Commentary on Gáspár Jékely's article in *EMBO reports*, July 2002

In his article, Gáspár Jékely praises the role that chemistry played in elucidating the structure of DNA. Rightly so, I must say, being educated as a chemist myself. However, I believe that some modesty is quite appropriate in this case and I would like to explain briefly why chemistry initially failed to grasp the real nature of DNA.

While reflecting on the sequencing of the human genome, Jékely alludes to 'Albrecht Kossel's *Baustein* hypothesis—the idea that large polymers can be built from repeated units of similar nature'. Referring to the reconstruction of proteins in the body from degraded proteins in food, Kossel said in a Harvey lecture in 1911, 'In order to understand fully the change we must remember that the proteins are composed of *Bausteine* united in very different ways. [...] The number of *Bausteine* which can take part in the formation of the proteins is about as large as the number of letters in the alphabet. When we consider that through the combination of letters an infinitely large number of thoughts may be expressed, we can understand how vast a number of the properties of the organism may be recorded in the small space which is occupied by the protein molecules [...].' But be careful, Kossel's explanation of his theory does not necessarily mean that he knew what a polymer was! A polymer, so self-evident for us today, was simply

unthinkable in 1911. The term *Bausteine* was not tantamount to Kossel's hypothesis 'that large polymers can be built from repeated units of similar nature', but it was simply his way of saying that the amino acids are the building blocks of proteins, as every biochemistry text book states today. Back in 1911, Kossel, however, believed that they were building blocks of just very small proteins; short peptides—he could imagine words but not sentences nor even books.

The polymer concept is closely connected with the name of another chemist: Hermann Staudinger. Staudinger gave a farewell lecture to the Zürich Chemical Society in 1926. A few eye-witness reports exist, and here I cite the words of Albert Frey-Wyssling: 'I remember Staudinger's lecture [...] on his high polymer thread molecules with a long series of Kekulé valence bonds. It was impossible to accommodate his view in the unit cell as established by X-ray analysis. All the great men present: the organic chemist, Karrer, the mineralogist, Niggli, the colloidal chemist, Wiegner, the physicist, Scherrer, and the X-ray crystallographer, Ott, tried in vain to convince Staudinger of the impossibility of his idea because it conflicted with exact scientific data. The stormy meeting ended with Staudinger shouting "*Hier stehe ich, ich kann nicht anders*" [Here I stand, I cannot do otherwise] in defiance of his critics.' Indeed,

Heinrich Wieland advised Staudinger in the late 1920s: 'Dear colleague, leave the concept of large molecules well alone: organic molecules with a molecular weight above 5000 do not exist. Purify your products, such as rubber, then they will crystallise and prove to be lower molecular substances.' Wieland's 'advice' sounds ridiculous to us, but makes perfect sense given that, shortly before Oswald Avery, it was virtually impossible to think of DNA as a biopolymer. This also explains partially why Phoebus Levene's tetranucleotide hypothesis remained so popular for such a long time.

What are the lessons from the polymer story—as well as many similar stories in science? (i) Chemists/scientists are only human beings. (ii) Scientists must not only consider exact data. Years of research may lead to a hypothesis which is later proven to be correct and accepted, but which at the time of verbalization expresses just the deep conviction—an emotion—of a single person. (iii) Emotions are the essence of life as they are the essence of science.

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