

The Effects of Contrast Agents on Hyperpolarised [1-¹³C]-Pyruvic Acid

L Friesen Waldner^{1,2}, T Scholl^{1,2}, A Chen³,
B Rutt^{1,4}, C McKenzie^{1,2}

¹Robarts Research Institute, Ontario

²The University of Western Ontario

³GE Healthcare, Toronto, Ontario,

⁴Stanford University, California



Introduction

- Addition of gadolinium (Gd) based contrast agents to ¹³C-enriched samples increases hyperpolarisation
(Ardenkjaer-Larsen *et. al.* Appl. Magn. Reson. (2008) 34:509-522)
- Gd decreases the relaxation time of the electron on the free radical that is added to the ¹³C-enriched substrate
- Increased electron relaxation rate leads to increased efficiency of the transfer of polarisation from the electron to the ¹³C nucleus

Introduction

- Gd contrast agents also decrease T_1 of ¹³C
- In small concentrations, Gd has desired effect on electrons with minimal effect on ¹³C
- Optimal contrast agent and concentration yields:
 - Increased hyperpolarisation
 - Minimal effect on T_1 of ¹³C

Purpose

To study the effects of several contrast agents at varying concentrations on the hyperpolarisation of [1-¹³C] pyruvic acid.

Methods

Solution Preparation

- [1-¹³C]-pyruvic acid (CIL, Cambridge MA) with 15mM OX63 trityl radical (Oxford Instruments, Abingdon UK)
- 15μL aliquots doped with 1.5μL of diluted contrast agent to obtain 0, 0.5, 1, 2, or 3mM concentrations of:
 - Dotarem (Guerbet) - Omniscan (GE Healthcare)
 - ProHance (Bracco) - Magnevist (Bayer)
 - MultiHance (Bracco)

Methods

Polarisation and T_1 Measurement

- HyperSense DNP polariser (Oxford Instruments, Abingdon UK)
- T_1 decay curves in liquid state were acquired on 0.55T bench top spectrometer (Oxford Instruments):
 - small tip angle (5°) excitation pulse
 - 100 acquisitions
 - 4.9s intervals

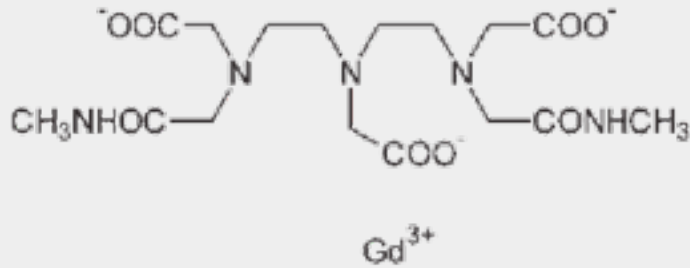
Methods

Data Analysis

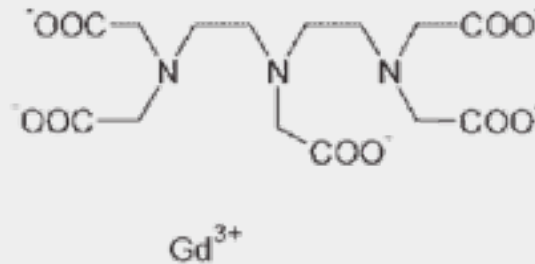
- Solid state enhancement of polarisation was determined from polarisation build-up curve
- Signal decay curves were fit to mono-exponential decay (Levenberg-Marquardt) to obtain T_1
- Liquid state enhancement of polarisation was determined from the y-intercept of decay curves
- Uncertainty in these measurements was determined from 10 polarisations of pyruvic acid/trityl radical (no contrast agent)

