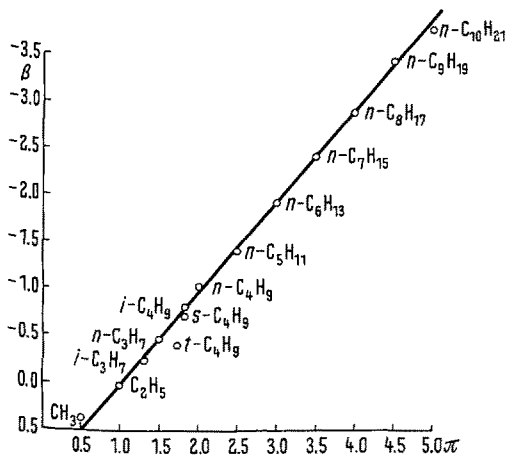
A Correlation Between Constants Used in Structure-Activity Relationships

Attempts to correlate quantitatively the magnitude of the biological activity and the chemical structure of organic compounds has recently met with increasing success. The principle consists in the application of linear free energy relationships, known from physical organic chemistry, to biological problems. If the efficiency-determining step is a chemical reaction, HAMMETT's[1] and TAFT's[2] equations can be used for this correlation successfully, and the group contributions to the activity can be expressed with the help of σ- or σ^*-constants. This was proved, for example, on the growth inhibition of *Staphylococcus aureus* by G-penicillins[3] or *Escherichia coli* by *m*- and *p*-substituted phenyl isothiocyanates[4] respectively.

About 10 years ago work was started dealing with studies on structure-activity relationships. In the first stage, this work was concentrated upon the group of compounds in which the efficiency-determining step is a physical phenomenon characterized by the solubility or partition coefficient, respectively. In a number of studies[5-8] constants were derived, characterizing the substituent independently of the nature of the biological object studied and the type of compounds. These constants, which ZAHRADNIK called β-constants, correlate with R_M-constants, as measured on thin layers by BOYCE and MILBORROW[9], and correlate therefore also with the partition coefficients of these substances. In recent years HANSCH and co-workers have applied the so-called π-constants to structure-activity relationships[10,11]. These constants characterize the contribution of a group to the partition coefficient. In their last work[12], which is solely dedicated to series of compounds whose biological activity is determined by a physical process, there are π-constants mentioned which excellently correlate with ZAHRADNIK's β-constants (see Figure). Both types of constants were successfully applied to a number of compound types as well as to biological objects[7,12]. We would like to stress the excellent mutual correlation of both sets of constants.



Zusammenfassung. Ein wechselseitiges Verhältnis zwischen den β-Konstanten von ZAHRADNIK und den π-Konstanten von HANSCH, die bei Strukturaktivität-Beziehungen verwendet werden, wird beschrieben.

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[1] L. P. HAMMETT, *Physical Organic Chemistry* (McGraw-Hill, New York 1940).
[2] R. W. TAFT JR., J. Am. chem. Soc. *75*, 4231 (1953).
[3] O. R. HANSEN, Acta chem. Scand. *16*, 1593 (1962).
[4] D. VLACHOVÁ and L. DROBNICA, Colln Czech. chem. Commun. (Engl. Edn.) *31*, 997 (1966).
[5] R. ZAHRADNÍK and M. CHVAPIL, Experientia *16*, 511 (1960).
[6] R. ZAHRADNÍK, Archs int. Pharmacodyn. Thér. *135*, 311 (1962).
[7] M. CHVAPIL, R. ZAHRADNÍK, and B. CMUCHALOVÁ, Archs int. Pharmacodyn. Thér. *135*, 330 (1962).
[8] R. ZAHRADNÍK, Experientia *18*, 534 (1962).
[9] C. B. C. BOYCE and B. V. MILBORROW, Nature *208*, 537 (1965).
[10] C. HANSCH, R. M. MUIR, T. FUJITA, P. P. MALONEY, F. GEIGER, and M. STREICH, J. Am. chem. Soc. *85*, 2817 (1963).
[11] C. HANSCH and T. FUJITA, J. Am. chem. Soc. *86*, 1616 (1964).
[12] C. HANSCH, A. R. STEWARD, J. IWASA, and E. W. DEUTSCH, Mol. Pharmacol. *1*, 205 (1965).

Regeneration of Feline Dorsal Roots

There is unanimous agreement regarding the capacity of the mammalian dorsal spinal nerve roots to regenerate as long as their regenerating axones are growing within the neurilemmal portion of the root (GUTH[1]). The growth of regenerating dorsal root fibres is inhibited at the zone of root entry, and the fibres are not capable of growing into the cord. However, histological observations of regenerating fibres have occasionally shown these to pass into the cord (CAMPBELL[2]).

This investigation dealt with the ability of feline dorsal root fibres to regenerate after their transection. For surgical restoration of the root continuity end-to-end, a tubulation technique with a Millipore microfilter was used. Judging from bioelectrical and histological data, severed lumbosacral dorsal root fibres were able to regenerate along their extramedullar portion (Figure 1). No physiological evidence of fibres transversing the neurilemmal-neuroglial junction could be demonstrated.

In a modification of the experimental technique, the distal part of the severed dorsal root was anastomosed to the proximal part of an adjacent (alien) ipsilateral dorsal root, which had been transected peripherally to its ganglion (Figure 2). Thus, the preganglionic portion of the rostral root used for anastomosing was left intact. The regenerative process could then proceed from the ganglion in a

[1] L. GUTH, Physiol. Rev. *36*, 441 (1956).
[2] J. B. CAMPBELL, Int. Congr. Neuropath. *3*, 453 (1962).