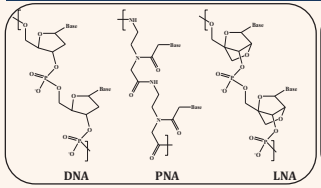
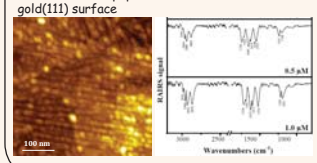
Functional Biointerfaces at Nanoscale: Biosensors, Bioelectronics and Single Molecule Biophysics at the *Mukhopadhyay Group*

Nanoscale Nucleic Acid Sensors



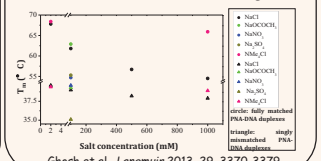
DNA and LNA are negatively charged whereas PNA is non-ionic.
- PNA and LNA exhibit nuclease resistance.
- Aq. solubility of PNA is less compared to DNA and LNA , which are almost fully aqueous soluble.
- Both PNA and LNA can form homoduplexes and heteroduplexes with natural and synthetic nucleic acid analogue with higher thermal stability compared to DNA.
- LNA is conformationally more rigid among the three.
- LNA forms the most stable homoduplexes yet discovered and the best probe so far for SNP detection in solution.

1. An atomic force microscopy investigation on self-assembled peptide nucleic acid structures on gold(111) surface



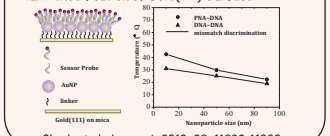
Ghosh et al., *J. Colloid Interface Sci.* 2011, 360, 52-60.

2. Facilitating Mismatch Discrimination by Surface-Affixed PNA Probes via Ionic Regulation



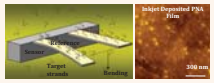
Ghosh et al., *Langmuir* 2013, 29, 3370-3379.

3. Enhancing On-Surface Mismatch Discrimination Capability of PNA Probes by AuNP Modification of Gold(111) Surface



Ghosh et al., *Langmuir* 2013, 29, 11982-11990.

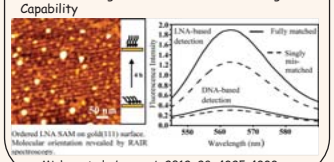
4. Enhancing sensitivity in a piezoresistive cantileverbased label-free DNA detection assay using ssPNA sensor probes



Sensitivity (ssPNA sensor probe): Sensitivity (ssDNA sensor probe) = 20:1

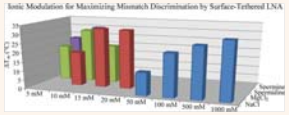
Ghosh et al., *J. Mater. Chem. B*, 2014, 2, 960-970.

5. Ordered Self-Assembled Locked Nucleic Acid (LNA) Structures on Gold(111) Surface with Enhanced Single Base Mismatch Recognition Capability



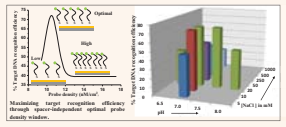
Mishra et al., *Langmuir* 2012, 28, 4325-4333.

6. Maximizing Mismatch Discrimination by Surface-Tethered Locked Nucleic Acid Probes via Ionic Tuning



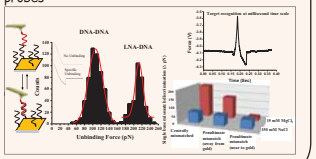
Mishra et al., *Anal. Chem.* 2013, 85, 1615-1623.

7. Regulating the On-Surface LNA Probe Density for the Highest Target Recognition Efficiency



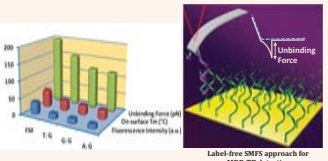
Mishra et al., *Langmuir* 2014 30, 10389-10397.