Contrast Agent Structures

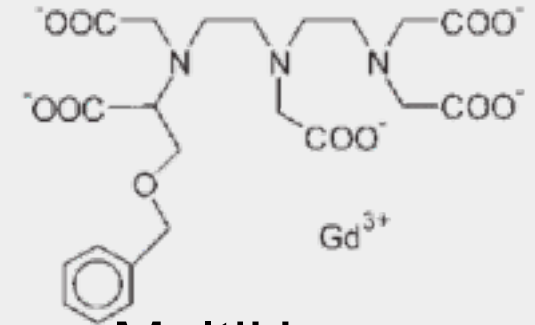
Open Chain Structures



Omniscan
Gadodiamide



Magnevist
Gadopentetate Dimeglumine

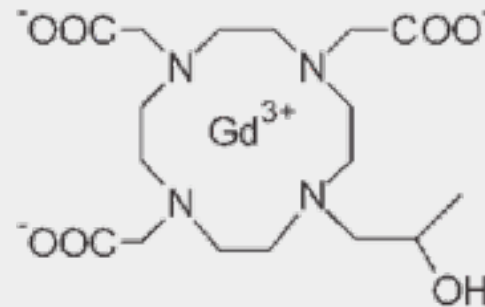


MultiHance
Gadobenate Dimeglumine

