Biological robotics and nanorobot red cells: Characterization and applications

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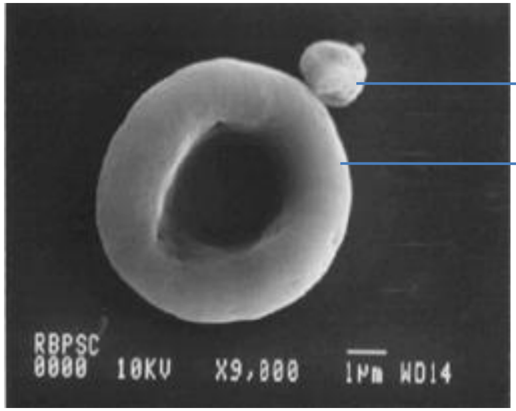
Red Blood Cells (RBC) as Robots

- 2 micron-scale red blood cell robot (1 micron = 10^{-6} meter) has hemoglobin and iron measuring nanoscale parts (1 nm = 10^{-9} meter)
- RBC robot can go everywhere across thinnest capillaries in blood stream
- Silicon, nitrogen, diamond or fullerene nanoparticles and nanocomposits can attach on RBC
- Magnetic field application controls the path of RBC and visualizes RBC-nanoparticle action

RBC as Payload of Nanomaterials

- RBC carry the nanomaterials sitting on surface of cell exterior in a controlled path pre-determined by applying magnetic field



Nanoparticle travelling over the Nanorobot RBC

Next Step: How Nanorobot path will be controlled by Magnetic Field application? Answer:

1. Measure Oxygen Biosensing (hematocrit) or
2. Measure magnetic moments or
3. NMR relaxation constants

Nanomedical Treatment

- RBC (carrier) along with antiviral peptide bound silicon (nanoparticle) sitting on its surface reaches at the infection site to combat the virus => Not established yet
- RBC (carrier) along with antimyoglobin bound iron (nanoparticles) sitting on surface tracks the muscle injury and recovery [Sharma(2009) US Patent 00220434]
- RBC (carrier) along with antitroponin bound iron (nanoparticles) sitting on surface tracks the leakage of troponin in infarction and recovery. [Sharma (2009) US Patent 0022434]
- RBC (carrier) along with antimyosin bound iron (nanoparticles) sitting on surface may track the muscle fibers??

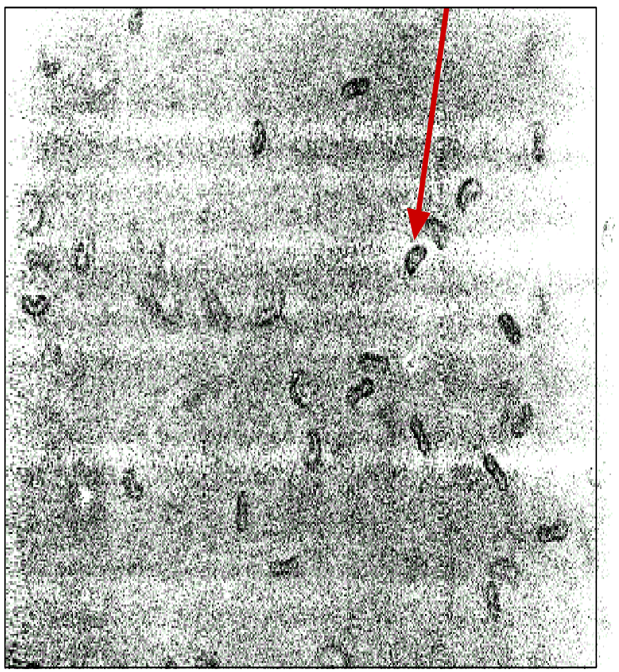
Where RBC NMR Property Takes Us?

