Reply to Pancheva, Panchev, and Pancheva

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TO THE EDITOR: We appreciate the feedback and the provocative comments of Dr. Pancheva and coworkers (2). On the basis of our recent study showing a direct interaction of Mb with mitochondria, Dr. Pancheva et al. proposed a theory about the immediate metabolism of oxygen, ATP, and PCr during muscle contraction: electrical current enhances O2 “detachment” from heme, mechanical contraction facilitates O2 release and allows Mb to serve as an excessive O2 scavenger, elevated temperature decreases O2 affinity of Mb, and CO2 induces Bohr effect in Mb.

The literature does contain a long history of reports that would cast invaluable perspectives on Pancheva et al.’s theory (3). Many studies have examined how electrostatics help Mb discriminate ligand binding and how the electric field could affect Mb movement. These studies, however, do not claim that a physiologically relevant electric field can alter the heme Fe-O2 covalent bond and facilitate the O2 “detachment” from the heme. In fact, many studies focus on the electrostatic effect on the ligand migration, which the authors’ restrictive definition of diffusion would appear to preclude (5).

Although a mechanical-chemical coupling could alter the Mb function, NMR studies suggest a minimal role for an overall protein effect, as implied in Pancheva et al.’s theory (1). The heme environment responds only to very high pressure to change the protein volume. How the discussion of mechanical-chemical coupling leads to evidence supporting the role of Mb as an O2 scavenger seems unclear.

Studies have already shown that increasing the temperature from 30°C to 35°C will decrease slightly the O2 affinity of Mb, as reflected in 1.21 to 1.98 mmHg change in the partial pressure of O2 to half saturate Mb (P50). But, in contrast to Hb, Mb exhibits no significant Bohr effect in the physiological range of pH.

Pancheva et al.’s comments, nevertheless, have raised provocative points and will help stimulate discussion on the mechanisms underlying the immediate release of O2 from Mb at the onset of muscle contraction, the function of Mb binding to mitochondria, and the cellular function of Mb (4).

DISCLOSURES
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AUTHOR CONTRIBUTIONS
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