Modular ^{31}P Wide-band Inversion Transfer for Integrative Analysis of ATP Metabolism, T_1 Relaxation and Molecular Dynamics in Skeletal Muscle at 7T

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Theory

As described previously (26), the Z-magnetization vector for a given spin exchange system after a B_1 perturbation evolves by

$$m(t) = \ I - e^{A \cdot t} \ (I - m(0)) \qquad [1]$$

where *m* represents the Z-magnetization normalized to its value at thermal equilibrium M^o; m(0) is the initial magnetization immediately after the B_1 perturbation at $t = 0$; *I* is unity vector, and *A* is the matrix describing the relaxation and exchange kinetic parameters of the spin system.

In the skeletal muscle, ATP is involved in chemical exchanges with both PCr and Pi and also undergoes intramolecular ^{31}P-^{31}P cross-relaxation effects (referred to as NOE). Together these three metabolites constitute a five-spin exchange system. The normalized magnetization vector, *m,* and exchange-relaxation (ER) parameter matrix, *A,* can be written as

$$m \ = \begin{bmatrix} m_{Pi} \\ m_{PCr} \\ m_{\gamma} \\ m_{\alpha} \\ m_{\beta} \end{bmatrix} \qquad [2]$$

and

$$A \ = \begin{bmatrix} -1/T_{1,Pi} - k_{Pi\to\gamma} & 0 & k_{Pi\to\gamma} & 0 & 0 \\ 0 & -1/T_{1,PCr} - k_{PCr\to\gamma} & k_{PCr\to\gamma} & 0 & 0 \\ k_{\gamma\to Pi} & k_{\gamma\to PCr} & -1/T_{1,\gamma} - k_{\gamma\to Pi} - k_{\gamma\to PCr} & 0 & -\sigma_{\beta\gamma} \\ 0 & 0 & 0 & -1/T_{1,\alpha} & -\sigma_{\beta\alpha} \\ 0 & 0 & -\sigma_{\gamma\beta} & -\sigma_{\alpha\beta} & -1/T_{1,\beta} \end{bmatrix} \qquad [3]$$

where the subscripts α, β, γ denote for α-, β- and γ-ATP, respectively, k denotes the first-order rate constant for the chemical exchanges with the forward and reverse reaction related by $k_{ji} = k_{ij} \frac{M_i^o}{M_j^o}$ (*k*, pseudo first order rate constant for ATP turnover; i, j = Pi, γ-ATP or PCr, γ-ATP); and σ denotes the rate constant of ATP ^{31}P-^{31}P cross-relaxation, which is assumed to be a constant within any two neighboring ATP spins ($\sigma_{\gamma\beta} = \sigma_{\beta\gamma} = \sigma_{\alpha\beta} = \sigma_{\gamma\alpha}$). The ER parameter matrix *A* is based on the coefficients of Bloch-McConnell-Solomon magnetization derivative formulism (21,26).

In a typical inversion-recovery experiment defined by repetitive pulse sequence (180° - t_d – 90° - τ)$_n$ (Figure 1b), the evolving of the Z-magnetization with inversion delay time t_d is given by

