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This Week's Citation Classic

Cairns J. The bacterial chromosome and its manner of replication as seen by autoradiography. *J. Mol. Biol.* **6**:208-13, 1963. [Dept. Microbiology, Australian Nat. Univ., Canberra, ACT, Australia]

Following the development of a method for visualizing DNA molecules by autoradiography after labeling with tritiated thymidine, the DNA of the bacterium *Escherichia coli* was shown in this paper to consist of a single molecule that is replicated at a moving locus (the replicating fork) at which both new DNA strands are being synthesized. [The *SCI*® indicates that this paper has been cited over 500 times since 1963.]

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"This paper on the structure of the chromosome of *Escherichia coli* (plus a more complete picture, published in the *Cold Spring Harbor Symposium* in the same year[1]) was almost the last work I published on the autoradiography of DNA, before I moved from Australia to the US and became totally embroiled in fund-raising at Cold Spring Harbor. The project began in 1960 when I spent a year working in Hershey's laboratory. There was at that time great uncertainty about the real size of DNA molecules, not least of all because there were no precise ways of measuring their molecular weight. Hershey had just devised ways of extracting T2 DNA as an intact single molecule of known molecular weight, and one of the next things to do was, therefore, to measure its length in order to find out whether it had two strands or four. Having had experience with autoradiography, when I worked on the pattern multiplication of vaccinia virus,[2] it was a natural thought that I should try to observe these isolated T2 DNA molecules by autoradiography (although it took months of messing around with other projects before I realized what I should be doing). It was soon clear that molecules could be visualized this way, and I returned to Australia with the intention of studying the structure and replication of bacterial DNA —a subject that had attracted me since the fall of 1957 when I did the washing-up in a house in Pasadena where Meselson was doing the cooking (and, at the same time, was completing the original density-transfer experiment that established semiconservative replication[3]).

"The autoradiography of DNA was a rather slow business. Exposure times were over two months. Therefore it took a couple *of* years to work out a technique for minimizing DNA breakage during extraction, and then it was only after quite a long search that I found any molecules that were sufficiently untangled to be interpretable.

"The other part of the paper concerned the structure of the replicating fork —namely, the fact that short pulses of ^{3}H-thymidine were found to label two new strands, both apparently growing overall in the same direction. The autoradiography of pulse-labeled DNA is a much more straightforward procedure because it does not require that the whole chromosome is laid out in an untangled state, and so I also included a few experiments on the replication of HeLa cell DNA, the results of which, because of the exigencies of my circumstances in the US, were not published for 3 years.[4]

"Rather than being innovative, the work was really an act of tidying (a bit like washing-up, in fact) because it showed that the bacterial chromosome was simply a molecule of DNA —albeit one organized in a rather unexpected way. If my paper has been often quoted, that is probably because it describes something very simple."

1. **Cairns J.** The chromosome of *Escherichia coli. Cold Spring Harbor Symp.* **28**:43-6, 1963.
2..... The initiation of vaccinia infection. *Virology* **11**:603-23, 1960.
3. **Meselson M & Stahl F W.** The replication of DNA in *Escherichia coli. Proc. Nat. Acad. Sci. US* **44**:671-82, 1958.
4. **Cairns J.** Autoradiography of HeLa cell DNA.*J. Mol. Biol.* **15**:372-3. 1966.