PREDICTION OF THE THREE-DIMENSIONAL STRUCTURE FOR RIBOSOMAL PROTEIN L25

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Received 14 October 1975

1. Introduction

Protein L25, contained in the 50 S subparticle of the *E.coli* ribosome, together with protein L18 forms a complex with 5 S RNA having an ATP- and GTP-ase activity [1]. The primary structure of this protein was recently determined by Ovchinnikov and his collaborators at our Institute [2]. Starting with the assumption that this protein has a globular structure in water environment we have attempted to determine its tertiary structure proceeding from the primary one. A search for such a structure was made with space filling CPK models by consecutive packing of regions with a regular secondary structure. At each stage we tried to obtain a maximum shielding from water of bulky hydrophobic groups and their possible densest packing, as well as the formation of the maximum number of hydrogen bonds and hydration of all the polar groups not forming intramolecular hydrogen bonds (cf. [3,4]).

2. Features of the primary structure

Protein L25 contains 30 bulky hydrophobic groups (Leu,Ile,Val,Met,Phe,Tyr), 17 positively charged groups (Arg and Lys) and 12 negatively charged groups (Asp and Glu). These groups are distributed along the primary structure as shown in table 1. Thus in the primary structure of protein L25 it is possible to distinguish two positively charged regions (9–25 and 68–86) and three regions saturated with a high percentage of massive hydrophobic groups (the central region 26–67 and two short terminal regions, 1–8 and 87–94). The positively charged region 68–86 contains a normal number of bulky hydrophobic groups while region 9–25 has only one such group.

Table 1

Chain region	Bulky hydrophobic groups	Positively charged groups	Negatively charged groups
1– 8	4 (50%)	0	1
9–25	1	7 (40%)	1
26–67	17 (40%)	3	7
68–86	5 (25%)	6 (30%)	2
87–94	3 (40%)	1	1
Total	30 (30%)	17 (20%)	12 (15%)

3. The secondary structure

The stereochemical theory of the secondary structure of globular proteins was developed in our laboratory by Lim [5]. Application of his algorithm [6] to the amino acid sequence of protein L25 predicts two α-helical regions, 4–12 and 53–69, and four β-structural region, 28–32, 38–42, 46–50 and 89–93. This localization of the regular secondary structure was taken as the zero approximation in constructing the model of the tertiary structure and was varied when necessary to obtain the optimum folding according to our criteria.

4. The central hydrophobic region

The central hydrophobic region of protein L25 includes the predicted β-structural regions βA (28–32),

βB (38–42), βC (46–50) and the helix βB (53–69) directly following each other along the chain. Therefore the conformation of this region was assumed to be a β-structural sheet, the hydrophobic surface of which is shielded by the hydrophobic surface of the α-helix. The β-structural hair-pin βA–βB represented in fig.1 has the greatest number of hydrogen bonds and hydrophobic contacts per one fixed residue. The βC region can be adjusted to this hair-pin in two ways (see fig.1). Both the obtained β-structural sheets have a marked hydrophobic surface which can be shielded by the hydrophobic surface of the helix αB as shown in fig.1. From the two obtained structures structure I′ seems to be more probable. Both structures of the central hydrophobic region leave unshielded the dihedral hydrophobic surface, formed by the hair-pin βA–βB and the adjacent side of the helix αB, as well as the opposite hydrophobic surface of this helix.

5. Adjusting the terminal regions

In both structures the N-terminal helix αA (4–12) and the preceding residues of the chain coiled into the helix 3_{10} shield well the above-mentioned dihedral surface while the positively charged region between αA and βA can be adjusted to the region βA, forming one more β-structural region 17–23 (βA′). The region of the chain following αB can be joined to βC as a β-structural hair-pin from regions 71–74 (βD) and 77–80 (βE). In the connecting region 66–70 between regions αB and βD a system of bends similar to helix 3_{10} can be formed.

As a result two structures, I and II are obtained (see fig.2) representing an approximately mirror

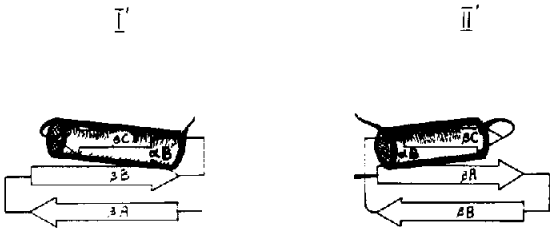

Fig.1. The most probable structures of the central hydrophobic region of protein L25. The hydrophobic surface of the β-structural sheet is turned to the viewer.

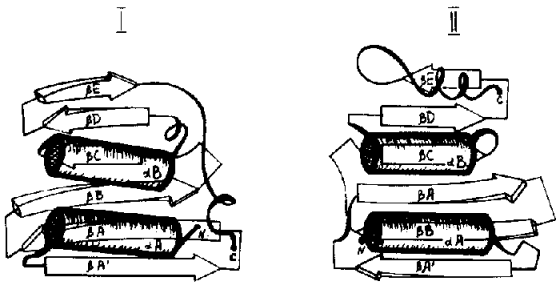

Fig.2. Hypothetical three-dimensional structures of protein L25. Structure I seems the more probable.

reflection of each other and differing by the interchange of regions βA and βB. In both structures two relatively small hydrophobic surfaces remain unshielded: at the junction between the helix αB and hair-pin βD–βE (at the top of the figure), and at the junction between the helix αA N-terminus and the helix αB C-terminus with the β-structural sheet. Each of these surfaces can be shielded both by the C-terminal hydrophobic region 87–91 coiled into the helix 3_{10}, and by deformation of the corresponding regions of the β-structure. The most probable ways of adjusting the C-terminal region to structures I and II are shown in fig.2, though the alternative joining of the C-terminus cannot be excluded for each of them.

