Direct Molecular Solution of Hyperpolarized 129Xe through Hollow Fiber Membranes

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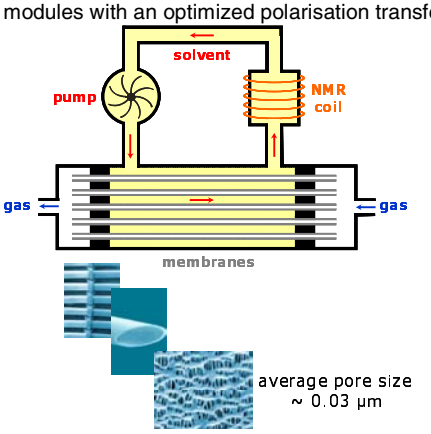
Motivation:

Xenon atoms are small enough to pass even the blood brain barrier. Therefore dissolved hyperpolarized (HP) Xenon is an interesting candidate for a new (free diffusive) MRI contrast agent. To dissolve Xenon in blood via inhalation is quite problematic due to the presence of oxygen in the lung and the slow passage into the cardiovascular system. These problems can be overcome by dissolving Xe in a suitable carrier liquid and injection. Care has to be taken to avoid the formation of stable foams. So far HP-Xe is typically frozen out, vaporized in the presence of the liquid and dissolved by shaking. This process is hard to control and not suitable to be applied in hospitals.

The aim of this study is the development of a technique to dissolve HP-Xe easily and continuously in different liquids using oxygenator membranes modules with an optimized polarisation transfer and without foam building.



Principle:

The solvent is circulated through the membrane module from a reservoir driven by a nonmagnetic membrane pump. At the same time HP-Xenon counter-flows through the hollow membranes and dissolves into the liquid. When the liquid enrichment of Xenon has reached a certain point it can be removed and injected as a contrast agent.

Realization:

Usage of hollow-fiber oxygenator membranes (like in heart-lung machines) in special modules to dissolve HP-Xenon in various biocompatible solvents.

To study the dissolution process or to conduct other spectroscopic experiments the reservoir can be put into a NMR probe.

Two prototypes ("Xenonizer") are already realized.

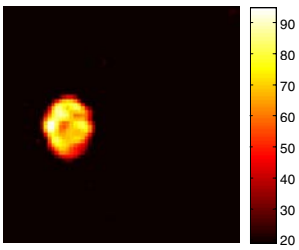
Results and Discussion:

In order to demonstrate the capabilities of our new approach, we have studied HP ^{129}Xe spectroscopy in water, DMSO, and a solution containing phospholipid bicelles used in high resolution NMR studies of proteins. There is no observable loss of polarisation or shortening of T_1, the continuous operation allows signal averaging and, therefore, multidimensional NMR. 2D EXSY (**Ex**change **S**pectroscop**y**) was performed for the first time using HP ^{129}Xe in solution. We also show first in vitro ^{129}Xe MRI images obtained with this method at a clinical scanner.

Our method significantly simplifies the application of HP ^{129}Xe in NMR and MRI by improving the gas dissolution process. Hopefully, this will widen the applications of hyperpolarised gases in this growing field of research. The feasibility of the method was shown by imaging dissolved HP-Xe in Lipofundin on a clinical Siemens Magnetom 1.5T scanner. A setup similar to the prototype was used (CELGARD® membranes).

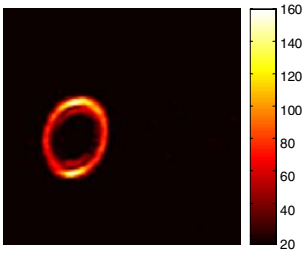
Xe images accomplished by "shaking" and using the membrane approach to dissolve the gas were compared. SNR ratio of both methods are in the same order (~ 2.8 : 1). Next experiments to get in vivo images in small animals (e.g. rats) are being planned.

Syringe with 5ml dissolved HP-Xe



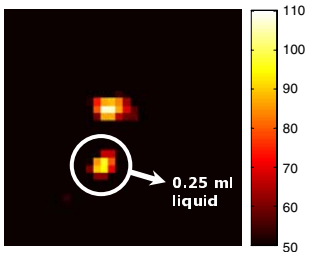
32x32, FOV 100mm, SNR 12.7

Phantom of two winded tubes, continuous Xenon and liquid flow



axial projection, diameter 50mm, 64x64, FOV 200mm, SNR 24.0

Two single tubes, continuous Xenon and liquid flow



16x16, FOV 100mm, SNR 7.2

Conclusion and Outlook:

This new method to dissolve hyperpolarized Xenon in several solvents allows fast molecularly dissolution of gas, no formation of foams or bubbles, no observed loss of polarization and continuous operation is possible even at high pressures.

A Comparison with other methods of Xenon dissolution by NMR and direct measurement of partial pressures has shown the advantages of the membrane method. Increasing the efficiency of dissolution by applying pressure allowed the investigation of Xenon chemical shift in bicells.

Further improvement of the materials, modules and the method will lead to an apparatus for easy production of hyperpolarized Xenon solutions as a new class of contrast agents in MRI.