Physics of Relaxation

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Outline

- Fundamental relaxation Mechanisms
  - Magnetic dipole-dipole coupling
    - » Static coupling
    - » Dynamic coupling
  - Frequency dependence of relaxation Rate
  - Temperature dependence of relaxation rate
  - BPP theory of relaxation
    - » Nonviscous liquids
    - » Solids
    - » Viscous liquids
- Compartmentalization
  - Macromolecular hydration effects
    - » Three fraction model
  - Cross-relaxation
  - Molecular weight dependence of relaxation
- Determinants of tissue T1 and T2
- Mechanism of proton relaxation enhancement

Review

- T1 and T2 relation times
  - How T1 and T2 happens?
- T2*
- Relaxation rate (RR)
  - 1/T1 or 1/T2

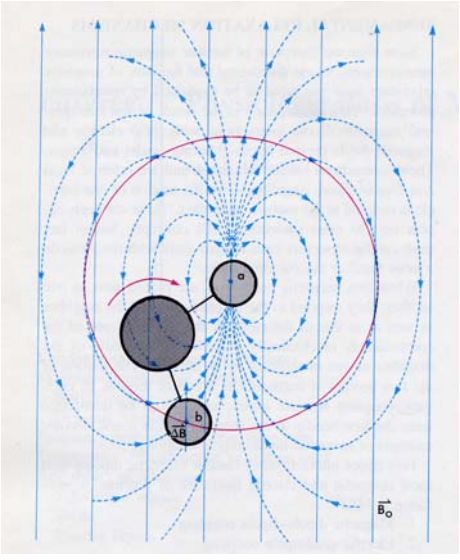
Why relaxation again?

- Molecular basis of relaxation is better understood
  - Predict the contrast change for pathologic condition.
  - Prospective select pulse sequence to optimize imaging
- Tissue are complex molecular systems with complex MR properties.
  - Relations of T1,T2 to properties of tissue are imperfectly understood.

Fundamental relaxation mechanisms

- Dipole coupling
  - Nuclear magnetic dipole interact with local electric and magnetic fields created by the neighboring nuclei and atoms ->induce relaxation
- Five major interactions
  - Magnetic dipole-dipole coupling
  - Electric quadrupole coupling
  - Chemical shift anisotropy
  - Scalar coupling
  - Spin-rotation interaction

Magnetic dipole-dipole coupling



- Proton b increase ΔB
- H_2O rotates
  - Magnitude and direction change
  - Local perturbation can be -10~10 gauss

Static coupling

- If H_2O molecule is fixed (ice)
  - ΔB is fixed
  - Fixed (static) magnetic field inhomogeneity cause proton on different molecules to precess at different frequencies.(what is the Δω?)
- Differences in resonant frequency result in
  - Dephasing in x-y plane
  - Shortening T2
  - Not affect T1
- Dephasing time
  - A proton process 2 πin 20 gauss
  - 1.2 $*10^{-5}$ sec

Correlation time

- Correlation time τ_c is the minimum time required for a molecule to rotate one radian($1/_{2\pi}$)
- If $\tau_c > 10^{-5}$ sec, fixed long enough for static dephasing of M_{xy}
- Any molecule large enough to have $\tau_c \sim 10^{-5}$ sec (rotating so slow), its magnetic field is essentially fixed with respect to MR measurement.

motional narrowing

- If the water molecules are moving rapidly in an isotropic fashion (as in bulk water τ_c ~10^{-12} sec), positive and negative contributions to the static phase shift of a given proton is averaged to zero; this is referred to as motional averaging or motional narrowing.
- Uniform rates of precession, slow dephasing, long T2

