

## Prof. Stephen Kent

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### *Bringing the Science of Proteins into the Realm of Organic Chemistry*

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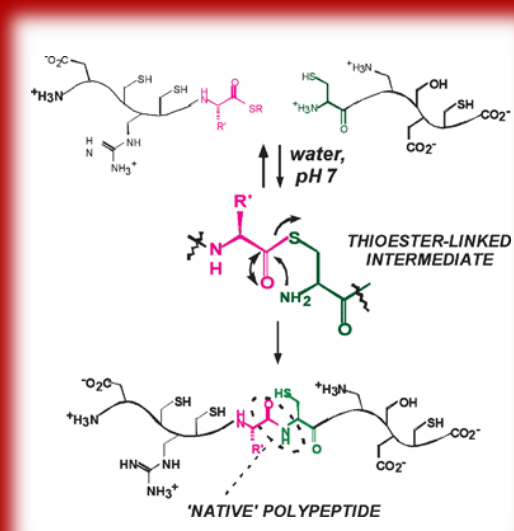
AULA I

Total chemical synthesis of proteins was one of the 'Grand Challenges' of 20<sup>th</sup> century synthetic organic chemistry, from the time of Emil Fischer. A general solution to this challenge was provided by the chemical ligation principle: *chemoselective covalent condensation of unprotected peptides enabled by formation of a non-native moiety at the ligation site* [1]. The most effective chemistry – 'native chemical ligation' [2] – is based on this principle and has enabled the robust total synthesis of a wide variety of protein molecules [3]. Application of synthetic organic chemistry to protein molecules enables novel protein science that can only be done by chemistry [4].

Examples include: total synthesis of mirror image proteins composed entirely of unnatural D-amino acids (and achiral glycine) [5,6]; design and synthesis of protein molecules with novel chemical features not found in Nature [7,8]; and, racemic & quasi-racemic crystallography enabled by total chemical synthesis for the determination of novel protein structures by X-ray diffraction [5,7; 9,10]

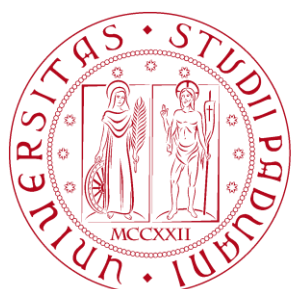
For selected references, see:

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7. Avital-Shmilovici, M.; Mandal, K.; Gates, Z.P.; Phillips, N.; Weiss, M.A.; Kent, S.B.H. Convergent chemical synthesis of ester insulin: determination of the high-resolution X-ray structure by racemic protein crystallography. *J. Am. Chem. Soc.* 2013, 135, 3173.
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9. Yeates, T.O.; Kent, S.B.H. Racemic protein crystallography. *Ann. Review Biophysics* 2012, 41, 41.
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La presenza della S. V. sarà molto gradita.

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