Macrocyclic Structures



Dotarem
Gadoteric Acid



ProHance
Gadoteridol

Fig 1: Solid State Polarisation Build-Up Curves for Dotarem

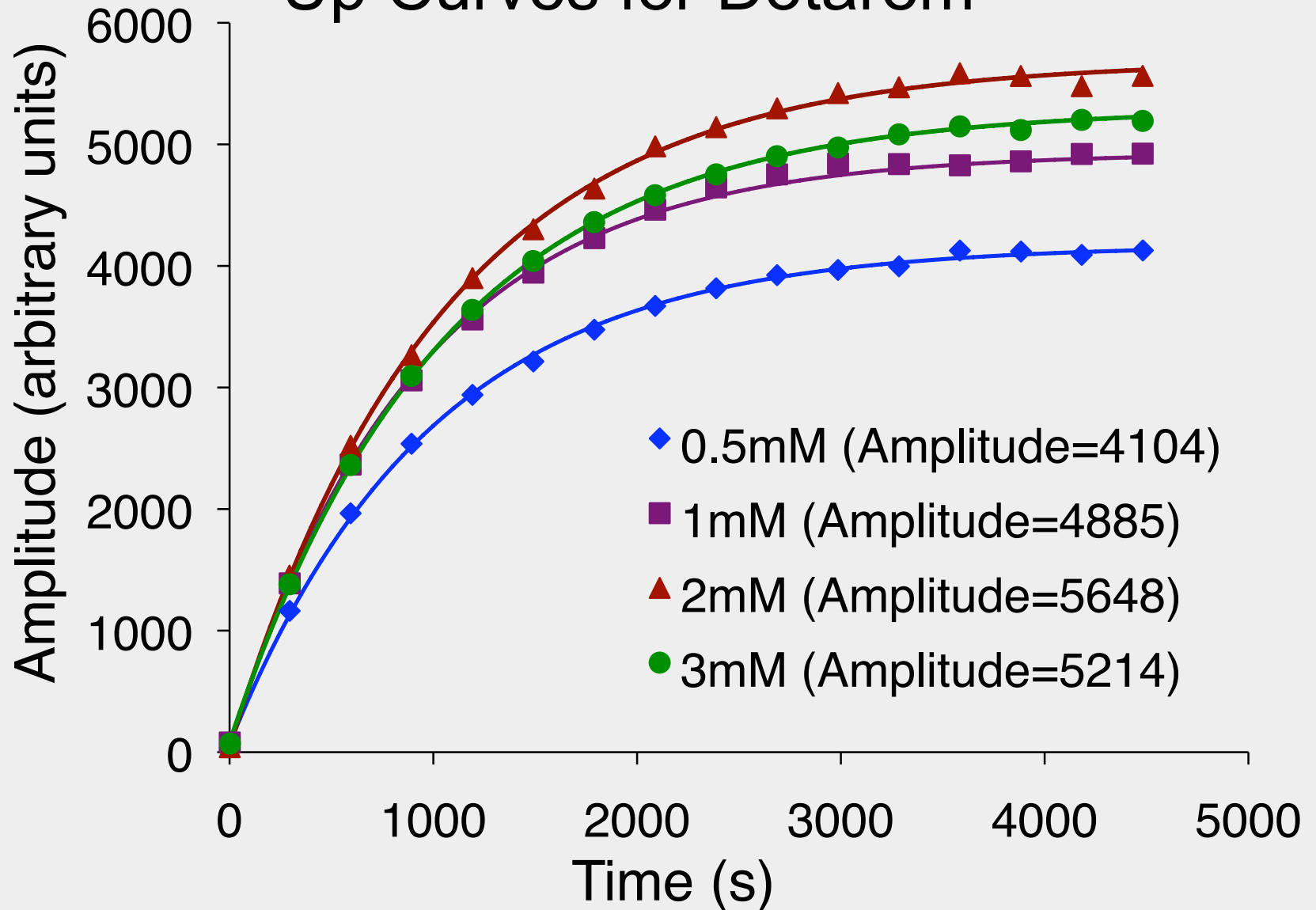


Fig 2: T_1 Decay Curves for Dotarem

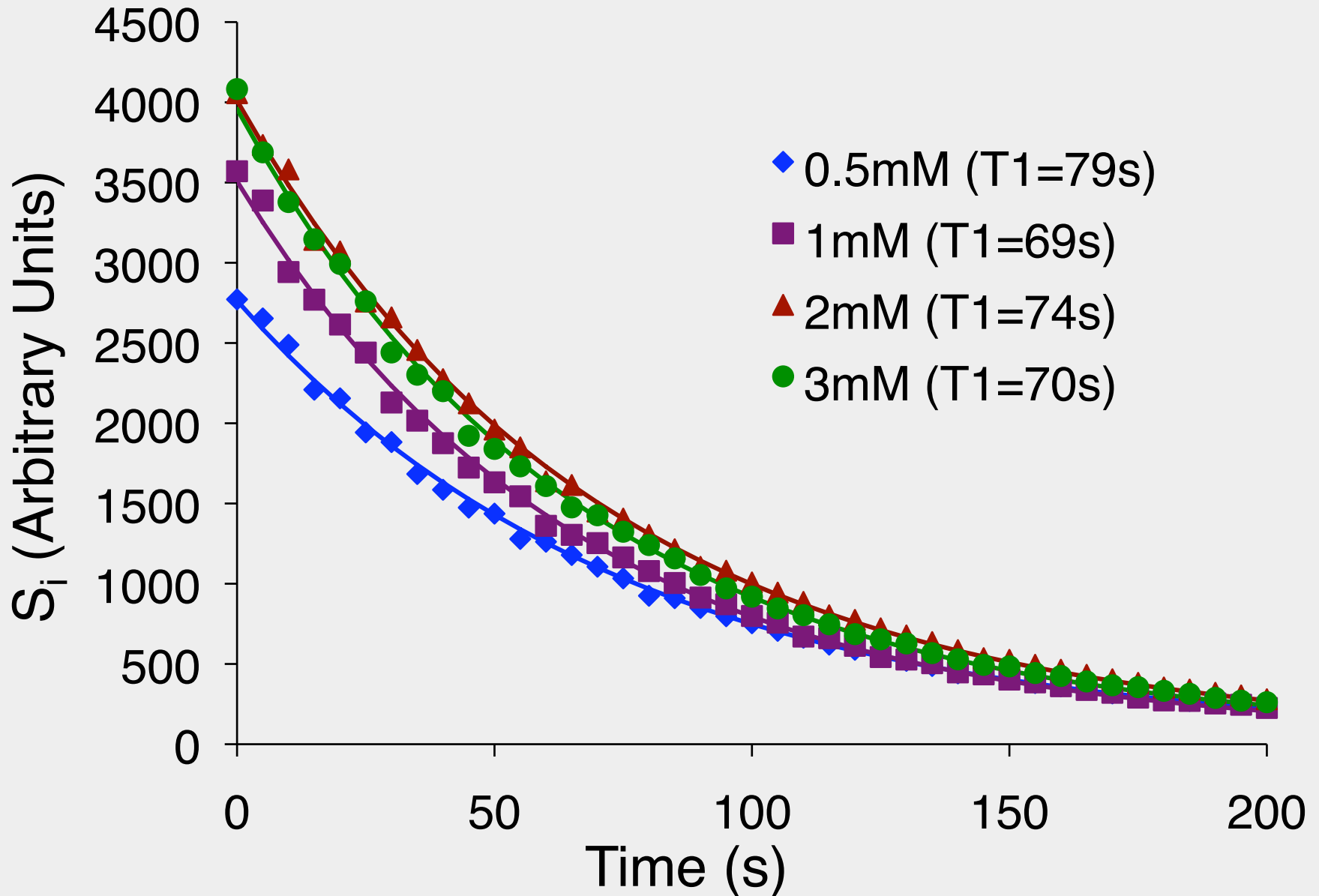


