between the cisternae. This hypothesis is supported by the observation of oriented elements in sections cut parallel or obliquely to the long plane of the cisternae (Fig. 3). Preliminary measurements indicate that these elongated elements are of the order of 70 to 80 Å in diameter. The elements are apparently essentially parallel, and appear, at least in some instances, to be arranged in lines from one intercisternal space to the next. In our preparations these elements were not in direct contact with the membranes of the cisternae.

What appear to be the same structures have now been demonstrated in several types of cells of different organisms. Whether they can be equated with the fine electron-dense lines seen earlier by Mollenhauer and then by others in this laboratory in cells of the root apex of maize has not yet been established. It is clear, however, that with the procedures used it is possible to demonstrate in some cells definite intercisternal structures in the Golgi apparatus. In some instances these intercisternal elements are more apparent toward one face of the apparatus than the other, possibly in relation to a progression of changes across the apparatus as seen in the production of secretory product (*2*). In other instances they are seen between all the cisternae. The difference could represent stages in the ontogeny of the apparatus. The demonstration of these intercisternal elements strengthens the concept of the apparatus as an organelle of which the cisternae are units, as opposed to the concept of the cisternae as simply being grouped in a Golgi zone. The elongated character of these elements and their parallel arrangement indicates a polarity that may prove to be important. Further study should clarify the functional aspects of these newly observed structures.

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Immunoglobulin Structure: Amino- and Carboxyl-Terminal Peptides of Type I Bence Jones Proteins

Abstract. *Analysis of the amino acid sequence in Bence Jones proteins permits study of the structure of L-chains of normal immunoglobulins. An amino-terminal octadecapeptide containing the sole methionine residue occurs in many but not all immunoglobulins of antigenic type I. The carboxyl-terminal octapeptide appears invariant in type I proteins and ends in cysteine, which may have a cross-linking function.*

The structure of the polypeptide L-chains of the immunoglobulins is deemed related to antibody function; however, on the basis of antigenic characteristics and peptide maps two wholly different types of L-chains exist, type I and type II (*1*). These are structurally similar to the two types of Bence Jones proteins and differentiate each of the three classes of serum immunoglobulins (γ_G, γ_A, and γ_M) into the corresponding two antigenic types (*2*). By comparison of the tryptic peptide maps of type I Bence Jones proteins, type I globulins from the serums of patients with lymphomatous diseases, and normal human γ-globulin we have established that all proteins of this antigenic type contain many tryptic peptides in common (*3*). Whether these peptides represent an identical L-chain or the common portion of a similar L-chain has yet to be established. However, since individual Bence Jones proteins of type I contain a common structural moiety, yet differ in some peptides, we have assumed that, in general, type I L-chains contain a fixed portion and also a mutable portion in which antibody specificity may reside (*4*). The fixed portion contains a series of tryptic peptides previously designated B_1, B_2, B_6, B_7, B_9, B_{11}, B_{13}, and B_{15} (*3–5*); the sequence of most of these has since been determined in our laboratory. A paramount question is whether type I L-chains share many identical sequences but differ at fixed points, for example, in the amino- or carboxyl-terminal peptides, or whether the differences in sequence are randomly located. Our results suggest that an octapeptide COOH-terminal sequence is identical but that differences occur in the NH_2-terminal portion.

A type I Bence Jones protein (Ag) was purified on a diethylaminoethyl (DEAE)-Sephadex column, reduced with mercaptoethanol, and alkylated by reaction with monoiodoacetic acid. A tryptic digest was prepared (with the *p*H-stat), and the soluble peptides were removed and fractionated. Seven basic peptides were separated from the fraction containing the neutral and acidic peptides by chromatography in a gradient elution system (0.5*M* pyridine–0.02*M* acetic acid to 2*M* pyridine–1*M* acetic acid on IRC-50, the column being 1.8 × 150 cm). The column was operated at 50°C, with a flow rate of 80 ml per hour. The fraction containing the neutral and acidic peptides was separated into a series of peptides by chromatography on Dowex 50-X2 (column, 1.8 × 150 cm) with a gradient elution system from 0.1*M* pyridine–formic acid (*p*H 3.1) to 1*M* pyridine–acetic acid (*p*H 5.0) at 40°C with a flow rate of 80 ml per hour. In all, 19 peptides have been obtained in yields ranging from 22 to 70 percent of theoretical. This excludes minor peptides and those present in the insoluble "core." The amino acid composition of many of these peptides is in accord with that previously reported (*5*).

By use of the dinitrophenyl (DNP) method and the phenylthiohydantoin method the probable sequence has been determined thus far for 11 peptides and partial sequences of others; this accounts all told for about one-half of the molecule. We confirm the sequence Gly-Glu-CySH (*6*) found in another type I Bence Jones protein by Milstein (*7*) for the tryptic peptide of this composition (B_1), which we previously reported to be COOH-terminal (*5*, *8*). For the COOH-terminal peptic peptide Milstein found the sequence Lys-Ser-Phe-AspNH_2-Arg-Gly-Glu-CySH; we have established the sequence of our tryptic peptide B_9 as: Ser-Phe-AspNH_2-Arg. Since B_1 and B_9 are present in the tryptic peptide maps of all type I Bence Jones proteins and immunoglobulins investigated in our laboratory, as well as in normal 7*S* γ-globulin, we suggest that this octapeptide sequence may be an invariant part of the structure of type I L-chains. Its apparent function is to provide the COOH-terminal cysteine residue which

is thought to bridge the H- and L-chains of the immunoglobulins (*7*).