Structure II contains approximately the same number of hydrogen bonds as structure I but has a smaller number of shielded bulky hydrophobic groups and a less compact packing.

6. Discussion

Thus, the structure satisfying best the adopted criteria is structure I, i.e. the β-structural sheet from 6 regions; 17–23 (βA′), 26–33 (βA). 35–42 (βB), 48–50 (βC), 71–74 (βD), 77–79 (βE) with the frontal hydrophobic surface shielded by α-helices 2–12 and 54–64 and the side one, by helix 3_{10} 87–91 (fig.3). It is possible, of course, that external parts of the β-sheet are more distorted than in our idealized model. Regions βC and βD are parallel to each other and all the other pairs of β-regions neighbouring along the chain are antiparallel and are connected by β-

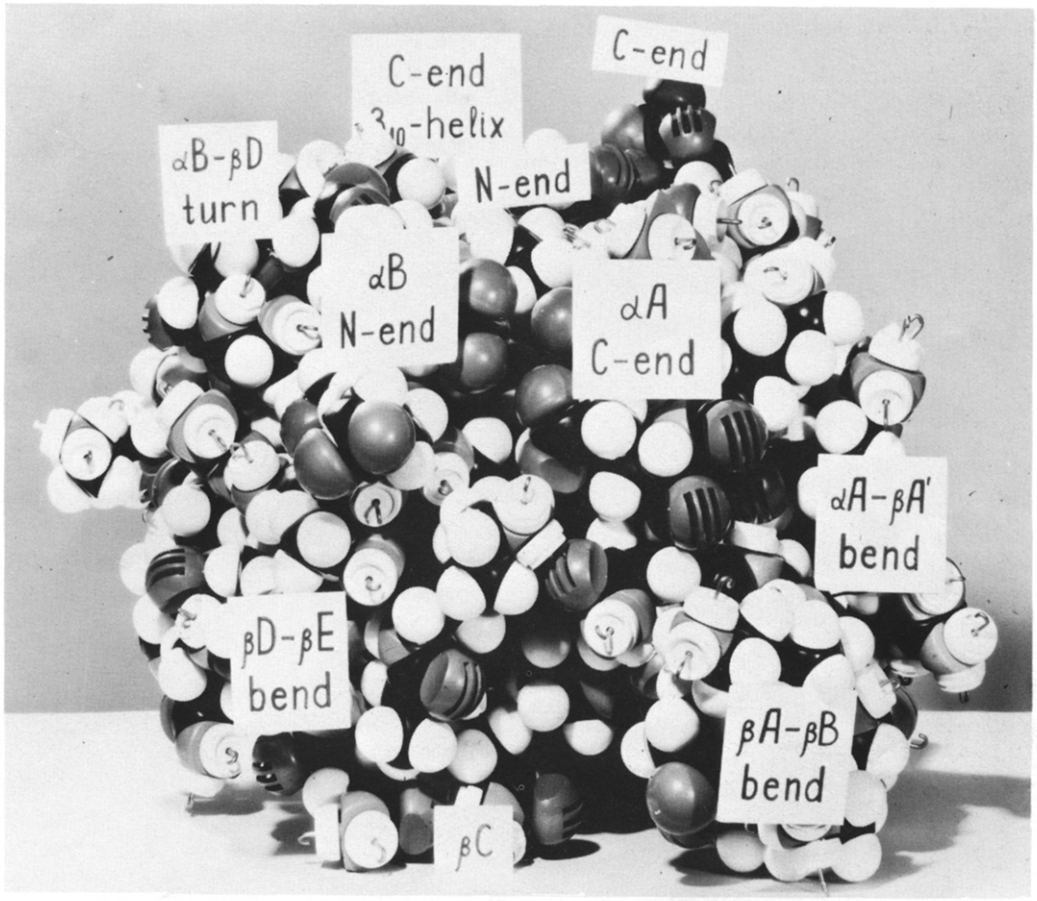

Fig.3. Space filling model of structure I (view from the C-terminus of the A helix and N-terminus of the B-helix).

bends. In both structures, I and II, the positively charged regions are located on the perimeter of the β-structural sheet, especially near the terminal β-structural strips βA′ and βE (cf. table 1). Therefore it can be expected that protein L25 can form complexes with at least two sites of 5 S RNA (cf. [7]).

It is interesting to note that the β-structural sheet formed of 5–6 regions (though parallel and not anti-parallel) and shielded from one side by α-helices, is the main motif of nucleotide-binding domains of dehydrogenases, kinases and other proteins [8,9]. We cannot say at present whether the similarity of the hypothetical structure of protein L25 with the structure of nucleotide-binding domains is a result of a random coincidence, convergency or just our error.

Acknowledgements

The authors thank O. A. Rakitina and A. G. Raiher for translating the manuscript into English.

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