brought to bear on her ideas. Nonetheless, the review sets forth a view of the chromosome that was reasonable and was based on notions that were certainly in the air at the time. A popular biochemistry textbook of the period devoted nearly half of its pages to discussions of colloids (micelles are a type of colloid particle).[†] A biochemistry textbook of today would hardly mention them.

Her model turned out to be wrong in virtually every particular. Nonetheless, it is instructive to read an argument that was highly plausible at the time... and to wonder how many beliefs that are widely held today will be absent from textbooks 80 years hence. More importantly, it is prudent to ask how we can recognize what is merely a widely held belief – possibly wrong – and what is an observation – beyond dispute -- that will remain in force so long as it remains in our collective memory.

[†] Gortner RA (1920). *Outlines of Biochemistry*. Reported in Dickerson RE (2005). *Present at the Flood: How Structural Molecular Biology Came About*. Sinauer Assoc, Sunderland MA. p.4