# Efficient detection of bound potassium and sodium using TQTPPI pulse sequence

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## Purpose

Ultra-high magnetic fields expand our capability to perform low gamma MRI. Triple quantum (TQ) signals are features unique to potassium and sodium nuclei, as they both have spin=3/2, thus detecting changes in binding and electrical field gradients *in vivo* (1,2). After calibration, TQ signal can also detect changes in the intracellular ion concentration (3). An improved way to detect the TQ signal is explored which does not utilize filtration.
It allows for the simultaneous detection of both the TQ and single quantum (SQ) signals under the same conditions. Separation of the TQ signal is achieved by concurrent time and phase increments (TPPI). In this case, no signals are lost and the TQ signals are observed separately at the triple frequency relative to a SQ signal. A comparison of the new TQ signals of potassium and sodium is performed *in vivo* in a rat head.

## Methods

The experiments were performed on a 21.1T magnet using Bruker MRI Avance III console (PV 5.1) and 64 mm gradient coil (RR Inc). Volume MRI coils for potassium (41.8 MHz) and sodium ($^{23}$Na, 238 MHz) were the same size with ID/L = 33/54 mm. A commonly used TQ filtering pulse sequence 90º(α) – t - 90º(α+β) - 90º (0) was modified so that the phase "α" was incremented by 45º at each step the time delay "t" was incremented. Phase "β" was alternated each scan (±90º) before incrementing the delay time to suppress in our case the double quantum (DQ) signal. The time increment in TQTPPI pulse sequence was 100 μs, duration of the 90º pulse for sodium was 120 μs, and 200 μs for potassium. Number of time steps was selected 256 or 512. SQ signal in TQTPPI spectrum was normalized to 100 %. The TQTPPI pulse sequence was verified in three male Fisher 344 rats (weight ~ 150 g *in vivo*) to compare the difference between the potassium and sodium TQ signals. All animal experiments were conducted according to the protocols approved by The Florida State University ACUC.

## Results and Discussion

The TQ and SQ signals for potassium and sodium in a rat head are presented on Fig. 1. The integral of the TQ signal for potassium was 40.9 ± 1.4 % relative to the SQ signal, while for sodium it was 20 ± 0.5 %. The observed two times difference in the TQ signals suggests that *in vivo* there is two times more probability of each potassium ion being bound rather than a sodium ion. As potassium is mainly intracellular, this result can indicate that ion binding in intracellular space is more efficient than in extracellular space. For comparison, polycrystalline KCl gives TQTPPI spectrum where the TQ signal is of 58.1 ± 1.7 % (Fig. 2). If polycrystalline KCl can be regarded as a model for 100% bound potassium we can conclude that in a rat head only 70 % (40.9/58.1) of potassium is bound, while the bound sodium is only 34.3 % of the total ion content. The advantage of the TQTPPI pulse sequence is that all SQ, TQ and potentially DQ signals are acquired at the same time under similar conditions, and all is performed without any signal losses. In contrast, during TQ filtration some losses of the TQ signals are expected, as the TQ signal is optimized only for those signals which generate the maximum for "t" delay of 2-3 ms or so. Thus, a possible distribution of the binding time will not be covered optimally in this case. The ions having stronger or weaker electric gradients or those experiencing changes during *in vivo* interventions will not be detected optimally.

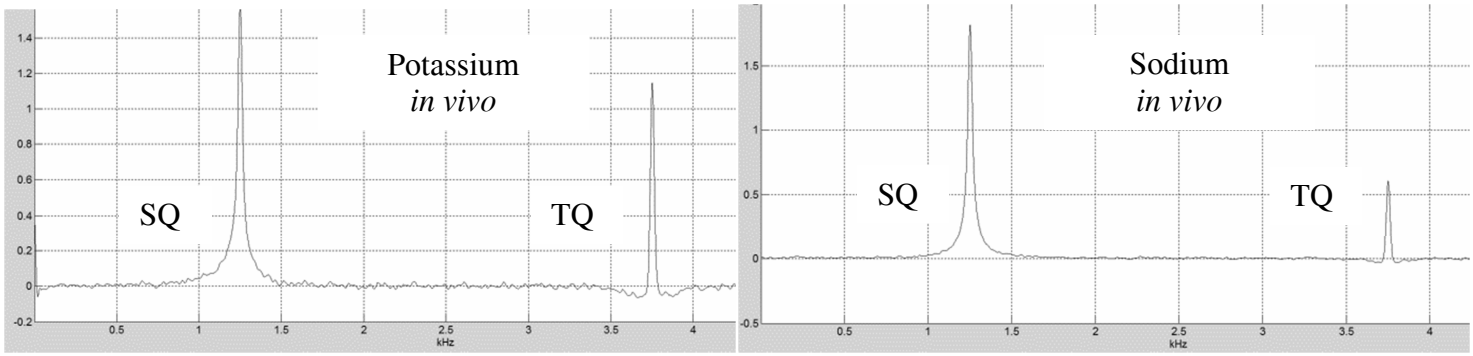


**Fig. 1.** Potassium (left) and sodium (right) TQTPPI signals from rat head. The right TQ peaks at 3.75 kHz represent bound potassium and sodium respectively, while peaks at 1.75 kHz are corresponding to SQ signals.

## Conclusion

Simultaneous detection of SQ and TQ signal for potassium and sodium was achieved using TQTPPI which demonstrates the efficient separation of signals from bound ions. The bound potassium and sodium signals are detected as separate peaks at the triple frequency relative to the SQ signal. In comparison to the TQ filtration method, TQTPPI detects bound ion signals optimally in a wide range of binding strength and a wide range of ion binding variations what is important during diseases or interventions.

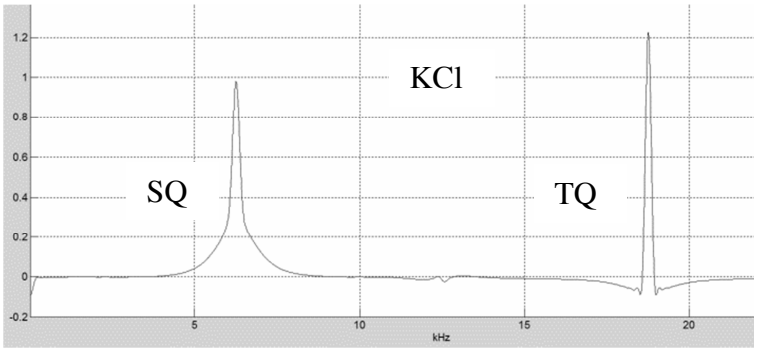


**Fig. 2.** Potassium TQTPPI signal in polycrystalline KCl, as a model for 100 % bound potassium.

## Acknowledgements

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