Dynamic coupling

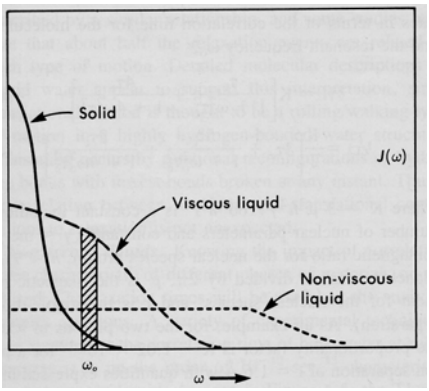
- Rapid molecular tumbling motion is the source.
- In bulk water, molecule rotate from 0 (fixed) to max freq ($1/\tau_c$)
- Rotation exposes each proton to a changing magnetic field similar to MR excitation process.
  - at resonant frequency, changing spin state (low to high, absorb energy)
- Source of changing magnetic field:
  - B1 during excitation
  - During relaxation, relative motion of proton magnetic moments attached to rotating molecule (source of dynamic component of dipole-dipole coupling)
- Spin exchange:
  - interaction of two protons
  - One lose and one gain energy

Dynamic coupling

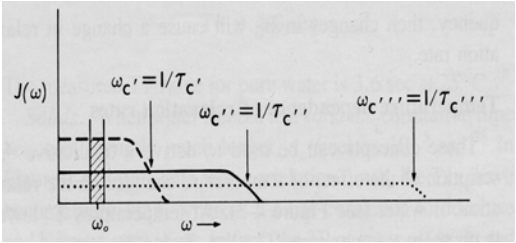
- Spin exchange -> random orientation of the dipole moments ->random dephasing in x-y plane-> T2 decay (true sample-related)
- During spin exchange, if excess energy are transferred to molecule motion (both spins end up in lower energy state), -> regrowth of longitudinal magnetization-> T1 relaxation.
- So T1,T2 decay are the result of dipole-dipole coupling.
- Why energy can be transferred to H2O?
  - Molecule tumbling at the resonant frequency
  - The more, the higher relaxation rate, the shorter T1.
- What determine the molecule tumbling rate?
  - Molecular weight, temperature, shape of the molecule

Frequency dependence of relaxation rates

- Molecules rotate from 0(fixed)~ max freq ($1/\tau_c$)
- Relaxation rate (RR) depends on the fraction of protons at the selected ω_0, relative all other available frequencies.
- If the population J(ω) is a function of frequency, then change of B0 will change RR.



Temperature dependence of relaxation rates



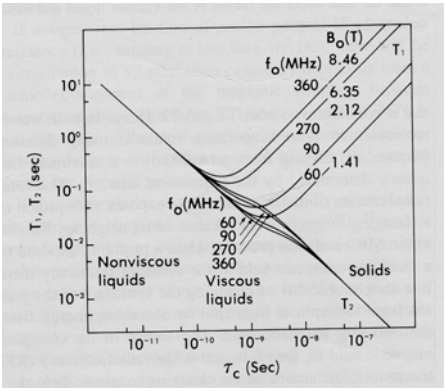
- T’ <25ºC, T’’ = 25ºC, T’’’ > 25ºC
- Area under the curves is same and proportional to the total number of protons
- Shaded area is proportional to the number in resonance
- What is the relation of T1 with temperature? How about T2s?
  - T1’<T1’’<T1’’’
  - T2’ < T2’’<T2’’’(why?)
- +temperature -> -τ_c -> - relaxation rate -> + T1,T2

BPP theory and relaxation

$$\frac{1}{T1} = K\left[\frac{\tau_c}{1+\omega_0^2\tau_c^2} + \frac{4\tau_c}{1+4\omega_0^4\tau_c^4}\right]$$

$$\frac{1}{T2} = \frac{K}{2}\left[3\tau_c + \frac{5\tau_c}{1+\omega_0^2\tau_c^2} + \frac{2\tau_c}{1+4\omega_0^4\tau_c^4}\right]$$

$$K = 3\mu^2\hbar^2\gamma^4/160\pi^2r^6$$



BPP theory and relaxation

- MRI freq range 1~100MHz, $\omega_0 = 2\pi f_0 = 6.4*10^6 \sim 10^8$ /sec
- Nonviscous liquids
  - For bulk water, $\tau_c \sim 10^{-12}$ sec
  - $\omega_0\tau_c << 1$
  - T1=T2

$$\frac{1}{T1} = K\left[\frac{\tau_c}{1} + \frac{4\tau_c}{1}\right] = 5K\tau_c \qquad \frac{1}{T2} = \frac{K}{2}\left[3\tau_c + \frac{5\tau_c}{1} + \frac{2\tau_c}{1}\right] = 5K\tau_c$$

