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# Are there differences in structural and mechanical properties of R15, R16 and R17 spectrin domains?

Spectrin is a cytoskeletal protein that plays an important role in maintenance of plasma membrane integrity and cytoskeletal structure. It determines the strength, mechanical stability and capacity for deformation of cells. Spectrin forms a reverse parallel heterodimer consisting of α- and beta-chains. This protein has an elongated shape consisting of repetitive rod-like units. Each unit of α-spectrin (repeat or domain) contains three α-helices forming the simple three-helix bundle with right-handedness (Fig. 1). Spectrin repeats are important for the functioning of the living cells.

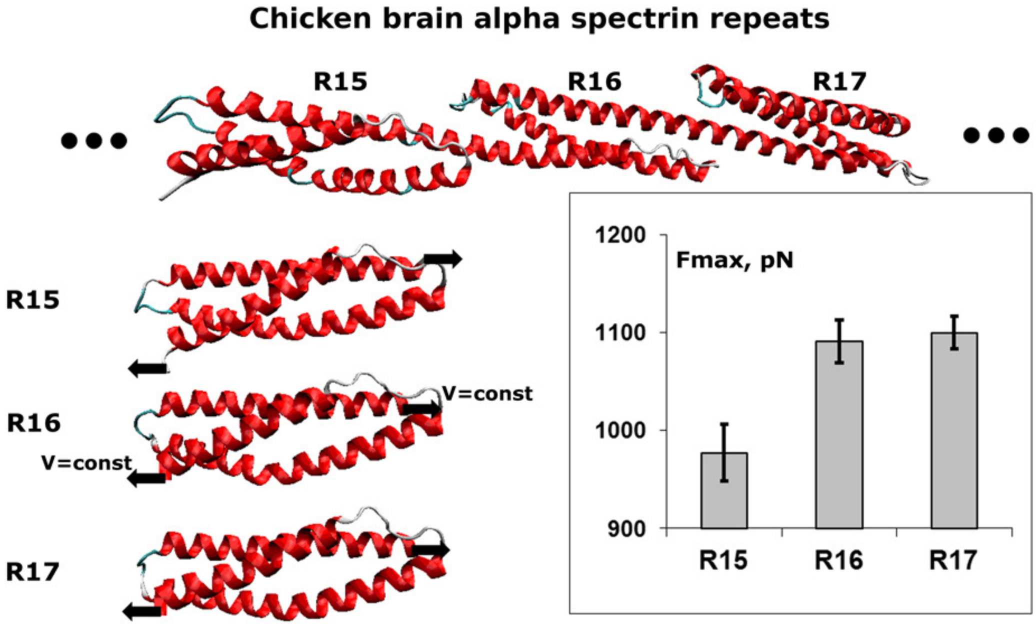

Fig. 1. Structure of R15, R16, R17 spectrin repeats and the maximum force required to extend each presented domain by the termini.

Here we consider the properties of only three well known repeats: R15, R16, and R17 of chicken brain α-spectrin. Despite their structural similarity (the sizes of α-helices, the fraction of residues in the secondary structure, angles between helices, the stabilities, the number of hydrogen bonds) experimentally it has been shown that these domains have different folding and unfolding rates, and also different folding mechanisms. Moreover, we have demonstrated that these domains have different mechanical stabilities. R15 is less mechanically stable than R16, which is less stable than R17. To explain such difference in mechanical stability we have found the additional properties, which can explain such behavior.

Analysis of the amino acid composition have been shown that although these domains have the same number of aromatic amino acid residues (10 in each domain), they differ in the number of aromatic residues involved in the aromatic clusters (Fig. 2A). R15 has one aromatic cluster including four amino acid residues, R16 has two (five amino acid residues), and R17 has three (seven amino acid residues) aromatic clusters (Fig. 2A). To find flexible and rigid regions in the spectrin domains we calculated the probability to be ordered or disordered per residue (Fig. 2B). As seen from Figure 2B, the average probability to be disordered per residue is 0.59 for R15, 0.49 for R16, and 0.38 for R17. Thus, domain R15 is more flexible than R16 and R17, in which the five and seven aromatic residues are included in the aromatic clusters. Therefore, we can suggest that R15 should be less mechanically stable than two other studied domains. To check this hypothesis we have performed steered molecular dynamics simulations. We modeled the process of stretching these spectrin domains by the termini with constant force and constant velocity. From the result of steered molecular dynamics simulations we can conclude that R15 is less mechanically stable than R16, which is less stable than R17 (Fig. 1), but these three spectrin domains have the same unfolding pathways.

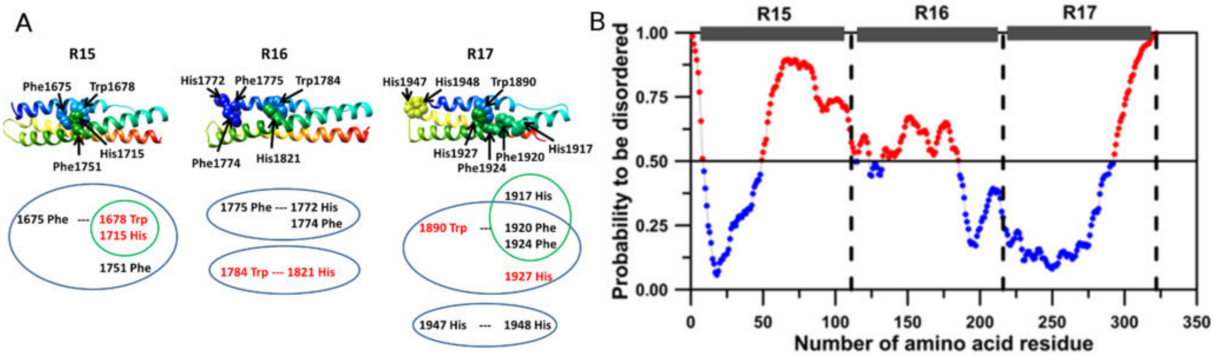

Fig. 2. A. Aromatic residues involved in the aromatic clusters in R15, R16 and R17 are shown as space-filling models. The first, second and third α-helices are colored blue, green and red, respectively. B. Probability of each amino acid residue to be ordered or disordered in three spectrin domains calculated using the IsUnstruct program (http://bioinfo.protres.ru/IsUnstruct/).

Thus, studying the structural and mechanical properties of R15, R16 and R17 spectrin domains we have revealed that they have different mechanical stabilities. R15 is less mechanically stable than R16, which is less stable than R17. The greater mechanical stability of spectrin domains 16 and 17 can be explained by the presence of a larger number of rigid regions and aromatic residues involved in the aromatic clusters. Therefore, the more mechanical stable spectrin domain the less flexible it is.

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## Publication

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