

Abstract 203

Investigating GluCEST for pH mapping at low temperatures: A feasibility study

Type: Scientific Session communications

Topic: Preclinical Studies and Basic Science / Novel contrasts and methods

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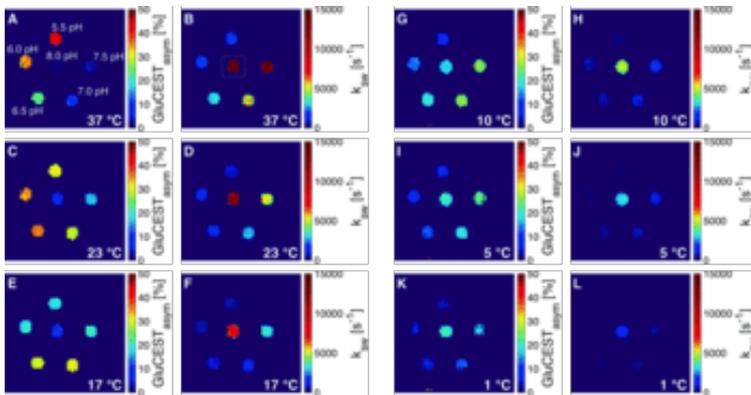
The CEST effect between amine protons of glutamate and protons of bulk water is concentration and pH dependent and therefore a potential technique for intracellular pH mapping.¹ An area of application might be the investigation of the physiological response of marine organism to the climate change.² Various studies have identified possible impacts for marine organisms, e.g., on acid-base balance and neurological disturbances.^{3,4} Therefore, it was the aim of this study to test the applicability of GluCEST for ectothermic animals, which are living at low temperatures of 0-15°C, by investigating the influence of lower temperatures on the GluCEST effect. In a first *in vivo* application the GluCEST approach was applied on a common marine ectotherm, the blue mussel *Mytilus edulis*.

Subjects and Methods

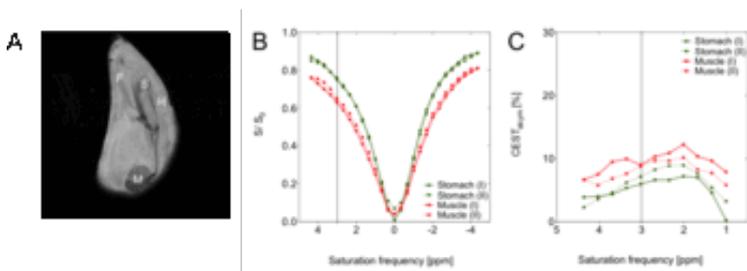
All NMR measurements were performed on a 7T animal scanner (Biospec 70/20 USR, Bruker Biospin, Ettlingen, Germany) equipped with a B₀ gradient system BGA-12S2 and a quadrature birdcage coil (72mm ø). CEST images were obtained by pre-saturated FISP imaging. Pre-saturation was accomplished by a train of 12 rectangular pulses (tp=1s, B₁=5.87µT). The phantom consisted of six NMR tubes filled with 10mM glutamate solutions dissolved in PBS, titrated to different pH values of 5.5-8.0. The observed temperature range was 1-37°C. The CEST asymmetry was calculated as $CEST_{asym} = (M_{sat}(-\Delta\omega) - M_{sat}(\Delta\omega)) / M_{sat}(-\Delta\omega)$. The exchange rates k_{sw} were determined by numerically fitting the Bloch-McConnell equations to the experimental data.

Results

The asymmetry images show that the GluCEST effect is still clearly visible for pH values greater than 6.5, especially at low temperatures (Figure 1). However, The exchange rates between the amine (-NH₂) protons of glutamate and water varied considerably for the examined range of pH values and temperatures.



The determined z-spectra and corresponding asymmetries from the muscle (M=9%) and stomach (S=6.5%) of the blue mussel show high differences in the GluCEST effect, indicating the suitability of the technique to marine organisms (Figure 2).

**Discussion/Conclusion**

The GluCEST effect (at 3ppm) on pH is non-bijective. In contrast, the exchange rates show a mono-exponential behaviour and a bijective dependence on pH at a given temperature as expected for base-catalysed exchange and the Arrhenius-equation, thus allowing pH measurements. In summary, GluCEST detection is feasible in the low temperature and physiological pH range. In addition, it can be used to detect relative differences in the GluCEST effect *in vivo* as demonstrated in the mussel *Mytilus edulis* at a temperature about 10°C.

References

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4. Munday, P. L. et al., *ProcNatlAcadSci*, **106**, 1848-1852 (2009)

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