Fig 3: Polarisation Enhancement in Solid State

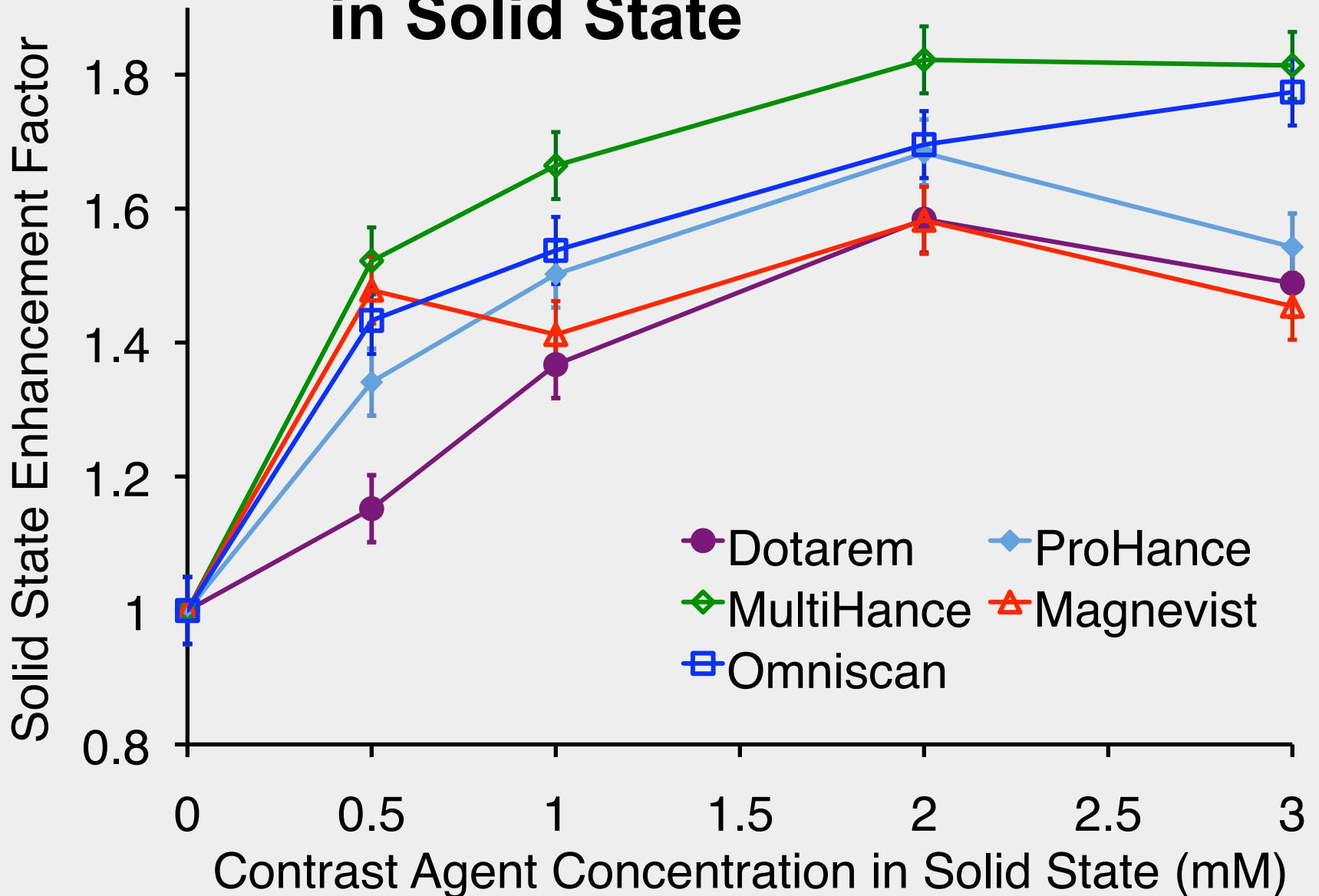


Fig 4: Change in Liquid State T_1 vs Contrast Agent Concentration

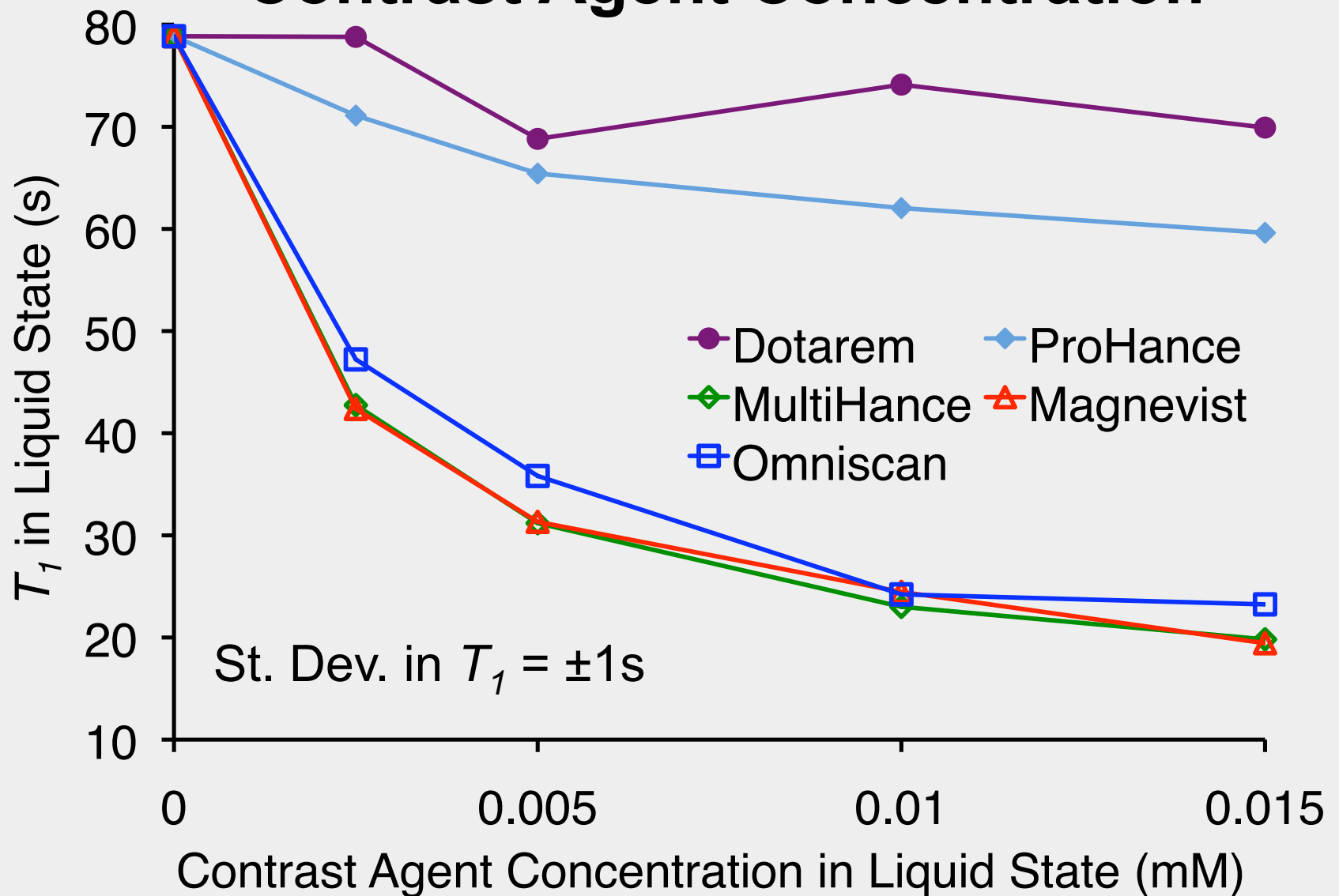
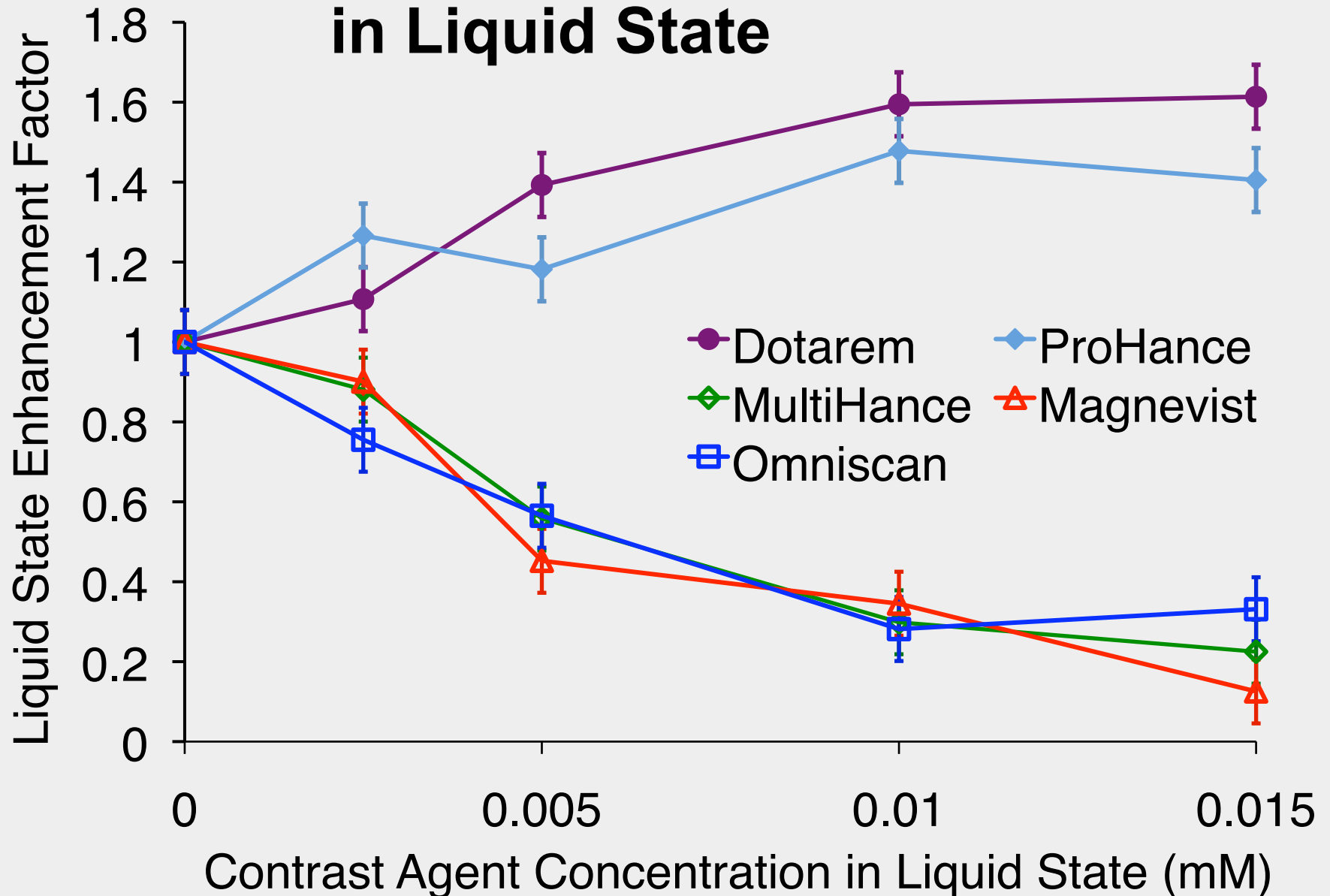


