



Inside cells, DNA generally occurs in two forms—linear strands and circular rings. In 1996, Mirkin invented and synthesized a new form, called spherical nucleic acids, or SNAs, which consist of densely packed, and highly oriented single- or double-stranded DNA templated on the surface of a nanoparticle core. Mirkin initially intended to create particles that could be programmed to bond together to form designer materials, an area that has spawned a new sub-field of materials science, but SNAs proved to be equally useful in biology and medicine. What drives the emerging biomedical application of SNAs are the unusual properties of this unusual class of nucleic acids. For example, SNAs can easily enter cells, without the need for a toxic co-carrier, a property not associated with natural forms of nucleic acids. This property stems from the ability of receptors on the surfaces of cells to recognize the three-dimensional SNA architecture and trigger an internalization process called endocytosis. Since it is the architecture of SNAs that enables these biological interactions, SNAs are compatible with a diversity of materials in the nanoparticle core, including inorganic, organic, and biological materials; this feature thereby expands the potential functionality of SNAs in biological systems.

The unique properties of SNAs have proven valuable in medical research and the development of diagnostics and treatments for disease. For example, many researchers now use SmartFlares™, intracellular probes based upon SNAs, to track the expression of genes in living cells. In this system, SNAs are complexed with short reporter oligonucleotides with fluorophore labels, bind to specific mRNA in a cell, and release the reporter strands, which can be detected by fluorescence imaging and flow cytometry techniques. The Verigene diagnostic system— developed and commercialized by Nanosphere, one of three companies launched by Mirkin—can rapidly and accurately detect many markers of infectious disease, cancer, and cardiac disease, and in many cases,

decrease the amount of time needed for a medical diagnosis. SNAs also have found use as nanotherapeutics, resulting in numerous lead-compounds for treatments for many forms of cancer, psoriasis, and diabetic wounds. Already more than 1,800 products have resulted from SNA technology, and SNAs are expected to provide further advances to human health and society.