Letter to the editor: “Interpretation of $^{31}$P NMR saturation transfer experiments: do not forget the spin relaxation properties”

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TO THE EDITOR: In an interesting Editorial Focus published last year in American Journal of Physiology-Cell Physiology, Balaban and Koretsky (1) drew attention to magnetization transfer (MT) effects that are observed in $^{31}$P magnetic resonance spectroscopy (MRS) experiments, in which the $\gamma$-ATP resonance is irradiated, leading to saturation transfer between $\gamma$-ATP and the $\alpha$- and $\beta$-ATP phosphates. The authors point out that the effects can be attributed to direct chemical exchange between small metabolite pools of ATP or ADP, which may be bound in enzyme-substrate complexes with resonances shifted to different frequencies and/or broad line shapes. Here we point out that magnetic interactions between phosphorous spins in metabolites have to be taken into account as well.

Magnetization transfer effects do not only arise from chemical exchange, but also from cross-relaxation effects. The latter phenomenon has been largely neglected in in vivo NMR spectroscopy. A case in point is the MT between the phosphates of ATP. In a recent article (3) we describe saturation transfer of equal magnitude between the $\alpha$- and $\beta$-ATP phosphates. In our figures; C.I.N. and C.W.H. drafted the manuscript; C.I.N., C.W.H., B.W., and A.H. interpreted the results; C.I.N. prepared the figures; C.I.N., C.W.H., and A.H. conception and design of the research; C.I.N. analysis and interpretation of the data; C.I.N., C.W.H., and A.H. conceived and designed the research; C.I.N., C.W.H., and A.H. conceived and designed the research; C.I.N., C.W.H., and A.H. analyzed the data; C.I.N., C.W.H., and A.H. reviewed the literature.

REFERENCES


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Fig. 1. Simulated line widths and line shapes for free ATP and ATP complexes. A: line width as a function of rotation correlation time $\tau_c$ for a $^{31}$P-31P spin system. Insert emphasizes the line widths for all three $^{31}$P resonances of ATP when bound to 50- to 100-kDa proteins, leading to $\tau_c$ of 10 to 100 ns ($\tau_c = 10^{-8}$ to $10^{-9}$). This figure demonstrates that complex formation of ATP with enzymes that catalyze ATP conversion reactions (e.g., creatine kinase or adenylate kinase or ATPases) will lead to a line broadening effect of maximally 60 Hz, not sufficient to explain magnetization transfer (MT) effects by direct cosaturation of resonances in bound ATP and subsequent exchange of ATP molecules between bound and free pools. This is also illustrated in B, where Lorentzian line shapes are plotted for free ATP ($\tau_c = 0.3$ ns) and for ATP bound to G-actin (ATP-complex), which has a $\tau_c = 40$ ns. The shifts are based on the in vitro experiments of Brauer and Sykes (2). The concentration of the bound ATP in the complex is at a 10-fold higher concentration than that of free ATP, to improve visibility and enable interpretation of line shapes. Clearly, the $\alpha$- and $\beta$- resonances of the ATP complex are not sufficiently broadened and shifted to be cosaturated with the $\gamma$-ATP resonance at $-328$ Hz. Simulations are performed for an interspin distance of 3 Å (for ATP), a chemical shift anisotropy $\delta = 180 \times 10^{-6}$, and a field strength of 7 T.