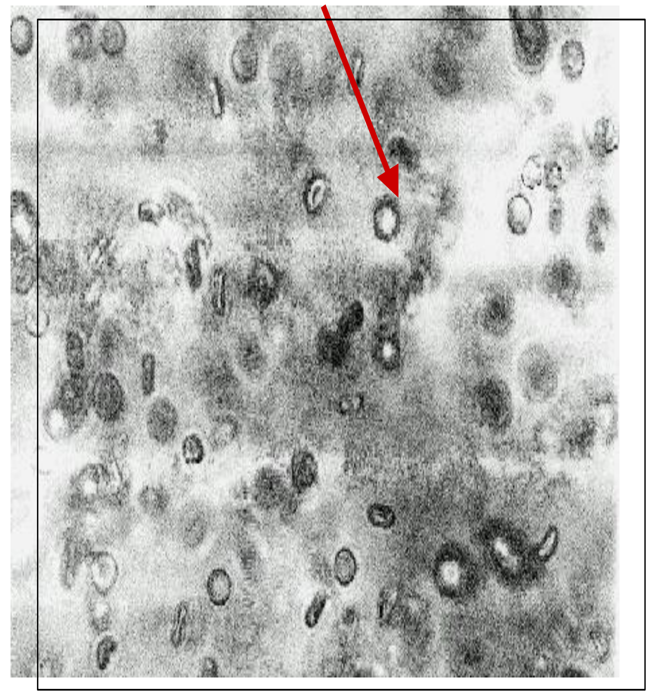
- RBC protons are NMR visible (specific 1/T1 constant values) => Blood **MR Angiography**
- RBC (Hemoglobin-iron) is Oxygen sensor (good for Physiological MRI or perfusion MRI or Diffusion MRI)
- RBC (Hemoglobin-iron) is magnetic field sensitive (keeps maximum RBC surface along the NMR magnetic field B1) or DISC rotates in parallel to B1 field
- Future of physiological MR angiography

Orientation of Red blood Cells with Applied Magnetic Field

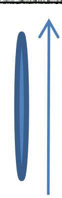
Under 8 tesla field Normal to the View

No magnetic field

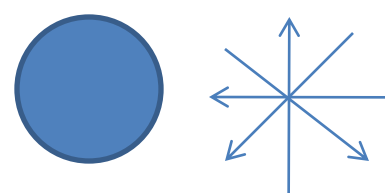




Phase Transition of Hemoglobin α $1/T_1$



B1 magnetic Field favors more surface area



Magnetic Field Changes The RBC Disc Rotation Along The B1 Magnetic Field Applied

Motivation:
What Property of RBC and Nanoparticles Are Significant?

- NMR sensitive RBC and Nanoparticle Relaxation constant rates (1/T1) measurement
- Dependence of 1/T1 on phase transition at different temperatures
- Enhancing the measurement sensitivity of relaxation rates (1/T1) by doping with $MnCl_2$

Experimental Set Up

- RBC
- Nanoparticles (maghemite Fe_2O_3)
- $MnCl_2$ (2.5% w/v)
- 90 MHz NMR Minispec® and 400 MHz NMR Oxford Spectrometer
- Temperature range: (150 K-500 K)
- 500 MHz NMR Microscopy of animal

NMR Relaxation times of RBC (Oxygen Biosensing)

- The diffusional water permeability (P_d) of the red blood cell (RBC) membrane in presence of Mn^+($MnCl_2$) at 400 MHz proportional with oxygen concentration in the blood (Oxygen Biosensor or hematocrit). (Hematocrit 45%).
- RBC rotational Reynolds number (due to specific nanomaterial load and oxygen uptake) and mass transfer => result with RBC disc rotation and increased $1/T_1$ or hematocrit

Phase dependence on RBC Relaxation Times

- $1/T1_{RBC} = 6A^2 M/h\nu_o\, J[\pi/16z]^{1/2}$

Where 'A' is hemoglobin(iron) energy ($A=2.21 \times 10^{-21}$ erg (0.665 MHz),

J is exchange coupling constant,

z is number of neighbors and

$h\nu_o/J \ll 1$ is extreme narrowing phase limit.

Moriya T.(1956) Prog. Theor.Phy.16,23.

