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Orthovanadate and orthophosphate inhibit muscle force via two different pathways of the myosin ATPase cycle

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Time course of force development

The time course of isometric force development (T_r) was fitted by means of the bi-exponential equation: $T_r = T_F(1-\exp(-r_F t)) + T_S(1-\exp(-r_S t))$, where t is the time elapsed from the start of force development following the end of shortening, T_F and T_S are the amplitudes and r_F and r_S are the rate constants of the fast and the slow exponentials, respectively. Table S1 reports the values of r_F and r_S in control and in 0.1 mM Vi. Neither rate is significantly affected by the addition of Vi according to the Student's *t-test*.

	Control	0.1 mM Vi	Paired <i>t</i> -test
r_F (s ⁻¹)	24.6 ± 1.0	24.3 ± 1.9	P > 0.8
r_S (s ⁻¹)	6.9 ± 0.4	5.2 ± 0.5	P > 0.2

Table S1. Mean values (±SEM, 4 fibers).

Set of rate constants used in Scheme 2

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
k_x	$10^6 \text{ M}^{-1} \text{s}^{-1}$	14 s^{-1}	21 s^{-1}	500 s^{-1}	8 s^{-1}	24 s^{-1}		$200 \cdot 10^3 \text{ M}^{-1} \text{s}^{-1}$	1.5 s^{-1}
k_{-x}	0.1 s^{-1}	9 s^{-1}	90 s^{-1}	$33 \cdot 10^3 \text{ M}^{-1} \text{s}^{-1}$	$10^5 \text{ M}^{-1} \text{s}^{-1}$	$8 \cdot 10^{-3} \text{ s}^{-1}$		180 s^{-1}	0.035 s^{-1}
K_x	10^7 M^{-1}	1.56	0.23	$15.2 \cdot 10^{-3} \text{ M}$	$8 \cdot 10^{-5} \text{ M}$	$3 \cdot 10^3$	$\geq 5 \cdot 10^2 \text{ M}$	$1.1 \cdot 10^3 \text{ M}^{-1}$	42.9

Table S2. Rate constants for the forward (k_x) and the backward (k_{-x}) transitions and corresponding equilibrium constants (K_x) in Scheme 2 reported in the manuscript. x is the step number, reported in brackets in the first row. In the simulation, [ATP]=5 mM; [ADP]=20 μM .