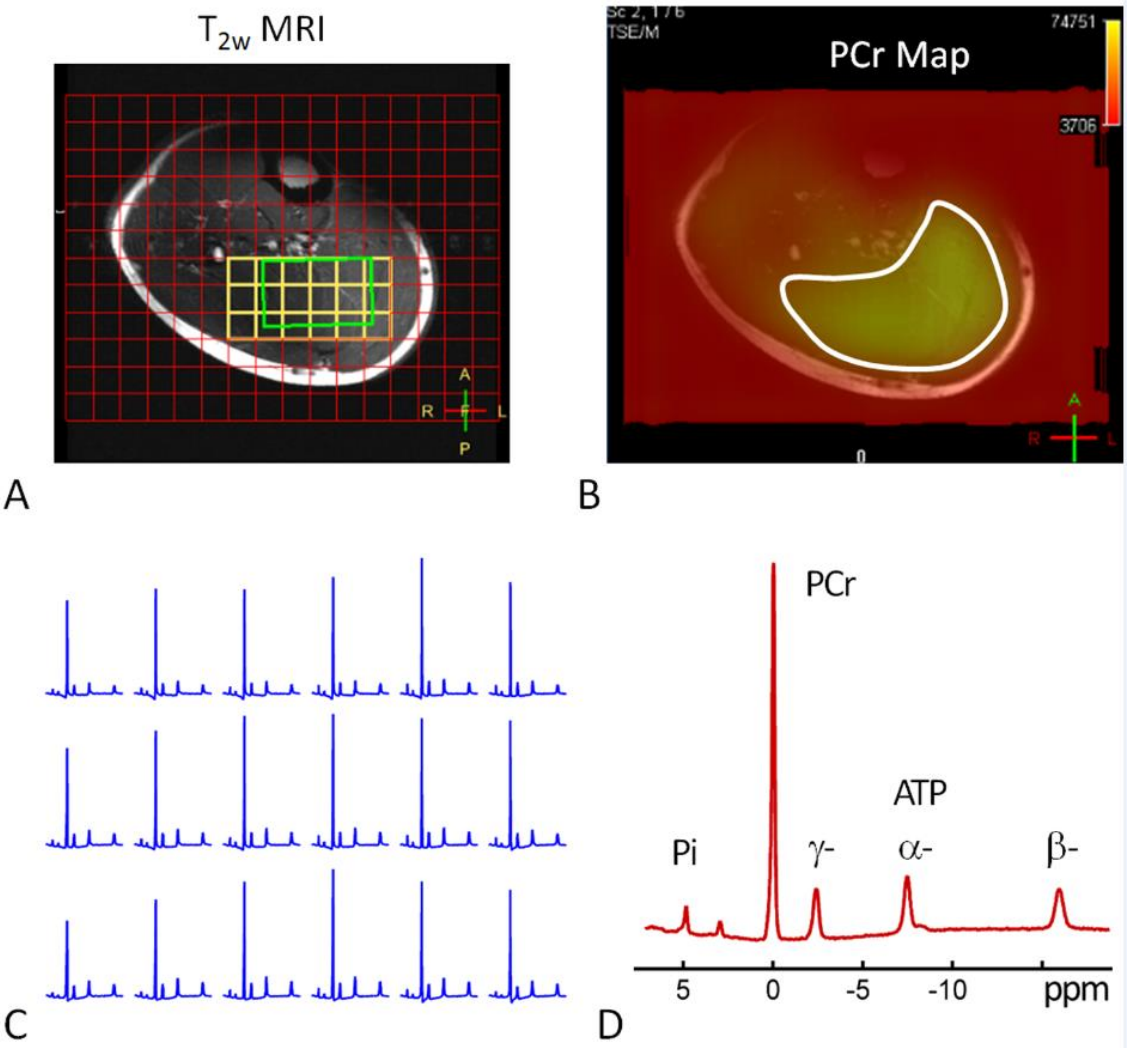
$$m(t_d) = I - e^{A \cdot t_d}(I - f \cdot (I - e^{A\,\tau}(I))) \quad [4]$$

where *f* represents the inversion fraction, ranging from *f* = -1 for fully inversion to *f* = 0 for no inversion, assuming a full magnetization recovery after each TR (= t_d + τ, ignoring pulse width). For partial recovery with short-TR, it is convenient to scale the Z-magnetization by, instead of M^o, the steady-state magnetization acquired with a reference sequence with the same TR but without inversion pulse. This results in the following normalized magnetization expression:

$$m(t_d) = \left(I - e^{A \cdot t_d}\left(I - f \cdot \left(I - e^{A\,\tau}(I)\right)\right)\right) / \left(I - e^{A \cdot TR}(I)\right) \quad [5]$$

Thus by analyzing the dependence of $m(t_d)$ on t_d, the relaxation and kinetic parameters encoded in ER matrix *A* can be determined.

Supporting Information Figure S1. 2D ^{31}P CSI acquired from human resting skeletal muscle at 7T with excitation by a nominal 90^{o} block pulse using a half-cylinder-shaped partial volume coil. (A) Matrix dimension 12x16 with 1 x 1 cm^2 spatial resolution. (B) PCr intensity map showing fair uniformity in RF sensitive soleus-gastrocnemius region. The highlighted muscle region accounting for > 90% of the total ^{31}P signals. (C) ^{31}P spectra from 3x6 voxels located in the sensitive region, as marked by yellow matrix in (A). (D) Averaged ^{31}P spectrum over the whole muscle.



Supporting Information Figure S2. (A) Simulated ^{31}P Z-magnetization against scan dynamic number **n** (= 1 – 9) at different flip angles (FA: 10°, 50°, 70° and 90°) and TRs (= T_1/5, T_1 and 5T_1 with T_1 = 6.5 s, by single-exponential function). (B) Dynamic 7T ^{31}P MR spectra acquired from human skeletal muscle at rest by a 90° block excitation pulse with TR = 7s, NA = 1 and nine consecutive dynamic scans. Note that all ^{31}P signals reached steady state after the 1st dynamic scan and that the dynamic pattern for PCr matches the simulated data for T_1 = 6.5 s and FA 90°.