Fig 5: Polarisation Enhancement in Liquid State



Discussion

- Open chain structures - Multihance, Omniscan - gave the largest enhancement in solid state polarisation (Fig 3), but bigger decreases in T_1 in solution (Fig 4)

Fig 3

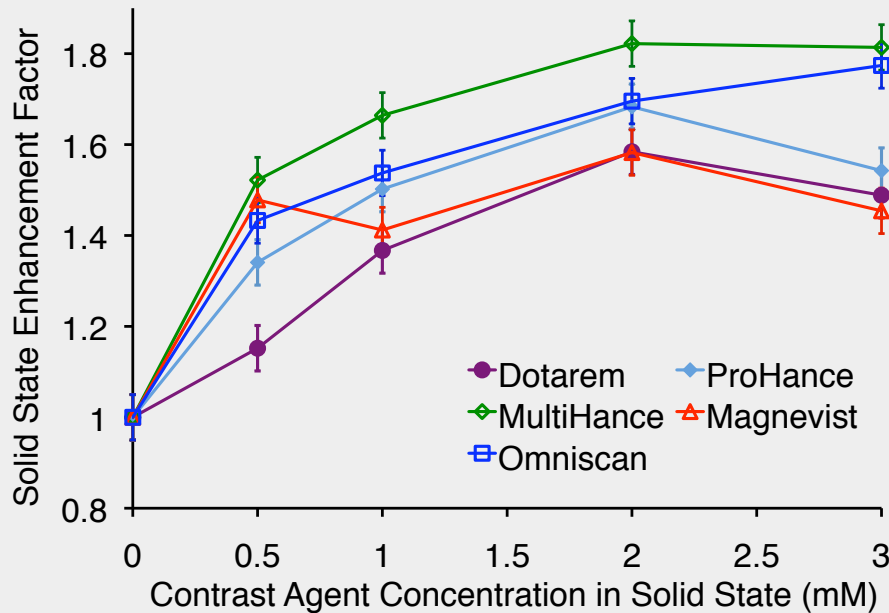
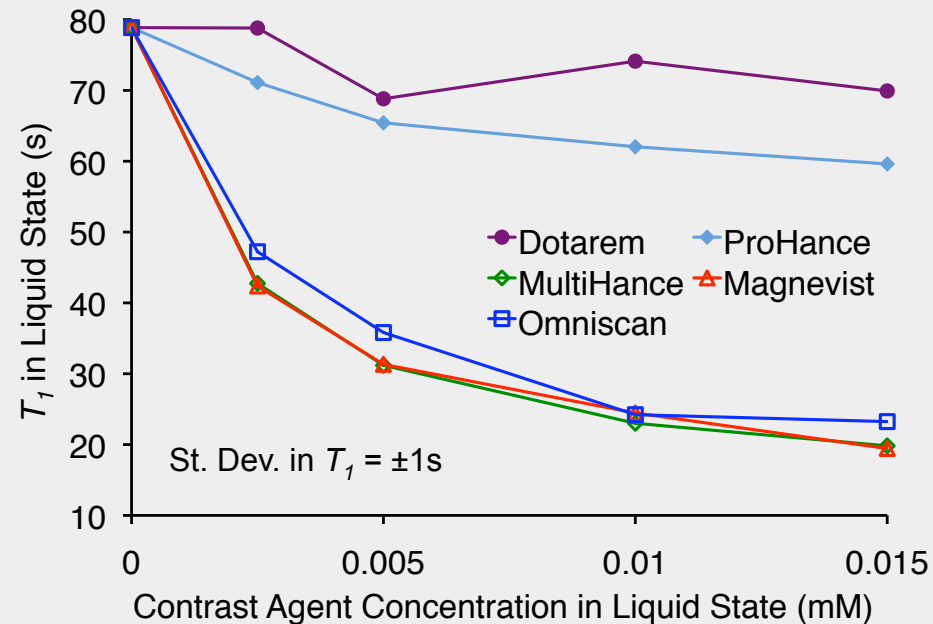