- Solids
  - $\tau_c \sim 10^{-5}$ sec;
  - $\omega_0\tau_c >> 1$
  - T1 very large
  - T2 small, $3\tau_c$, static magnetic field inhomogeneity
- In ice, no motional narrowing -> dephasing like the magnetic inhomogeneity in spin echo sequence, But diffusion so fast, that 180º pulse cannot rephase it.
- Viscous liquids (as lipids)
  - $\tau_c \sim 10^{-9}$ sec, $\omega_0\tau_c \sim 1$
  - T1 and T2 more nearly equal than for solid.
  - T1,T2 frequency dependent

Successes and problems of BPP theory

- Successes
  - Explained the relaxation of monomolecular solvents and solids
- Problems
  - Inadequate to describe multicomponent solutions, such as human tissue

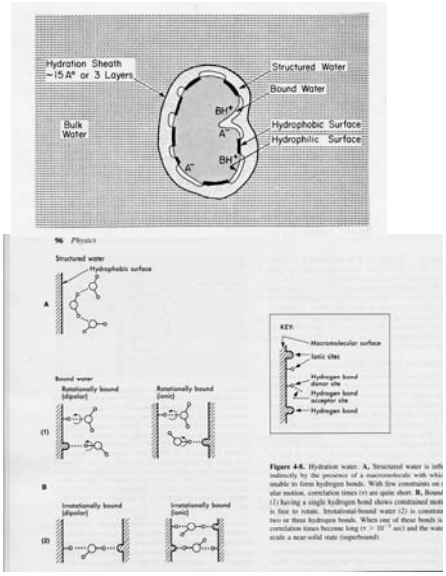
Fast exchange model

- MR relaxation of tissue can be better explained if:
  - a small fraction of cell water is highly immobilized on the surface of macromolecules with correlation time on the order of that of ice (τ_c ~ τ_c of ice)
- Water molecules in this layer undergo rapid turnover or fast exchange with bulk water molecules free in solution.

$$\frac{1}{T1} = \sum_i P_i \times \frac{1}{T1_i}$$

- Most investigators accept the fast exchange, but disagree over the extent and number of water compartments and their relaxation characteristics ->3 compartments model is sufficient for measurement on protein solution.

Three-fraction model



- MR relaxation rate of tissue is determined by the fast chemical exchange of water molecules between various sites on macromolecule surfaces
- Bulk water
- Hydration water
  - Structured water
  - Bound water
    - Rotationally bound water
    - Irrotationally bound water
- Most fat free tissues

Three-fraction model

- Fraction one
  - Bulk water and structured water
  - Mass: $M_w = f_w X$ (solvent mass)
  - R_w –relaxation rate
- Fraction two
  - Rotationally bound water
  - Mass fraction f_r
  - R_r
- Fraction three
  - Irrotationally bound water
  - Mass fraction f_i
  - R_i
- Ri >>Rr>Rw, irrotationally bond water dominate relaxation

$$f_w + f_r + f_i = 1$$

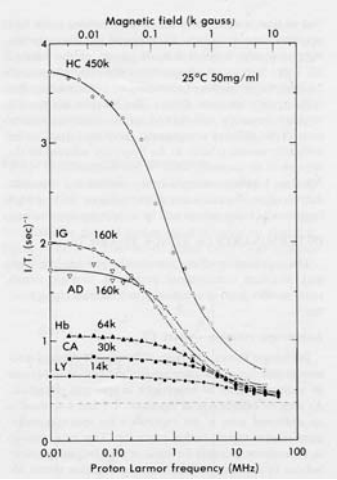
$$R1 = 1/T1 = f_w R_w + f_r R_r + f_i R_i$$

Cross-relaxation

- Protons of solids have wide ranges of resonance frequencies -> exchange excited spin energy.
- spin diffusion:
  - If a proton nucleus on one end of a chain is excited, it can pass the excitation energy to a neighbor down the chain until only proton on the other end of the chain remains excited.
  - This motion of spin energy is call spin diffusion.
  - Occurs in solids but not in mobile liquids
- Proteins move slowly -> This allows spin diffusion to side chain (possible bound water) which move rapidly and relax faster-> promote the spin-lattice relaxation of the whole molecule.

