There are other reasons why polyanions are useful genetic molecules, other than their resistance to nucleophilic attack. The biological form of DNA is a large double stranded polyanionic polymer, in contrast to RNA which is a single-stranded polyanion polymer and protein which are polymers with varying combination of anionic, cationic, and hydrophobic properties. Even with counterions, it would be difficult to fold DNA into complicated and compact 3D structures as occurs for proteins, given the large electrostatic repulsions among the charged phosphates. Rather it forms a elongated double stranded rod, not unlike the rod-like structure of proteins denatured with sodium dodecyl sulfate (used in SDS PAGE gels). The elonged rod-shaped structure of ds-DNA is critical for the molecule which is the main carrier of our genetic information since mutations in the bases (leading to a switch in base pairs) causes no change in the overall structure of dsDNA. This enables evolutionary changes in the genetic material to produce new functionalities. A single change an amino acid of a protein, however, can cause a large change in the structure of a whole protein, a feature unacceptable for a carrier of genetic information. RNA structure effectively lies between that of DNA and proteins. Since it has less charge density than dsDNA, it can actually form dsRNA helices, so it can carry genetic information, as well as form complex 3D shapes necessary for its activity as an ribozyme. Perhaps more importantly, steric interference prevents ribose in RNA from adopting the 2'endo conformation, and allows only the 3'endo form, precluding the occurrences of extended ds-B-RNA helices.

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