Fig 4



Discussion

- Macrocyclic structures - Dotarem, ProHance - yielded less enhancement in solid state polarisation (Fig 3), but had less impact on T_1 (Fig 4)

Fig 3

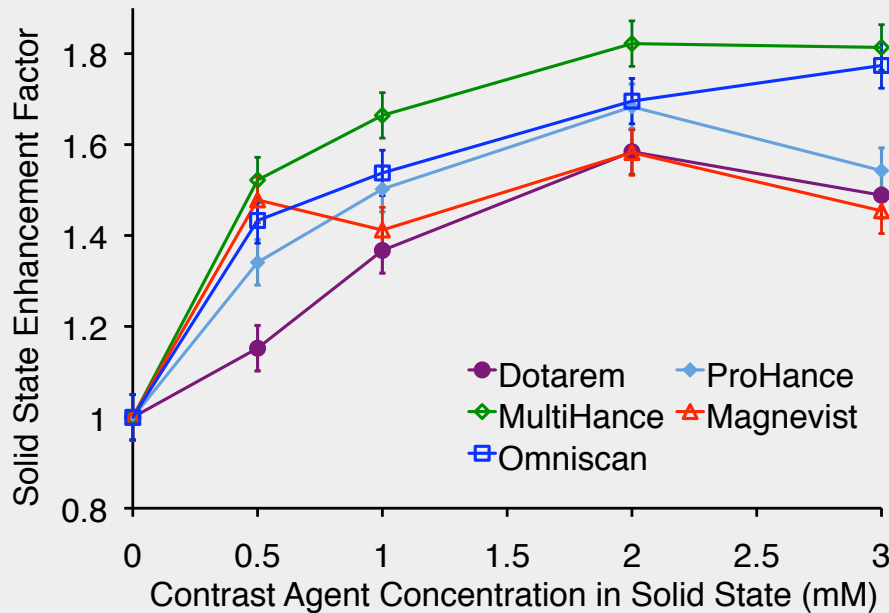
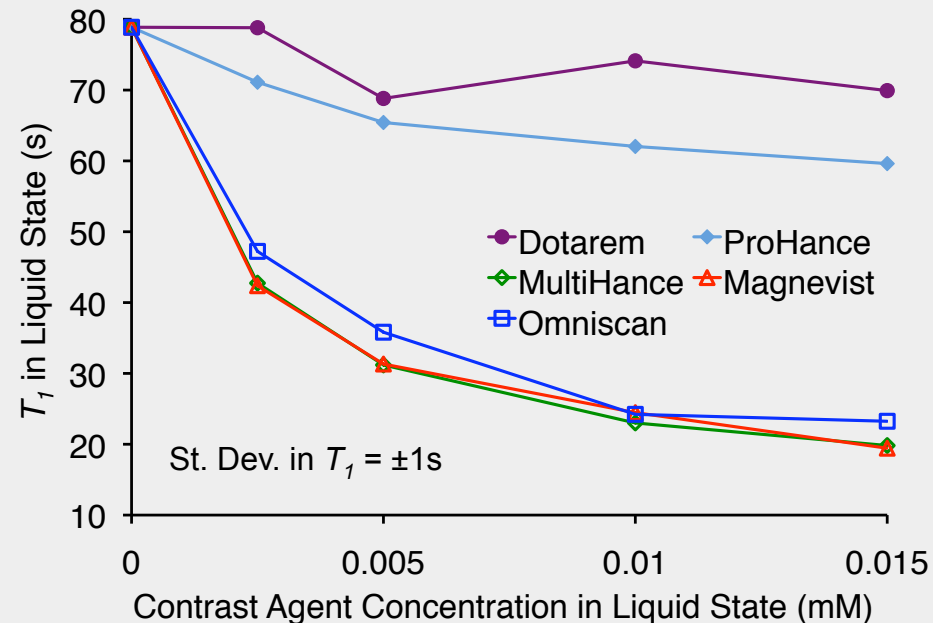