Molecular weight dependence of relaxation

- Cross-relaxation make the relaxation of water in a protein solution dependent on macromolecular solute motion
- Solvent proton spin-lattice relaxation rate depend on the molecular weight of the solute protein at 10kHz~50MHz
- Relaxation of solvent responds to macromolecular motion via cross-relaxation between protein and water.
- Tumbling rate is determined by the molecular weight and the shape of the protein.
  - Large proteins tumble slowly; small ones tumble rapidly
- At lower freq (roughly < 1MHz),macromolecular motion dominate relaxation characteristics of the solution. At high freq, water motion will be of primary importance.



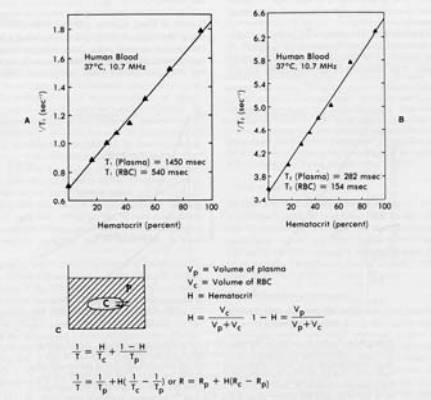
Determinants of tissue T1 and T2

- In tissue, Increasing size and mass of macromolecular structure -> anisotropic motion.
- Anisotropic rotation
  - Isotropic motion (motional average/narrowing)
  - Anisotropic motion of water -> shorten T2
  - In collagen, regular parallel molecular arrangement of collagen molecule surface -> bonded water is rotating anisotropically and display strong orientational dependance.->shorter T2

Determinants of tissue T1 and T2

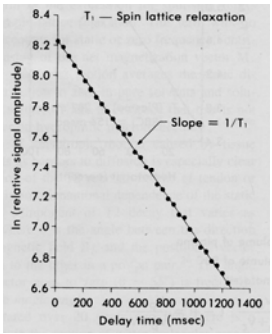
- Fast exchange --- cellular suspensions
  - Blood (a cellular suspension) is an example of the macroscopic significance of fast exchange

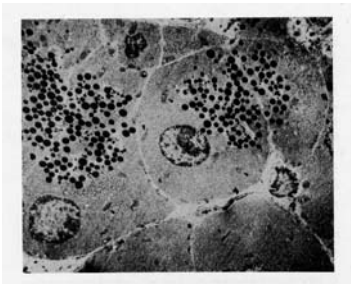
- The linear relationship confirm fast exchange between intracellular and extracellular water
- Because of the fast exchange, Relaxation is a weighted average of the two fractions of RBC and plasma.



Determinants of tissue T1 and T2

- Fast exchange---soft tissue
  - Spin-lattice relaxation rate for most tissue organs are generally single component in character, just as in blood.
  - Microstructures -> widely varying water and macromolecule in different portion of the cell





Determinants of tissue T1 and T2

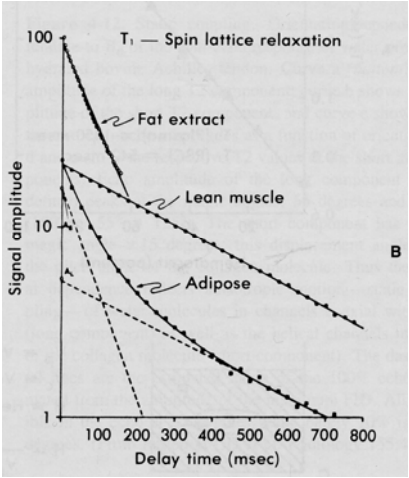
- Fast exchange---soft tissue
  - The observed relaxation rate is a weighted average of all the components within a diffusion radius, including one cell or more cells in most cases.
- The radius is determined by:
  - Water diffusion characters of tissue.
  - Frequency of MR device.