8. Molecularly resolved label-free sensing of single nucleobase mismatches by interfacial LNA probes



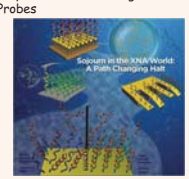
Mishra et al., *Nucleic Acids Res.* 2016, 44, 3739-3749.

9. Discriminating unalike single nucleobase mismatches using a molecularly resolved, label-free, interfacial LNA-based assay



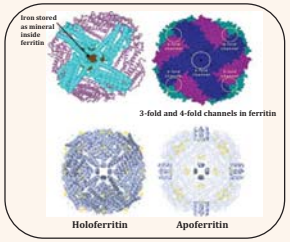
Lahiri et al., *Analyst* 2016, 141, 4035-4043

10. Nanoscale Nucleic Acid Recognition at the Solid-Liquid Interface Using Xeno Nucleic Acid Probes



Lahiri et al., *Langmuir* 2019, 35, 8875–8888 (Invited Feature Article)

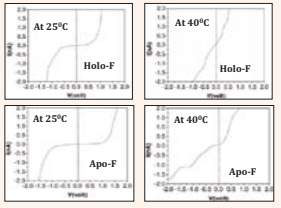
Nanoscale Protein-based Bioelectronics



Applicability of Ferritins for Bioelectronics
- Ferritin is an iron storage redox protein that is found in both prokaryotes and eukaryotes. It is also a globular protein which is soluble & non-toxic in nature.
- It has a unique ordered arrangement of 24 subunits that leads to the formation of a hollow sphere with an external diameter of approximately 12 nm and an internal diameter of 7 to 8 nm. As it is centrosymmetric in nature so the metals present inside the protein are easily accesible.
- It is structurally robust and functions well up to 80°C temperature in aqueous environment within a pH range of 4.0-9.0.
- Ferritin, which contain iron inside the hollow sphere as ferrihydrite phosphate called holoferritin and which is devoid of iron called Apoferritin.

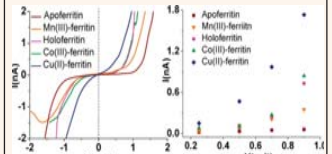
Correlating electrical transport characteristics of ferritin with its structural and mechanical properties

1. Near-Metallic Behavior of Warm Holoferritin Molecules on a Gold(111) Surface



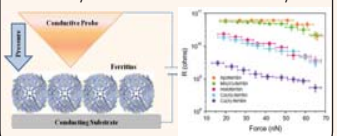
Rakshit et al., *Langmuir* 2010, 26(20), 16005–16012.

2. Tuning Band Gap of Holoferritin by Metal Core Reconstitution with Cu, Co, and Mn



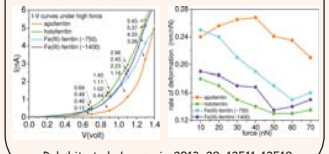
Rakshit et al., *Langmuir* 2011, 27, 9681-9686.

3. Solid-state Electron Transport in Mn-, Co-, holo-, and Cu-ferritins: Force-induced Modulation is Inversely Linked to the Protein Conductivity



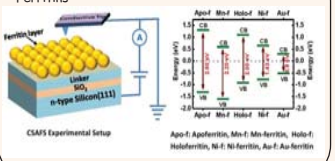
Rakshit et al., *J. Colloid Interface Sci.* 2012, 388, 282-292

4. Nanoscale Mechano-Electronic Behaviour of a Metalloprotein as a Variable of Metal Content



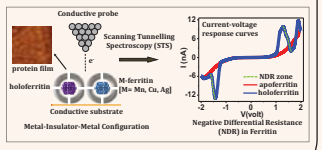
Rakshit et al., *Langmuir* 2013, 29, 12511–12519.

5. Nanoscale On-Silico Electron Transport via Ferritins



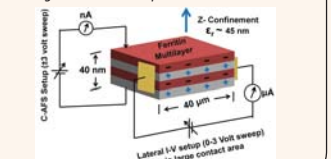
Bera et al., *Langmuir* 2017, 33, 1951-1958.

