CURRICULUM VITAE

Nina Sidorova

Work Address: National Institutes of Health
LPSB/NICHD, Bldg.9, Rm.1E-108
Bethesda, MD 20892

Phone: (301) 402-4698 (w)

E-mail: sidorova@mail.nih.gov

Education:

1991	Ph.D. in Molecular Biology, V.A.Engelhardt Institute of Molecular Biology Russian Academy of Sciences. Ph.D. Thesis: "Synthetic Peptides which Can Form Specific Complexes with DNA"
1983	M.S. in physics. Moscow State University, Department of Physics
1978-1983	student, Moscow State University, Department of Physics

Research and professional experience:

Extensive experience in characterizing DNA-drug, DNA-peptide and DNA-protein interactions.

Specific Projects:

- Design and detailed description of peptides and peptide-netropsin (antitumor antibiotic) conjugates that bind DNA in the minor groove in a sequence-specific manner.
- Measurements of the amount of water displaced in the process of a synthetic netropsin analogue binding to DNA. This was the first application of the osmotic stress technique to DNA-drug interactions demonstrating the ability to measure changes in water binding associated with the netropsin analogue interaction to different DNA sequences.
- Development of a restriction nuclease footprinting assay for the quantitating specific DNA-netropsin binding constants. It has been shown that though netropsin binds in a

DNA minor groove, and restriction endonuclease EcoRI binds in a DNA major groove, both netropsin and a netropsin analogue protect DNA from EcoRI restriction nuclease cleavage by inhibiting the binding of EcoRI to its recognition site.

- Direct measurement of differences in sequestered waters between specific and nonspecific EcoRI-DNA complexes using a competitive equilibrium binding under conditions of osmotic stress. It has been demonstrated that a competitive binding method allows a direct measurement of number of waters released in formation specific versus non-specific EcoRI-DNA complex. About 110 more water molecules are being retained in the nonspecific complex to compare with the specific complex.
- Kinetics of the EcoRI binding to DNA under conditions of osmotic stress. Linkage of EcoRI dissociation from its specific DNA recognition site to water activity, salt concentration, and pH. The observed dependence of the binding equilibrium constant on water activity is reflected in the dissociation rate of the EcoRI from its specific site as well. Osmotic stress dramatically slows down the dissociation of the EcoRI from its specific site on DNA. We find that the dependence of the dissociation rate on water activity is dominated by the difference in 110 sequestered water molecules between the specific and nonspecific binding modes of the protein. The salt and pH dependence of the overall off rate is dominated by the dissociation of the nonspecifically bound protein from the DNA.
- Development of the self-cleavage assay for the restriction endonucleases EcoRI and BamHI. Using osmotic stress technique as a practical way of manipulating dissociation rates controllably, a method was developed for using the nuclease activity of two restriction endonucleases to measure sensitively their specific binding. This self-cleavage assay allows measurement of binding equilibrium and kinetics avoiding intrinsic problems of the techniques based on separation of free and bound species (such as gel mobility shift assay and filter-binding assay). There is the possibility of using such a technique for any protein possessing DNA cleavage activity given that its interactions with DNA are sensitive to osmotic stress.

- Measurement of the difference in sequestered water between the specific EcoRI complex and a 'star-site' noncognate complex and of the work needed to remove water from the 'star-site' complex using equilibrium and kinetic measurements. As seen at low osmotic pressures complexes of EcoRI with 'star-sites' that differ by only a single base pair from the specific recognition site sequesters as many waters as the nonspecific complex. At high enough osmotic pressures, however, in contrast to nonspecific complexes, the complex between EcoRI and the 'star-sequence' can be strongly dehydrated. It has been proposed that the modulation of 'nonspecific' and 'specific' modes of EcoRI binding to 'star' sequences by neutral solutes could play a key role in the enzymatic activity at these sites.
- Sensitivity of a *Thermus aquaticus* MutS-DNA specific binding to salt, pH and water activity. Among large group of proteins required for mismatch repair, only MutS recognizes and binds to heteroduplex DNA containing mispaired or unpaired bases, and by doing so triggers cascade of events. Studies are in progress now to investigate influence of salt, pH, and water activity on MutS-DNA binding to different mismatches to determine parameters crucial for this protein binding strength and specificity.
- Water release in the BamHI restriction endonuclease binding. The work is in progress on measuring differences in water release between specific and nonspecific BamHI-DNA binding. The strong advantage of the BamHI system is that both specific and nonspecific complex structures are available. Our osmotic measurements can be directly related to the structural data.

