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Comment

Modeling of DNA curvature
Comment on "Sequence-dependent collective properties of DNAs and their role in biological systems" by Pasquale De Santis and Anita Scipioni

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Since the pioneering works of Trifonov [1,2] the idea of DNA sequence dependent intrinsic properties, which are involved or even govern many biological processes, has become widely accepted. The review of De Santis and Scipioni [3] is devoted to such superstructural DNA features, which they call "sequence-dependent collective properties of DNA", mainly having in mind DNA curvature and bendability. The authors of this broad and detailed review do not share Trifonov's opinion [4,5] that these are rather different properties that require separate models and study approaches. Moreover, De Santis and Scipioni even do not mention that there are researchers clearly distinguishing between intrinsic DNA curvature that is primarily the property of naked DNA and DNA bendability particularly evident in the case of sequence dependent DNA–histone octamer association. The great advantage of the review is in the consistent attitude, which I deeply appreciate and share the assurance of the authors that in this case it is the only correct scientific approach. It is in description of the **physical** model that explores different aspects of DNA collective properties instead of application by some means irrelevant models related to signal processing, machine learning and data mining. (In the text of the review these approaches are called "the bioinformatic approaches".) Because of the space limitations I would like to comment on the DNA curvature model, exclusively.

De Santis and Scipioni use the term curvature from the classical mathematical point of view. Though, we want to measure DNA curvature associated with a certain base pair. I do not see any sense in usage of the regular mathematical definition of the trajectory line curvature, even De Santis and Scipioni appeal to the Landau and Lifshitz [6] authorities. The DNA 'axis', i.e. the broken line passing through the base pair centers, or DNA strand, i.e. the broken line connecting the phosphates, cannot strictly be described in terms of curvature, unless represented as smooth curves. DNA molecule may be presented as a line in space only in the frame of the certain model, which should be clearly stated. In our model [7,8] we proposed to describe the overall DNA curvature of a relatively small DNA fragment by a curvature of an arc approximating to the path of the axis of the given DNA fragment. Overall DNA shape is a meaningful notion only if the length of the DNA molecule is substantially larger than its diameter. This is, only fragments longer than 20 bp, with elongated shape, could have that shape curved. To predict the mentioned above DNA axis from the DNA sequence we used the nearest-neighbor approximation of the wedge model for the DNA

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double helix [7] as it was also done by others [9–11]. De Santis et al. used twist, roll and tilt angles, while we used more suitable 'Eulerian' angles [8,12]: twist (Ω), wedge (σ) and direction of wedge (δ) angles where the twist angles are taken from [13] and other angles are from [7]. Today there are several sets of wedge angles but, surprisingly (or not), the sets are poorly correlated. Actually, Fig. 2 from [3] shows it pretty well for the three sets.

De Santis and Scipioni claim that their set of the angles [10,11] shows the best correlation with the results brought in [14]. Milton et al. [14] mutagenized a 60 base-pair region of a certain DNA fragment to determine base-pairs that are critical for the fragment to bend. The mobility of each mutated fragment was measured by polyacrylamide electrophoresis at 4 °C and at 65 °C to assess the degree of bend. To my opinion the experiments in [14] cannot provide any additional evidence which set is better because the dependence of DNA mobility anomalies on peculiarities of unknown DNA shape changes as a result of the mutagenesis is too complex to be included in the theoretical model of the migration anomaly of DNA fragments in polyacrylamide gels. We can only hope that further investigations will clarify which set is better in the frame of the nearest-neighbor model. Of course, it will be important only in case that this model will stay relevant for the description of the curved DNA.

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