Higher 1/T1 indicates bound metallic state of Hb molecule phase at low temperature

How Nanofullerenes change the Relaxation constants

$$\frac{1}{T_1} \approx \frac{2\pi\sqrt{6}}{9\hbar} A_{\rm dip}^2 N(E_F)^2 k_B T \ .$$

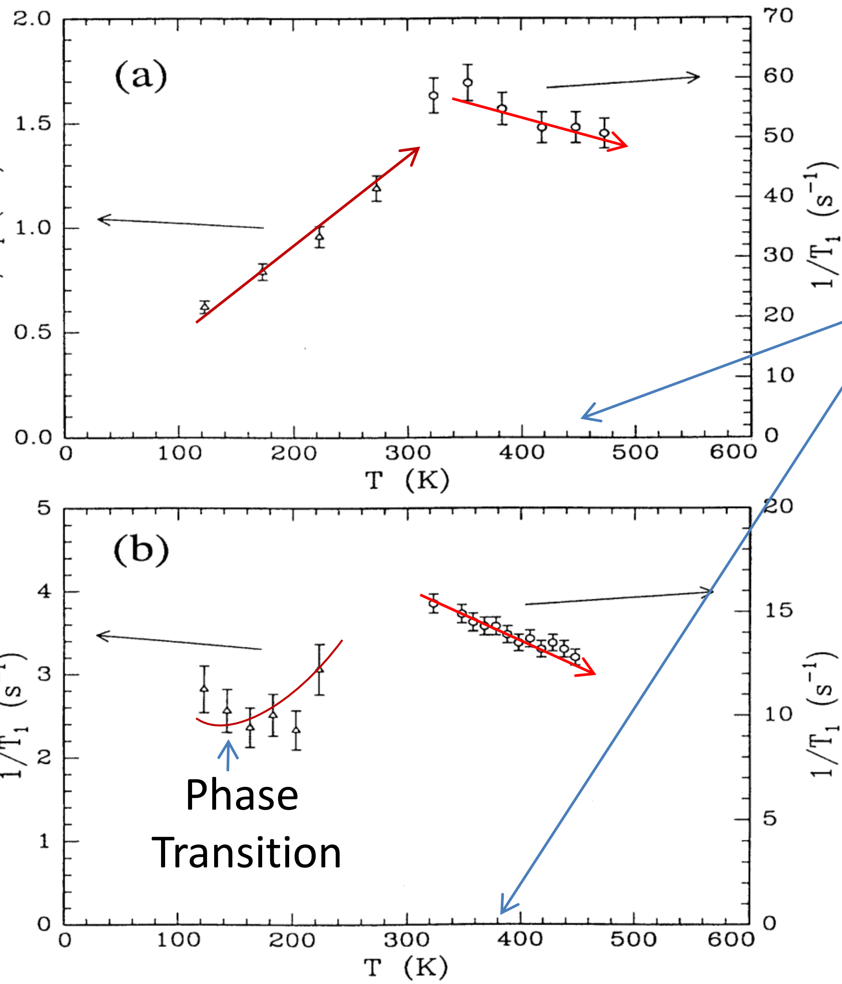
The dipolar couplings and orbitals from $2p_z$ functions show 1/ T1 dependence on temperature because of $A_{\rm dip}^2 N(E_F)^2$;

where Fermi energy A_{dip} = 1 x 10^{-20} erg and $N(E_F)^2$=34 eV^{-1} per fullerene molecule. T is temperature in K.