  Techniques used: osmotic stress technique modified to perform solution studies; gel-electrophoresis of DNA and DNA-protein complexes (specifically gel mobility shift assay in agarose and polyacrilamide gels); DNA isolation and purification; PCR; DNA cloning; HPLC; stop-flow technique; optical spectroscopy (fluorescence, circular dichroism).

2004 – till now Staff Scientist in the National Institutes of Health, National

	Institute of Child Health and Human Development, Laboratory of Physical and Structural Biology
2002-2004	Research Fellow in the National Institutes of Health, National Institute of Child Health and Human Development, Laboratory of Physical and Structural Biology
1997-2002	IRTA Fellow in the National Institutes of Health, National Institute of Child Health and Human Development, Laboratory of Physical and Structural Biology
1994- 1997	Visiting Fellow in the National Institutes of Health, Division of Computer Research and Technology, Laboratory of Structural Biology
1992 - 1994	Visiting Fellow in the National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Laboratory of Biochemistry and Metabolism
1983 - 1992	Junior Researcher and Research Scientist in the Engelhardt Institute of Molecular Biology RAN, Laboratory of Physics of Biopolymers

Research interests:

Molecular recognition, particularly DNA-protein binding. Distinguishing between factors that are in common and factors that are different for specific and nonspecific binding. Demonstration of the general importance of water in the specific DNA-protein binding. Linking thermodynamics and structure through water release. Practical applications of the osmotic stress technique for stabilizing of labile DNA-protein complexes.

PUBLICATIONS

1. Sidorova N.Yu., Semenov T.E., Surovaya A.N., Vengerov Yu.Yu. Streltsov S.A., Khorlin A.A., Gottikh B.P., Zhuze A.L., Gursky G.V. /Interaction of a Synthetic Pentapeptide with DNA: Binding Specificity and Compaction of DNA/ (1987) *Mol. Biol. (Mosk)* **21**, 1250-1264.
2. Vengerov Yu.A., Semenov T.E., Surovaya A.N., Sidorova N.Yu., Streltsov S.A., Khorlin A.A., Zhuze A.L., Gursky G.V. /Electron Microscopic and Physico-Chemical Studies of DNA Complexes with Synthetic Oligopeptides: Binding Specificity and DNA Compact Structures/ (1988) *J. Biomol. Struct. and Dynam.* **6**, 311-330.
3. Grokhovsky S.L., Surovaya A.N., Sidorova N.Yu., Votavova H., Sponar J., Frich I., Gursky G.V. /Design and Synthesis of Peptides Capable of Specific Binding to DNA/ (1988) *Mol. Biol. (Mosk)* **22**, 1056-1073.
4. Grokhovsky S.L., Surovaya A.N., Sidorova N.Yu., Gursky G.V. /Synthesis of a Nonlinear DNA-Binding Peptide with Specificity Determinants Close to Those of the 434 Cro Repressor/ (1989) *Mol. Biol.(Mosk)* **23**, 1226-1244.
5. Leinsoo T.A., Nikolaev V.A., Grokhovsky S.L., Surovaya A.N., Sidorova N.Yu., Streltsov S.A., Zasedatelev A.S., Zhuze A.L., Gursky G.V. /Synthetic DNA-Binding Ligands Containing Reaction Centers Specific for AT and GC Base Pairs/ (1989) *Mol. Biol. (Mosk)* **23**, 1274-1292.
6. Grokhovsky S.L., Surovaya A.N., Brussov R.V., Chernov B.K., Sidorova N.Yu., Gursky G.V. /Design and Synthesis of Sequence-Specific DNA-Binding Peptides/ (1991) *J. Biomol. Struct. and Dynam.* **8**, 989-1025.
7. Sidorova N.Yu., Nikolaev V.A., Surovaya A.N., Zhuze A.L., G.V.Gursky /Interactions Between DNA and Cystine Peptide/ (1991) *Mol. Biol. (Mosk)* **25**, 571-580.
8. Grokhovsky S.L., Nikolaev V.A., Zubarev V.E., Surovaya A.N., Zhuze A.L., Chernov B.K., Sidorova N.Yu., Zasedatelev A.S., Gursky G.V. /Sequence-Specific Cleavage of DNA by Netropsin Analogue Containing a Copper (II)-Chelating Peptide Gly-Gly-His/ (1992) *Mol. Biol. (Mosk)* **26**, 832-838

