CC/NUMBER 22 MAY 28, 1990

This Week's Citation Classic*

Wu T T. A model for three-point analysis of random general transduction. Genetics 54:405-10, 1966. [Department of Biological Chemistry, Harvard Medical School, Boston, MA]

A model was presented so that three-point analysis of random general transduction can be used to calculate the distances between the markers with respect to the average length of the transducing particle. [The SCI® indicates that this paper has been cited in over 315 publications.]

From Cotransduction Frequencies to Linkage Maps

Tai Te Wu Departments of Biochemistry, Molecular Biology, and Cell Biology; Biomedical Engineering; and Engineering Sciences and Applied Mathematics Northwestern University Evanston, IL 60201 and Cancer Center Northwestern University Medical School Chicago, IL 60611

February 26, 1990

During my stay at Harvard Medical School, I was learning bacterial genetics in Dr. Edmund C.C. Lin's laboratory. At that time transduction was the most precise method of locating genetic markers. Cotransduction frequencies were used to estimate distances between markers. A formula had been developed by C. Yanofsky1 but was not very accurate. Threepoint analysis² provided more accurate estimates by experimentally measuring 12 frequencies.

One day, my wife was sick from a chemical that she synthesized in her laboratory. So I

staved home to cook dinner for the two of us. While staring at many sets of 12 frequencies from different three-point analysis experiments on the kitchen table. I decided that there had to be an easier way of interpreting these numbers. Using standard model construction methods in engineering and applied mathematics, I wrote down some integrals, all of which could be readily solved. In one hour I got a set of equations relating the 12 frequencies to the two distances between the three genetic markers. In other words, the experimental data from a three-point analysis could be converted to two distances.

A week later I asked Ed whether my result was worthwhile for publication. Ed was very encouraging and suggested that I should send it to Genetics. It was soon published, but I had forgotten about it completely since I moved on to other problems. It was brought to my attention that these equations were quite useful when the National Science Foundation asked me to submit a research proposal on this work. Unfortunately, it was rather difficult for me to explain that I finished my project in one hour.

The genetic map of Escherichia coli initially constructed by A.L. Taylor and C.D. Trotter³ has been refined by B.J. Bachmann⁴ and M. Singer et al.⁵ using my equations to provide precise locations of over 1,000 known markers. Recently, similar equations have been employed to construct the linkage map of Salmonella typhimurium.6

After the development of nucleotide sequencing, complete sequences of some plasmids and viruses were determined. To analyze DNA sequences of more complicated organisms, genetic mapping is an essential intermediate step. My analysis provides this intermediate step by indicating how accurate linkage maps can be constructed for E. coli and S. typhimurium from classical genetic measurements.

4. Bachmann B J. Linkage map of Escherichia coli K-12, edition 7. Microbiol. Rev. 47:180-230, 1983. (Cited 1,060 times.)

1A-20

20

^{1.} Yanofsky C & Lennox E S. Transduction and recombination study of linkage relationships among genes controlling tryptophan synthesis in Escherichia coli. Virology 8:425-47, 1959. (Cited 265 times.)

^{2.} Gross J & Englesberg E. Determination of the order of mutational sites governing L-arabinose utilization in

Escherichia coli B/r by transduction with phage P1bt. Virology 9:314-31, 1959. (Cited 120 times.) 3. Taylor A L & Trotter C D. The genetic map of Escherichia coli K-12. Genetics 50:659-77, 1964. (Cited 230 times.)

^{5.} Singer M, Baker T A, Schnitzler G, Deischel S M, Goel M, Dove W, Jaacks K J, Grossman A D, Erickson J W & Gross C A. A collection of strains containing genetically linked alternating antibiotic resistance elements for genetic mapping of Escherichia coli. Microbiol. Rev. 53:1-24, 1989.

^{6.} Sanderson K E & Roth J R. Linkage map of Salmonella typhimurium, edition VII. Mircobiol. Rev. 52:485-532, 1988. (Cited 30 times.)