Higher 1/T1 indicates bound metallic state of molecule phase at low temperature

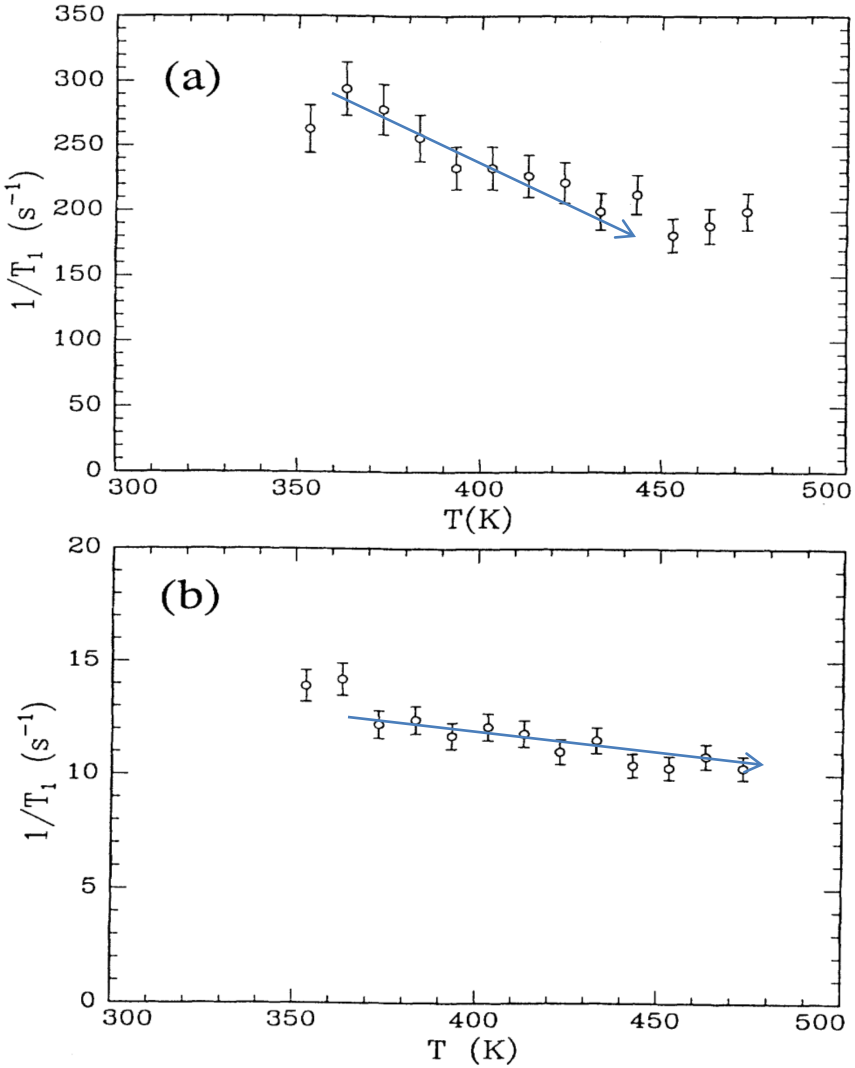
Change in T1 Relaxation constants of RBC in Presence of Nanoparticles

Nature Precedings : doi:10.1038/npre.2010.4262.1 : Posted 4 Mar 2010



- Structural Phase transition occurs due to <u>high temperature</u> paramagnetic unpaired protons in nanoparticle attached.
- (a) No nanoparticle attached on RBC
- (b) Nanoparticle attached

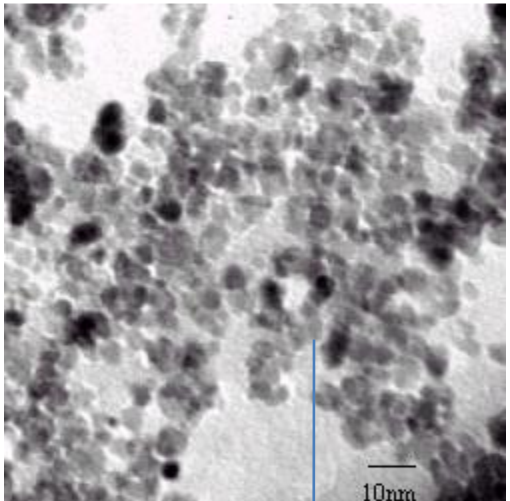
Effect of $MnCl_2$ on Relaxation constants of RBC: A Method to Increase Sensitivity of RBC to NMR

