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Moffitt W & Yang J T. The optical rotatory dispersion of simple polypeptides. I. *Proc. Nat. Acad. Sci. US* 42:596-603, 1956.
[Department of Chemistry, Harvard University, Cambridge, MA]

The optical rotatory dispersion of polypeptides can be expressed by an equation that can be linearized to provide a parameter b_0, which measures the degree of α-helicity. For a 100 percent helix, $b_0 = -630$ deg cm^2 dmol^{-1}. [The *SCI*® indicates that this paper has been cited in over 820 publications since 1956.]

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In my graduate days at Iowa State, I studied protein conformation by optical rotation with the late J.F. Foster. Globular proteins are levorotatory at the Na D line and become more so upon denaturation. The discovery of the α-helix[1] in 1951 seemed to provide an explanation if the helix was presumed to be dextrorotatory at this wavelength. The obvious test would be to measure the optical rotatory dispersion (ORD) of helical polypeptides, which had been found in "poor" solvents.[2] (Biot had inaugurated the ORD era during 1812-1838, which ended with the invention in 1866 of the Bunsen burner with its nearly monochromatic Na light.[3])

The idea of optically active helices was anticipated by Pasteur[4] in 1860 but was viewed with skepticism in the 1950s. (An L-polypeptide was then thought to have an equal probability of winding into a right- or left-handed helix, making no net contribution to the optical activity.) But this ORD test remained on my mind when I went to work on polypeptides with P. Doty at Harvard in 1954. One evening in April 1955 in a darkened room, I used a crude polarimeter with a Na lamp and borrowed a Hg lamp with filters to isolate lines at three more wavelengths. To my deep satisfaction, all four optical rotations were dextrorotatory, and the dispersion was not simple and monotonic. Later work—still painful and time-consuming—was done on a Rudolph spectropolarimeter.

I had treated my data with a two-term Drude equation (one term for the helical contribution). Unknown to me, the late W. Moffitt was working on the theory of ORD of the helix[5] because he had heard us chemists constantly talk about this structure. When I learned of Moffitt's equation, I simply recast it in an experimentally useful form in terms of three parameters a_0, b_0, and λ_0. By trial and error, I found that $\lambda_0 = 212$ nm led to a linear plot; b_0 then gave a measure of the α-helicity, being about -630 deg cm^2 dmol^{-1} for a fully helical chain. (Moffitt thought it incredible to fit the data without a computer program, and I, as a mere experimentalist, had to convince him at the blackboard that this simple method was valid.)

In the spring of 1956, there was a sudden demand for my data. D.D. Fitts and the late J.G. Kirkwood had developed an alternative theory of helical rotation.[6,7] At first, I declined to be a coauthor with Moffitt because of the ensuing argument between the theoreticians. Ironically, Moffitt's theory[5] came out in the same month as this *Citation Classic*. Today, we recognize the Moffitt equation as phenomenological and the prediction of a right-handed helix for L-polypeptides as fortuitous.[8]

Our paper was highly cited for two decades because it gave a means of detecting, and to some extent quantifying, α-helix in proteins in solution.[9,10] It reassured the X-ray crystallographers that their structural inferences about right-handed helices were correct and persisted in solution. Most of all, perhaps it renewed our interest in the development of new methodology for the study of chiroptical phenomena (ORD and CD) of proteins,[10] and later nucleic acids, and with it opened up a whole new avenue of biophysical inquiry.

1. **Pauling L, Corey R B & Branson H R.** The structure of proteins: two hydrogen-bonded helical configurations of the polypeptide chain. *Proc. Nat. Acad. Sci. US* 37:205-11. 1951. (Cited 515 times since 1955.)
2. **Doty P, Bradbury J H & Holtzer A M.** Polypeptides. IV. The molecular weight, configuration and association of poly-γ-benzyl-L-glutamate in various solvents. *J. Amer. Chem. Soc.* 78:947-54. 1956. (Cited 460 times.)
3. **Lowry T M.** *Optical rotatory power*. London: Longmans, Green. 1935. 483 p.
4. **Pasteur L.** *Researches on the molecular dissymmetry of natural organic products*. Lectures presented to the Chemical Society of Paris, 20 January and 3 February 1860.
5. **Moffitt W.** Optical rotatory dispersion of helical polymers. *J. Chem. Phys.* 25:467-78, 1956. (Cited 420 times.)
6. **Fitts D D & Kirkwood J G.** The optical rotatory power of helical molecules. *Proc. Nat. Acad. Sci. US* 42:33-6, 1956. (Cited 55 times.)
7. ----------. The optical rotatory power of polyamino acids and proteins. *J. Amer. Chem. Soc.* 78:2650-1, 1956. (Cited 35 times.)
8. **Moffitt W, Fitts D D & Kirkwood J G.** Critique of the theory of optical activity of helical polymers. *Proc. Nat. Acad. Sci. US* 43:723-30, 1957. (Cited 175 times.)
9. **Urnes P & Doty P.** Optical rotation and the conformation of polypeptides and proteins. *Advan. Prot. Chem.* 16:401-544. 1961. (Cited 490 times.)
10. **Yang J T, Chen G C & Jirgensons B.** Optical rotatory dispersion and circular dichroism. (Fasman G D, ed.) *CRC handbook of biochemistry and molecular biology. Proteins—Volume III*. Cleveland, OH: CRC Press. 1976. p. 3-140.