

# 講義スケジュール

- I: 混沌の時代から繊維写真の時代
- 2:サイクロール説
- 3:二次構造の解明
- 4: DNAの構造
- 5:結晶構造解析法の発展
- 6:高分解能構造解析の始まり

# 1930's - 1960's

1930s /	Astbury	ケラチンの繊維写真
1934 E	Bernal & Hodgkin	ペプシンの結晶回折
1935 H	Hodgkin	インスリンの結晶化
1936	Wrinch	サイクロール説を提唱
1938 F	Perutz	ヘモグロビン結晶から回折
1939 F	Pauling	サイクロール説を批判
1950 F	Pauling	αヘリックスの構造
1953	Watson & Crick	DNAの構造
1954 F	Perutz	重原子同型置換法を構造解析に導入
1957 H	Kendrew	ミオグロビンのソーセージモデル
1959 H	Kendrew	ミオグロビンの2Å構造

1930's の背景

## Protein dilemma

- •discrete macromolecular compounds?
- •only colloidal suspensions?
- •have fixed molecular weights?
- •definite amino acid compositions?
- •how amino acids linked together?
- •sequences are random?

### 1930's の背景

# **DNA** dilemma

- •How are nucleotides linked together?
- •order of bases is random?
- •what purpose?
- •how could anyone think that DNA could be the storehouse?

Molecular biology is essentially the practice of biochemistry without a license (E. Chargaff 1963)





![](_page_2_Figure_0.jpeg)

![](_page_3_Figure_0.jpeg)

![](_page_3_Figure_1.jpeg)

![](_page_3_Figure_2.jpeg)

![](_page_3_Figure_3.jpeg)

## key paper

X-Ray Studies of the Structure of Hair, Wool, and Related Fibres. II.—The Molecular Structure and Elastic Properties of Hair Keratin.

By W. T. ASTBURY and H. J. WOODS, Textile Physics Research Laboratory, The University, Leeds.

(Communicated by Sir WILLIAM BRAGG, O.M., F.R.S.)

(Received June 30, 1933.)

Phil. Trans. Roy. Soc. London (1934) A232, 333-394

![](_page_4_Figure_6.jpeg)

# 2種類の蛋白質

球状蛋白質

### 繊維状蛋白質

# 繊維写真の父:Astbury

![](_page_4_Picture_11.jpeg)

1898 - 1961

![](_page_4_Picture_12.jpeg)

Mozartの髪の毛の回折写真

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![](_page_5_Picture_0.jpeg)

![](_page_5_Figure_1.jpeg)

![](_page_5_Picture_2.jpeg)

![](_page_5_Figure_3.jpeg)

![](_page_6_Picture_0.jpeg)

![](_page_6_Figure_1.jpeg)

# 

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#### р.333 - 334

Briefly, the whole argument rests on the discovery<sup>†</sup> that the X-ray "fibre photograph" which appears to be common to all mammalian hairs, human hair, wool, whalebone, nails, horn, porcupine quills, etc., and which is undoubtedly the diffraction pattern of crystalline, or pseudo-crystalline, keratin, the common fibre substance of all these biological growths, is changed into a quite different fibre photograph when the hair is stretched. The change is a reversible one, recalling that previously discovered by KATZ<sup>‡</sup> in rubber, because when the hair is returned to its initial unstretched length, the normal keratin photograph reappears. It is clear that the X-ray effects give a diffraction record of a reversible transformation involving not merely an internal slipping of the fibre substance or a rotation of "micelles" into stricter alignment, but a definite elastic elongation and contraction of the keratin complex itself. It has been proposed, I, to call the two forms of keratin thus revealed by X-ray analysis  $\alpha$ -keratin and  $\beta$ -keratin, the former being the shorter, normal form.

# 伸び縮みの可逆的な変化が 可能な蛋白質の構造とは?

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knowledge of the elastic properties, we must now conclude that the whole process of extension and recovery in the hair fibre is based on a protein chain-system which, under the proper conditions, is capable of being stretched to twice or contracted to half its normal length. These (approximate) limits rest on exhaustive experimental tests of numerous actual fibres, and also find a complete quantitative interpretation in all the available X-ray data, not only of keratin itself, but of other protein fibres also.\* The true starting-point of the line of argument is the observation that the X-ray photograph of  $\beta$ -keratin (stretched hair) is in all essentials analogous to that of the fibroin of natural silk, which is the same whether stretched or unstretched. From every point of view we must assume that fibroin is built from *fully-extended* polypeptide chains lying closely side by side to form long, thin crystalline "bundles" or micelles, and that the effective length of each amino-acid residue in such a system is  $3.5 \text{ A.}^+$ 

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Putting aside for the moment the question of the analysis of the normal fibre photograph ( $\alpha$ ), it is to be noticed at once that the photograph of stretched hair ( $\beta$ ) is closely analogous to that always given by the protein of natural silk\*, fibroin, whether unstretched or stretched, and there is every reason to believe<sup>†</sup>, both from X-ray and general physical and chemical evidence, that the fibre substance of silk is for the most part built of fully-extended polypeptide chains of the simple kind postulated by FISCHER. It follows, therefore, that  $\beta$ -keratin is most probably also based on fullyextended polypeptide chains, while a-keratin must be constructed out of the same chains in some shorter, folded form. Natural silk is thus virtually non-elastic, while mammalian hairs, on account of the inherent configurational instability of the extended keratin complex, show long-range elasticity of a most valuable and instructive character.

