

Progress towards an accurate molecular muscle model.

Sam Walcott

Dept. of Mathematics, University of California, Davis
email: swalcott@math.ucdavis.edu

Motivation

Understanding legged locomotion depends on understanding muscle contraction. For example, why an animal prefers to move one way over another depends on how muscles use energy. Although phenomenological muscle models exist, each has drawbacks and none captures all of muscle’s complex behavior. This lack of reliable models, particularly for energy consumption, has led some movement scientists to call for more muscle experiments [1]. Yet biologists have been studying muscle for decades. Recent work has focused on the molecular level. We hope to use these existing measurements to make a better model.

State of the Art

Molecular muscle models have a long history, starting with the “Huxley” model [2]. This simple molecular model correctly predicts some macro-scale muscle behavior (e.g. the force-velocity relationship [3]). Subsequent work made the model consistent with both biochemical measurements and thermodynamic laws [4]. Such models are still used today [5].

These models are unsuitable for locomotion studies because they are too complex and because they do not capture all of muscle’s behavior. While methods exist to simplify the models [6], there is no reason to do so while simpler phenomenological models are equally accurate. We want to make the molecular models more reliable.

Our Approach

We develop molecular models based on molecular measurements. The advantage of this approach is that such measurements are performed under simplified conditions. As a result, we model virtually every aspect of the experiment, from molecular mechanics to data analysis. The model’s predictions can thus be compared very precisely to measurements.

Current Results

Under simplified conditions, we developed a molecular model that fits measurements performed with arbitrary numbers of molecules both in the absence and presence of external force [7]. The model provides insight into some puzzling experimental observations [8]. We recently added regulation [9], allowing the model to work under conditions where the Huxley model fails (since regulation violates Huxley’s assumption that each molecule works independently). We are now extending this work to more complex physiological conditions.

Best Possible Outcome

We progress towards a molecular model that gives a quantitative description of muscle contraction. Such a model would relate muscular force, contraction speed and energy consumption, allowing a more quantitative understanding of legged locomotion. Additionally, such a model would provide deeper understanding of genetic muscle diseases.

References

- [1] R. M. Alexander, (2005). *J. Exp. Biol.*, 208:1645–1652.
- [2] A. F. Huxley, (1957). *Prog. Biophys. Biophys. Chem.*, 7:255–318.
- [3] A. V. Hill, (1938). *Proc. Royal Soc. B: Biol. Sci.*, 126:136–195.
- [4] T. L. Hill, (1974). *Prog. Biophys. Mol. Biol.*, 28:267–340.
- [5] A. Månsson, (2010). *Biophys. J.*, 98:1237–1246.
- [6] G. I. Zahalak (1981). *Math. Biosci.*, 55:89–114.
- [7] S. Walcott, D. M. Warshaw, E. P. Debold (2012). *Biophys. J.*, 103:501–510.
- [8] J. E. Baker, et al. (2002). *Biophys. J.* 82: 2134–2147.
- [9] S. Walcott (2013). *Cell. Mol. Bioeng.* (In Press)