9. Nikolaev V.A., Surovaya A.N., Sidorova N.Yu., Grokhovsky S.L., Zasedatelev A.S., Gursky G.V., Zhuze A.L. /DNA-base pair sequence-specific ligands. X. Synthesis and binding DNA an analogue of netropsin containing copper-chelating tripeptide/ (1993) *Mol. Biol. (Mosk.)* **27**, 117-128.
10. Sidorova N., Rau D.C. /The osmotic sensitivity of netropsin analogue binding to DNA/ (1995) *Biopolymers* **35**, 377-384.
11. Sidorova N., Gazoni P., Rau D.C. /Competition between Netropsin and Restriction Nuclease EcoRI for DNA Binding/ (1995) *Journal of Biomol. Structure & Dynamics* **13**, 367-385.
12. Nikolaev V.A., Grokhovsky S.L., Surovaya A.N., Leinsoo T.A., Sidorova N.Yu., Zasedatelev A.S., Zhuze A.L., Strahan G.A., Shafer R.H. and Gursky G.V. /Design of Sequence-Specific DNA Binding Ligands that Use a Two-Stranded peptide Motif for DNA Sequence Recognition/ (1996) *Journal of Biomol. Structure & Dynamics* **14**, 31-47.
13. Sidorova N.Yu. and Rau D.C. /Differences in Water Release for the Binding of EcoRI to Specific and Nonspecific DNA sequences/ (1996) *Proc. Natl. Acad. Sci USA* **93**, 12272-12277.
14. Sidorova N.Y. and Rau D.C. /Removing Water From an EcoRI-Noncognate DNA Complex With Osmotic Stress/ (1999) *Journal of Biomol. Structure & Dynamics* **17**, 19-31.
15. Sidorova N.Y. and Rau D.C. /The Dissociation Rate of the EcoRI-DNA Specific Complex Strongly Linked to Water Activity/ (2000) *Biopolymers Rapid Communications* **53**, 363-368.
16. Sidorova N.Y. and Rau D.C. / Linkage of EcoRI Dissociation from its Specific DNA Recognition Site to Water Activity, Salt Concentration, and pH: Separating their Roles in Specific and Non-specific Binding/ (2001) *JMB* **310**, 801-816.
17. Sidorova N.Y. and Rau D.C. /Role of Water in the EcoRI-DNA Binding/ (2004) *In the book on Restriction Nucleases*, Springer Verlag, editor Alfred M. Pingoud, *Nucleic Acids and Molecular Biology* **14**, 319-335.
18. Sidorova N.Y. and Rau D.C. /Differences between EcoRI nonspecific and 'star' sequence complexes revealed by the osmotic stress technique/ (2004) *Biophys. J* **87** (in press).