The NH_2-terminal peptide of this type I Bence Jones protein is the peptide previously identified by us as B_3 (*5*). In accord with the composition reported earlier, its probable sequence is: Asp-Ileu-GluNH_2-Met-Thr-GluNH_2-Pro-Ser-Ser-Ser-Leu-Ser-Ala-Ser-Val-Gly-Asp-Arg. There is some uncertainty still about the Pro-Ser and Gly-Asp positions, but the remainder has been verified by comparison of overlaps in five peptic peptides derived from B_3. The NH_2-terminal position of this peptide is in accord with the presence of aspartic acid as NH_2-terminal in Bence Jones protein Ag, with the proximity of methionine to the amino end as cleavage by cyanogen bromide indicates, and with the presence of DNP-aspartic acid, isoleucine, and glutamic acid in the DNP-peptide obtained by pronase digestion of the DNP-protein. The significant features of the composition of the NH_2-terminal peptide are the absence of aromatic amino acids and cysteine, the presence of the single methionine, and the concentration of one-fifth of the serine residues of the whole protein within one heptapeptide sequence.

Although B_3 has been identified in the tryptic peptide maps of a number of type I Bence Jones proteins, the myeloma globulin from the same patient (Ag), and in normal 7*S* γ-globulin (*3, 4, 5*), it is absent in several type I Bence Jones proteins including specimen Lo, which has NH_2-terminal glutamic acid and lacks methionine (*4*). This indicates that the NH_2-terminal portion of type I L-chains is one locus subject to individual variation. Other peptides present in Ag but absent in some type I proteins are B_{16} which tentatively has been assigned the sequence Leu-Glu-Ileu-Lys and B_8 which has the sequence Thr-Phe-Gly-GluNH_2-Gly-Thr-Lys.

Variation in the NH_2-terminal portion but constancy in the COOH-terminal portion may have general structural significance for both type I and type II Bence Jones proteins. In the type II proteins the NH_2-terminal amino acid is either undetectable or varies considerably with the individual specimen (*9*). On the other hand, the acidic peptide A_1 is present in all 11 type II Bence Jones proteins that we have examined (*4*). Apparently A_1 is COOH-terminal since it lacks lysine and arginine; its composition is: Thr_2,Ser,Glu,Pro,Ala,-Val,CyS. Milstein (*7*) has suggested that the COOH-terminal cysteine in type I L-chains provides the disulfide bridge to the H-chain in type I globulins. Whether the cysteine in the COOH-terminal peptide of type II proteins has a function similar to that of the terminal cysteine in type I proteins remains to be established.

The heterogeneity of normal γ-globulin (*1, 2*) and the nonidentity of Bence Jones proteins (*9*) have hitherto diminished the incentive for sequence analysis of these related proteins. However, the successful elucidation of the sequence of the NH_2- and COOH-terminal peptides of a type I Bence Jones protein and the identification of these and other peptides in normal γ-globulin verifies the value of this approach to structural study of the immunoglobulins. For this purpose complete amino acid sequence analysis of several Bence Jones proteins of each antigenic type will be essential.

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6. Abbreviations for amino acid residues: Gly, glycine; Glu, glutamic acid; CySH, cysteine; Lys, lysine; Ser, serine; Phe, phenylalanine; Arg, arginine; $AspNH_2$, asparagine; Asp, aspartic acid; Ileu, isoleucine; $GluNH_2$, glutamine; Met, methionine; Thr, threonine; Pro, proline; Ala, alanine; Val, valine; Leu, leucine; CyS, half-cystine.
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Intermolecular Forces in Association of Purines with Polybenzenoid Hydrocarbons

Abstract. *The interactions in solution between purine or pyrimidine bases and polybenzenoid aromatic hydrocarbons probably consist in a vertical, stacking-type physical association. By molecular orbital calculations the role of the Van der Waals-London intermolecular forces in these interactions is determined. The electrostatic dipole-dipole forces are negligible, the polarization (or induction) dipole–induced dipole forces are contributory, but most important are the dispersion (or fluctuation) forces. This loose, physical type of interaction should not show any specificity with respect to the carcinogenic activity of the hydrocarbons.*

The molecular associations between purine and pyrimidine bases or their nucleosides and polycyclic aromatic hydrocarbons correspond, to a large extent, to the long-known phenomenon in which aromatic molecules are made soluble by purines, first studied by Weil-Malherbe in 1946 (*1*) and investigated by Boyland and Green (*2*). From studies, particularly those of Ts'o and co-workers (*3*), on the interaction and association of purine bases with themselves or the aromatic amino acids of proteins or hydrocarbons, it appears that these interactions consist in a vertical, stacking-type association of the parallel-oriented partners, with an intermolecular separation of 3 to 4 Å. A similar type of interaction seems to exist also between the aromatic hydrocarbons and the nucleic acids themselves (*4*). Some authors (*5*) but not others (*6*) consider that it corresponds to the intercalation of the hydrocarbon into the nucleic acid between successive base-pairs.

With regard to the nature of these physical interactions between the purines and the hydrocarbons a correlation has been shown to exist (*7, 8*) between the solubilizing power of the purines and their electron donor properties. This correlation indicates that charge transfer forces represent a significant component in the overall binding forces. However, as no charge transfer band is observed in these interactions, and as the compounds taking part are not particularly outstanding electron donors or acceptors, one could