We may picture a polypeptide chain as a long series of  $\alpha$ -amino-acid residues,

each of the general formula (H, NH) – a kind of molecular centipede whose

legs represent the various univalent "side-chains" denoted in the general formula by the letter R; and in a fibre such as hair, built, as X-rays show, from a system of

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#### p.343

It follows therefore that if the postulated analogy between  $\beta$ -keratin and fibroin is sound, the characteristic meridian spacing of  $\beta$ -keratin, I, 3.4 A (approximately), corresponds to the average length of an amino-acid residue in the fully-extended keratin chains, so that to explain the occurrence of the normal  $\alpha$ -form of hair, we have to decide on a method of folding these chains which will satisfy both the quantitative requirements of the  $\alpha$ -photograph and the 100% extension revealed by the generalized load/extension curve. In addition, the molecular model must give, at least, a qualitative interpretation of the main physico-chemical differences between  $\alpha$ - and  $\beta$ -keratin, and also promise a basis for a quantitative treatment of the super-contraction phenomenon. The type of intramolecular transformation which best satisfies all these various requirements is shown diagrammatically as follows :----

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The  $\beta$ -form is thus represented by fully-extended peptide chains in which each amino-acid residue takes up, on the average, a length along the fibre-axis of  $3 \cdot 4$  A, while the  $\alpha$ -form is represented by a series of pseudo-diketopiperazine rings which follow each other according to a pattern of length  $5 \cdot 1$  A. The unfolding of the rings is clearly accompanied by an elongation of 100%, and the suggested pattern offers an explanation of both the characteristic meridian reflection of the  $\alpha$ -form (5  $\cdot 1$  A) and of the decrease of resistance of the  $\beta$ -form, as compared with the  $\alpha$ -form, to the action of reagents such as steam, etc.

# Astburyのモデル

![](_page_8_Picture_3.jpeg)

http://www.leeds.ac.uk/heritage/Astbury/

![](_page_8_Figure_5.jpeg)

# β patternの詳細な考察

![](_page_9_Picture_0.jpeg)

#### р.372

chains. In silk fibroin the apparent cell given by the X-ray photographs (a = 9.68 A., b = 7.0 A., c = 8.80 A.,  $\beta = 75^{\circ} 50'$ ) is associated with a weight equivalent to four glycine residues and four alanine residues,\* from which the simplest conclusion seems to be that the chains are for the most part built out of alternate glycine and alanine residues, thus; :--

![](_page_9_Picture_3.jpeg)

and that four parallel chains constitute a crystallographic group.

### p.371

repetition of pattern parallel to the fibre axis. For silk the period in this direction is about 7 A.,\* while for  $\beta$ -keratin it is rather less, something between 6.7 and 6.8 A.† (for the detailed description of the two keratin photographs, see I). It is not at all probable—for keratin at least (see above)—that lengths such as these represent the true period along a polypeptide chain-system, but are rather an expression of the fact that in the simplest formulation of the fully-extended general chain :—

![](_page_9_Figure_7.jpeg)

![](_page_9_Figure_8.jpeg)

#### p.372-373

The X-ray photograph of  $\beta$ -keratin, I, is most conveniently referred to an orthogonal cell of dimensions,  $a = 9 \cdot 3 \text{ A}$ ,  $b_i = 6 \cdot 7 - 6 \cdot 8 \text{ A}$ , and  $c = 9 \cdot 8 \text{ A}$  (see footnote<sup>†</sup>, p. 371), of which b is the most prominent period along the molecular chains, while a and c are "side-spacings." With regard to the latter two points emerge, (i) that the equatorial "spot" nearer the centre which gives the c-spacing is preserved more or less unchanged when the  $\alpha$ -photograph is transformed to the  $\beta$ -photograph, and (ii) that the transformation calls into existence on the equator a very strong spot of spacing a/2, *i.e.*,  $4 \cdot 65 \text{ A}$ . From a study of existing X-ray data on proteins§ the interpretation of these results seems clear, that, in fact, the spacing  $9 \cdot 8 \text{ A}$ . common to both  $\alpha$ - and  $\beta$ -photographs arises from the lateral extension of the side-chains (the R-groups of the general formula given above), while the spacing  $4 \cdot 65 \text{ A}$ . If represents the distance of approach of the main-chains on those sides free from side-chains. The controlling factor in this closest approach of neighbouring "backbones" is most probably attraction between (= NH) and (= CO) groups. \* † ‡, whereby the chains are grouped in pairs; thus :--

![](_page_10_Figure_2.jpeg)

![](_page_10_Figure_3.jpeg)

![](_page_10_Figure_4.jpeg)

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#### p.344

The  $\beta$ -form is thus represented by fully-extended peptide chains in which each amino-acid residue takes up, on the average, a length along the fibre-axis of  $3 \cdot 4$  A, while the  $\alpha$ -form is represented by a series of pseudo-diketopiperazine rings which follow each other according to a pattern of length  $5 \cdot 1$  A. The unfolding of the rings is clearly accompanied by an elongation of 100%, and the suggested pattern offers an explanation of both the characteristic meridian reflection of the  $\alpha$ -form (5  $\cdot 1$  A) and of the decrease of resistance of the  $\beta$ -form, as compared with the  $\alpha$ -form, to the action of reagents such as steam, etc.

![](_page_11_Picture_2.jpeg)

次回の key paper			
Wrinch は Astbury の 繊維写真の解釈を	The Pattern of Proteins By Dr. D. M. Wrinch, Mathematical Institute, Oxford Nature (1936) 137,411-412		
とっ誤っ(所釈し( しまったのか	The Cyclol Theory and the 'Globular' Proteins* By Dr. D. M. Wrinch Nature (1937) 139,972-973		
化学結合論による論考	The Structure of Proteins By Linus Pauling and Carl Niemann JACS (1939) 61, 1860-1867		
Wrinchの反論	The Geometrical Attack on Protein Structure By Dorothy M. WRINCH JACS (1941) 63, 330-333		