6. Negative Differential Resistance Behavior of the Iron Storage Protein Ferritin



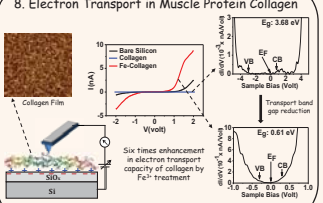
Kolay et al., *Langmuir* 2018, 34, 3126-3135.

7. Long-range solid-state electron transport through ferritin multilayers



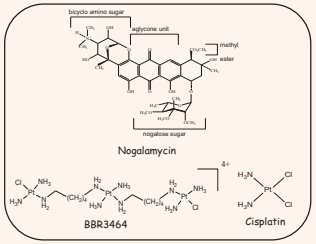
Bera et al., *J. Mater. Chem. C* 2019, 7, 9038-9048.

8. Electron Transport in Muscle Protein Collagen



Kolay et al., *Langmuir* 2019, 35, 11950-11957.

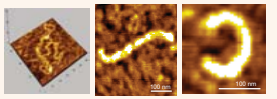
Single Molecule Level Structural Biology



- The antibiotic antitumour nogalamycin is a naturally-occurring DNA threading intercalator. Its structure consists of a central anthracycline unit (aglycon part) and two bulky groups - a nogalose sugar and a bicyclo amino sugar, at the two ends.
- BBR3464 $[\{trans\text{-}PtCl(NH_3)_2\}_2\text{-}\mu\text{-}trans\text{-}Pt(NH_3)_2\{NH_2(CH_2)_6NH_2\}_2]^{4+}$, is a new generation platinum chemotherapeutic agent, which exhibits cytotoxicity at 10 to 1000 times lower dose limit compared to the well-known platinum drug cisplatin. DNA is thought to be the primary cellular target of BBR3464 and cisplatin.
- High-resolution AFM is applied to obtain molecularly resolved information on drug-induced DNA structural changes.

Molecularly resolved features of drug-treated dsDNA reveal details relevant to the mode of drug action

1. The AFM topographs of DNA–nogalamycin complex, incubated for 12 and 48 h, revealing a gradual change from the circular supercoiled form to the compact plectonemic superhelix, confirming intercalative binding.

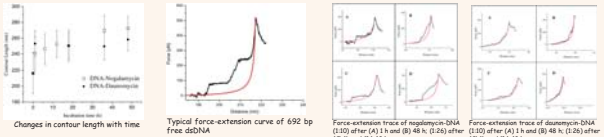


Banerjee et al., *Biochemical and Biophysical Research Communications* 2008, 374, 264–268.

2. Macroloop with knot formation and/or microloop formation along the DNA contour, and overall compaction are indicative of drug treatment.

Banerjee et al., *Biochimie* 2010, 92, 846-851.
Banerjee et al., *Biochimie* 2012, 94, 494-502.

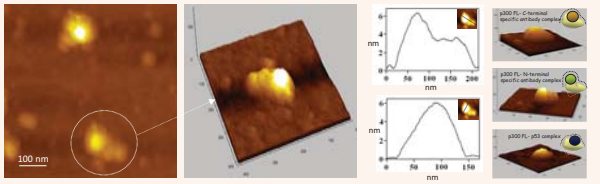
3. Discriminating intercalative effect of threading and classical intercalator by force spectroscopy



Banerjee et al., *PLOS ONE* 2016, 11(5), e0154666

Structural aspects of proteins and protein-protein assemblies at single molecule level using scanning probe microscopy approach

1. Structural features of human histone acetyltransferase p300 and its complex with p53



Banerjee et al., *FEBS Letters* 2012, 586, 3793-3798

2. Direct observation of binding of human histone acetyltransferase p300 to histone/HMGB1 protein and probing the force of interaction by single molecule atomic force spectroscopy

Molecular partners	Unbinding force (pN) at loading rate 3 nN/s	
	Non-acetylating condition	Acetylating condition
p300 FL/ histone octamer	95±2	66±2
p300 FL/histone H3	117±2	97±2
p300 FL/HMGB1	122±3	102±3

Banerjee et al., *J Phys Chem B* 2015, 119, 13278-13287