# NMR Relaxation Measurements of Solid-Solid Phase Transitions in Complex Lipid Systems

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Lipids are complex macromolecular mixtures with interesting and complicated solid polymorphic crystal states. Understanding and creating techniques to explore these systems, which are crucial components in pharmaceutical drug delivery, food science and membrane biology, will improve understanding of material properties and their relation to material function. Nuclear magnetic resonance (NMR) is uniquely qualified to study these complex structures in real time without disturbing the microstructural domains. A universal method for detecting transitions between solid-solid or solid-liquid configurations is differential scanning calorimetry (DSC), in which the temperature of a system is changed, as the heat capacity is measured. However, this method can be invasive, in melting certain domains, and dependent on the rate of temperature change. Solid state $^{13}$C NMR has been implemented to probe the dynamics with temperature to obtain information about transitions between and mixing of polymorphic domains[1].

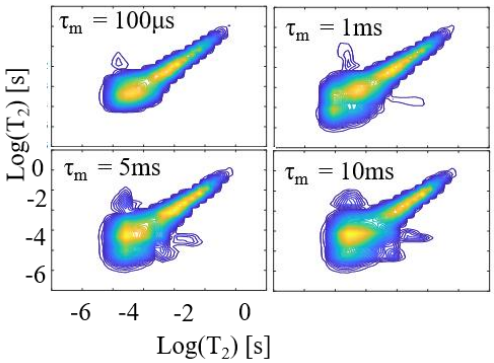


**Fig. 1**: $T_2$-$T_2$ exchange plots of beeswax at 50˚C for increasing $\tau_m$ times.

It is also well established that multidimensional relaxometry is useful to characterize exchange with mass transport between domains[2-4]. In systems with no mass transfer, solid state methods, using spin diffusion magnetization exchange during an evolution period after selection based on dipolar coupling, are well established for characterizing domain size in polymer[5] and lipid[6] systems with domains of varying $T_2$ relaxation. The influence of spin diffusion, or flip-flop secular dipolar interactions, on $T_2$-$T_2$ experiments were indicated by Hills and coworkers for aqueous protein gels[7] and Washburn for kerogen in shales[8]. Here, NMR relaxometry is used to characterize temperature dependent solid-solid phase transitions in terms of relaxation distributions and magnetization exchange for lipid systems.

The two complex lipid systems in this work, beeswax and glyceryl behenate, exhibit exchange without mass transport. Data for $T_1$-$T_2$ correlation experiments, $T_2$-$T_2$ exchange experiments and $T_2$ distribution dispersion (varying echo time τ) experiments[9] are presented. The measured exchange times between domains, shown for beeswax in Fig. 1, are of the order of 0.1-100 ms, consistent with spin diffusion of the order of $10^{-16}$ to $10^{-18}$ m$^2$/s with average domain separations 0.1-10 nm[5,10]. The complexity and variability in a natural product like beeswax makes association of specific domains with $T_2$ more complicated. The glyceryl behenate system allows reproduceable deconstruction in terms of its triglycerides. In doing so, we determine domain sizes, the partitioning of mono-, di-, and tri- components within the domains. This is done through $T_2$ distribution dispersion measurements. Decomposing the triglyceride provides an in-depth analysis of the relaxation distribution properties of glyceryl behenate, the base of many drug delivery techniques, extending the ability of NMR relaxometry to characterize lipid systems.

**References:**

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