Determinants of tissue T1 and T2

- Slow exchange --- soft tissue (fat).
  - Lipids in adipose are hydrophobic molecules -> rejected by water
  - Lack of hydrogen bonding sites also limits the cross-relaxation possibilities between fat and water.
- Two components relax

Slow exchange --- soft tissue

- T1 relaxation is Biphasic in character
- The relaxation rate of the water-protein fraction of fat cell is nearly identical to that of muscle
- The relaxation rate of the short component of the adipose tissue is identical to that of fat extract



Slow exchange --- soft tissue

- Separate fat and water.
  - Distinctly different local magnetic field contribution ---Dixon Method
  - Relaxation time difference.
  - not make the lipid fraction in brain visible
    - Polar and organize in vivo into membranes.
    - Bilayer sheet

Determinants of tissue T1 and T2

- Water content
  - Primary factor in determining the relaxation time
  - Significant on contrast

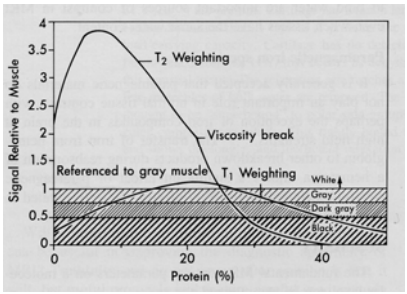


Table 4-2. Tissue water content and predicted contrast

Organ	Percent water	Calculated contrast	
		T1 weighted	T2 weighted
CSF	99+	Dark	Bright
Blood	81	Bright	Bright
Brain	79	Bright gray	Bright gray
Lens	68	Dark gray	Dark
Tongue	65	Dark gray	Dark
Bone	<45	Black	Black

*From Figure 4-17, assuming contrast similar to a protein solution.

Determinants of tissue T1 and T2

- Lipid content
  - High lipids content causes shorter net tissue T1 relaxation times
- Homework
  - Fat relax rapidly compared to water ,why?
    - Clue: Slower tumbling rate;12% w/w protons in fat compared to 11% w/w in water
  - T2 of nonpolar storage fat is longer than that of many other tissue, why?
  - How about lipids in brain?

Determinants of tissue T1 and T2

- Perturbed water motion
  - The ability of tissue to perturb the motion of water on or near their molecular surface is an important secondary source of tissue T1 and T2 difference
- Paramagnetic iron species
  - Don’t play an important role in normal tissue contrast except iron compounds in the brain at high field strength.

Summary of MR contrast parameters on molecular level

- Water content –contrast
- Perturbed water motion – varying ability of the macromolecules of different tissue to bind and structure water in their vicinity.
- Macromolecular motion
- Lipid content
- Paramagnetic species.

Mechanism of proton relaxation enhancement

- Enhancement: processes that shorten either T1 or T2 are said to “enhance” protein relaxation.
- Paramagnetic substance dissolved in water expose the water protons to fluctuating magnetic fields from unpaired electrons flipping up and down.
- When these electronic magnetic moments fluctuate at or near the Larmor frequency, both T1 and T2 are shortened.
- In biologic substances,T1 are 5~10 times longer than T2, -> T1 shortening is observed at lower concentration of paramagnetic agent than are needed to produce T2 shortening.

Next lecture

- Contrast agents
  - Definition and classification
  - Design requirements
  - MR contrast mechanisms
  - Relaxivity theory of CA
  - Gadolinium complex
  - Tissue specific contrast agents(application)
- MR Molecular imaging

- Reference:
  - Magnetic resonance Imaging (2nd edition) David D. Stark, William G. Bradley, JR.
  - Magnetic resonance Imaging (3nd edition) David D. Stark, William G. Bradley, JR
  - N. Bloembergen, E. M. Purcell, and R. V. Pound. Relaxation Effects in Nuclear Magnetic Resonance Absorption. 1948,73:679-712