Fig 4



Discussion

- Short T_1 's lead to rapid loss of polarisation when the pyruvic acid is removed from the polariser
- Shorter T_1 's for open chain structures lead to significantly less polarisation in the liquid state than for macrocyclic structures

Fig 4

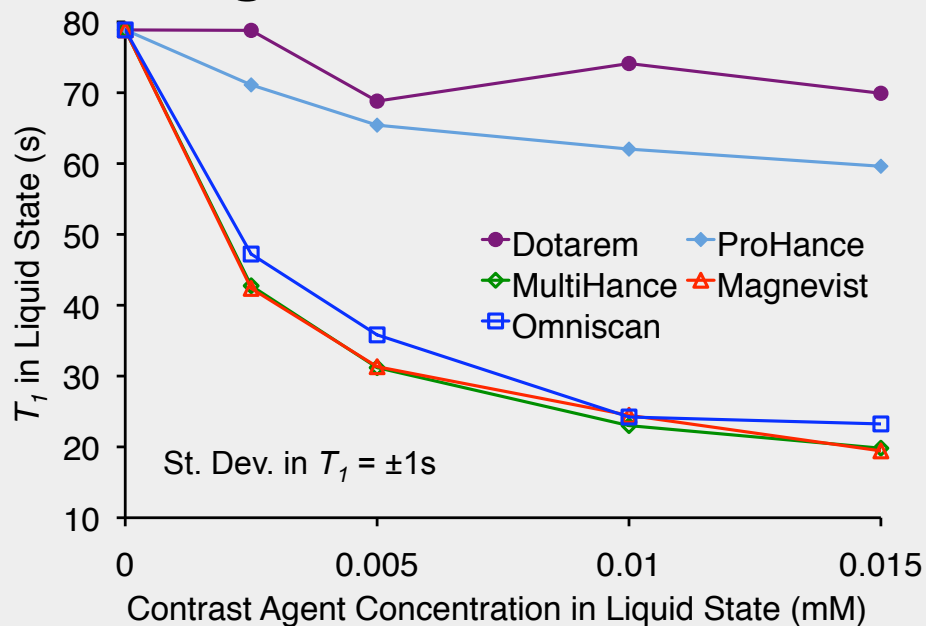
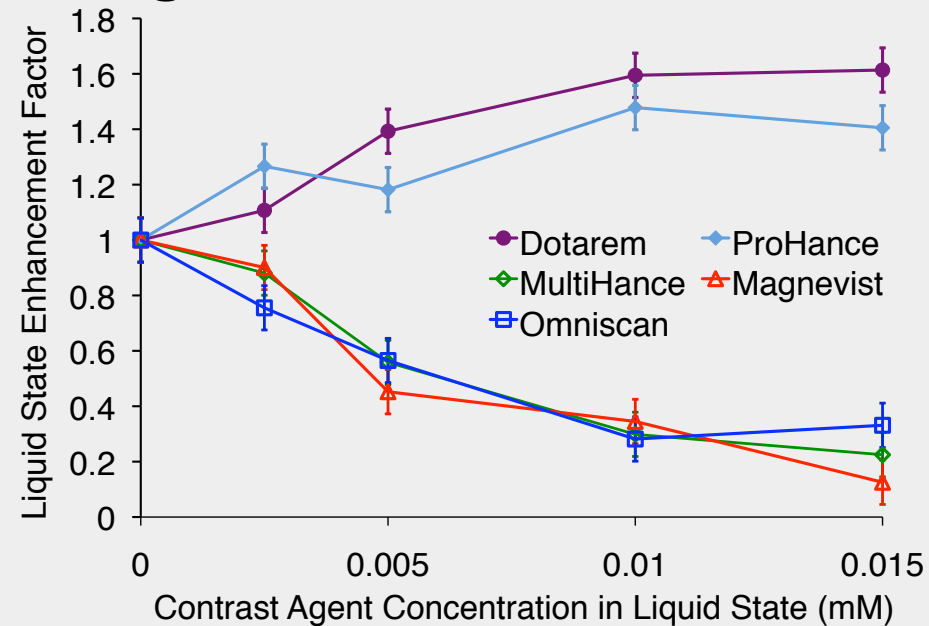
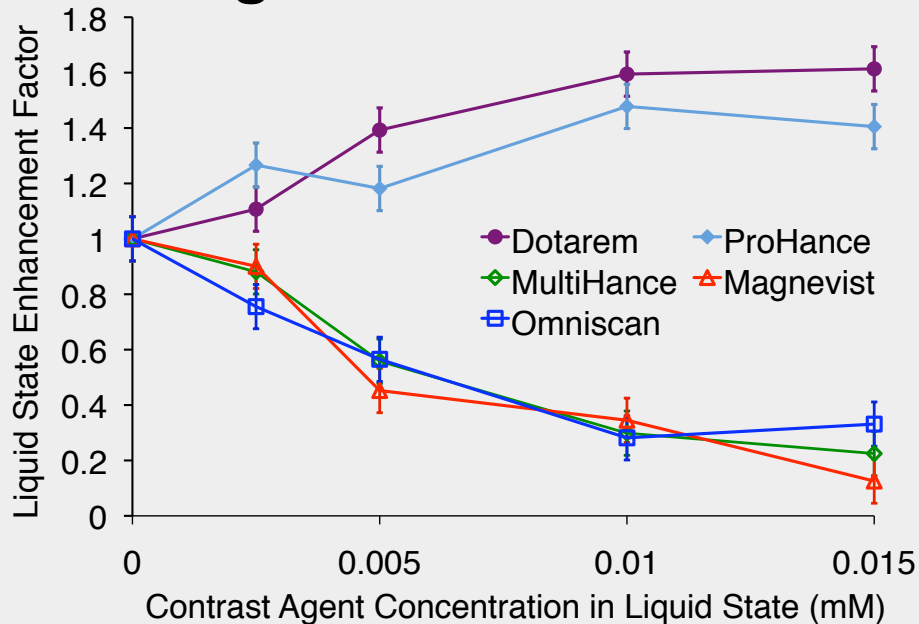