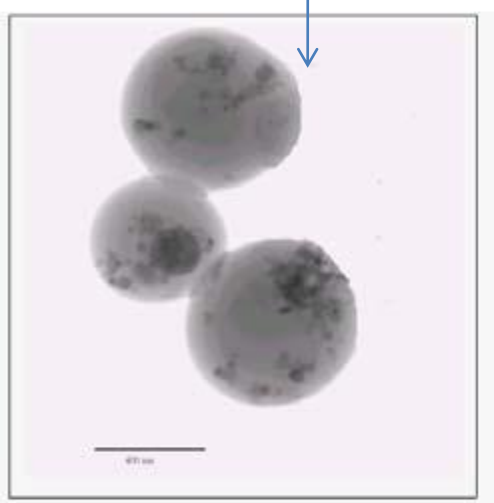


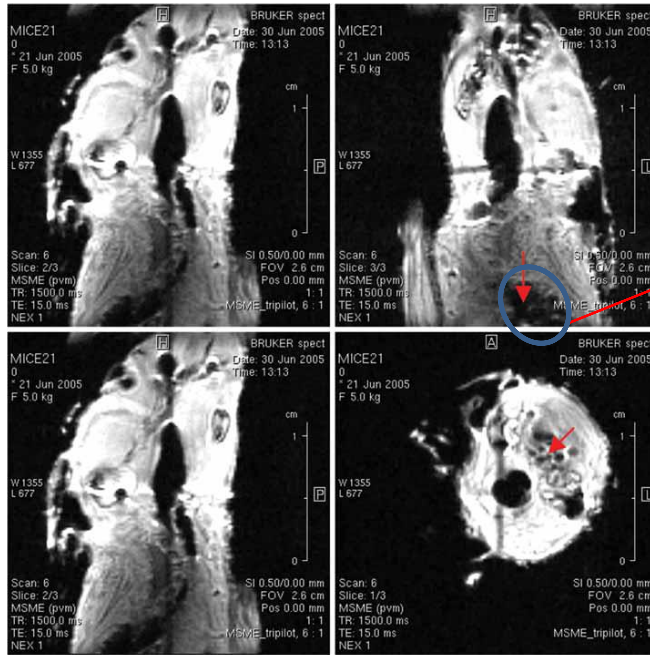
- $MnCl_2$ is a doping subtance and enhances the sensitivity of relxation constant measurements

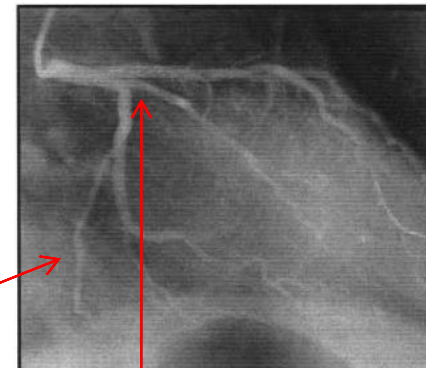
- At high temperatures, Mangenese doping increases the T1 constant values or less 1/T1 constant value changes

RBC in magnetic Field and MR Angiography



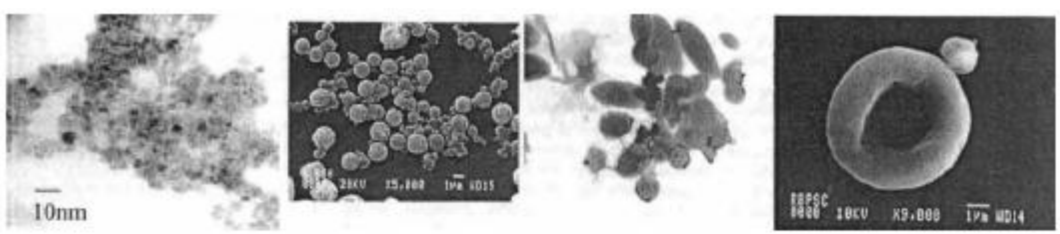






MR Angiography is a method to Visualize the presence of RBC (Blood Imaging)

Sharma R, Kwon S(2007) JAN:2(2) 139-146
http://www.informaworld.com/smpp/content~content=a773313197~db=all~order=page



What Are Potentials of RBC Nanorobots?

- RBC as carrier and Nanomaterials bound with(physiological or biochemical or immunological, biosensor, drug compounds) serve as Magnetic field controlled Robot
- They can be used in:
  1. Monitoring disease or therapy;
  2. Targeted delivery of RBC with specific properties;
  3. Sensing physiology signals or structural-function property of enzymes, hormones, active neurotransmitters

Other possibilities of RBC Nanorobots

- Use as respirocytes by ^{13}C NMR spectroscopy
- Use of 13C-fullerene based MR Angiography
- RBC can hold nanocomputers in future to function and travel in blood.
- Use of RBC as nanosystems embedded inside as "functional physiology lab". Risk: attack by viruses and bacteria on RBC
- RBC can work as biochemical genomic SSN
- Future nanorobot programming

Conclusion

- Red blood cells contain hemoglobin with iron as paramagnetic and sensitive to magnetic field.
- Under the effect of magnetic field their path can be controlled and tracked by their magnetic moments and NMR relaxation constants.
- Red blood cells have capability of carrying payload of nanoparticles.
- NMR relaxation constants predict physiological function of red blood cells in the target organ.