Fig 5



Discussion

Fig 5



- For open chain structures, lower amounts of liquid state polarisation may limit their usefulness (Fig 5)
- There is evidence that filtering out contrast

agents while in the liquid state may restore T_1 , and may reduce polarisation loss in solution (Van Criekinge, *et. al.* 49th ENC (2008) #189)

Discussion

- Increases in solid state enhancement are obtained up to a concentration of 2mM
- For macrocyclic structures, there are minimal changes in T_1 and loss of liquid state polarisation at concentrations of 2mM

Fig 3

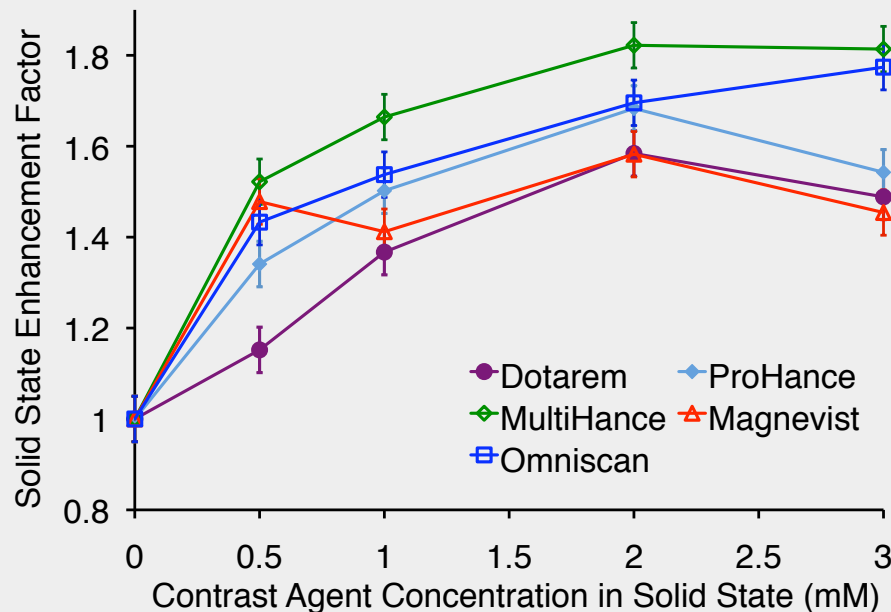
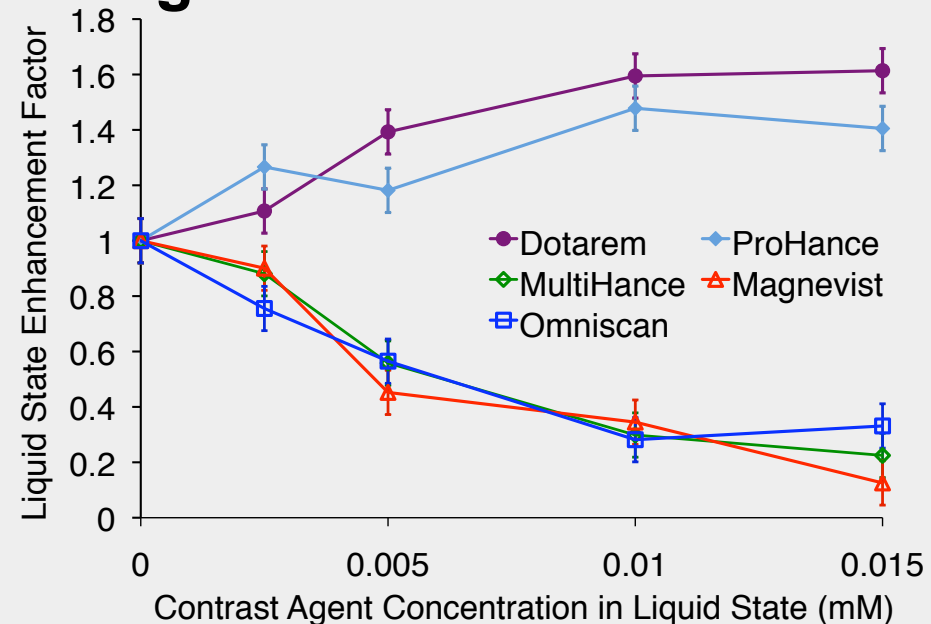


Fig 5



Conclusions

- Macrocyclic contrast agents provide:
 - largest enhancement of polarisation in liquid state with minimal shortening of T_1
 - increased polarisation in solid and liquid states at concentrations up to 2mM
- Open chain contrast agents are undesirable:
 - larger loss of liquid state polarisation
 - decreased T_1

Acknowledgements

- Elizabeth Gillies for helpful discussions

