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How Muscles Function - The Work Loop Technique

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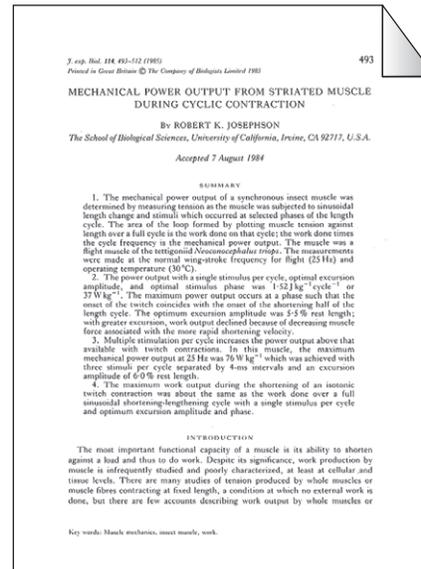## HOW MUSCLES FUNCTION – THE WORK LOOP TECHNIQUE

Anna Ahn discusses Bob Josephson's 1985 paper entitled: 'Mechanical power output from striated muscle during cyclic contraction'.

A copy of the paper can be obtained from http://jeb.biologists.org/content/114/1/493.short

The primary function of muscle is to generate force and produce movement in animals. Before 1985, muscle function had typically been examined under maximally stimulated conditions, while held at a constant length or allowed to shorten at a constant force. Although crucial for understanding fundamental mechanisms and properties of muscle, these contractions at a constant length (isometric) or under a constant load (isotonic) while maximally stimulated are seldom physiologically relevant to an animal.

In 1985, Bob Josephson developed a technique that took a monumental step towards measuring and understanding muscle function during everyday behaviours such as running, flying, swimming, breathing, sound production, eating, or even the beating of a heart. Commonly referred to as the 'work loop technique', this method determines mechanical function while simulating *in vivo*-like conditions. Typically, rhythmic behaviours are phasically controlled in animals, where a pulse or burst of neural activation occurs with each cycle of movement (Fig. 1). In response to activation, muscle then generates force and usually shortens. In a work loop experiment, cyclic length changes and phasic stimulation patterns can be imposed on an isolated muscle while force is measured. A plot of force *versus* length provides a loop, within which the area equals the mechanical work performed by the muscle. The area under the curve during the shortening phase of a muscular contraction represents the work output from the muscle on its environment. Likewise, the area under the curve during lengthening represents the work input to the muscle from its environment to re-lengthen it. Subtracting the work input during lengthening (Fig. 1C) from the work output during shortening (Fig. 1D) gives the net work per cycle performed by the muscle, or the area inside the 'work loop' (Fig. 1E). Generally, a muscle performs positive work, which is represented by a loop that rotates counterclockwise, with force peaking during shortening (Fig. 1). Muscle power can be calculated as the work, or the area inside the work loop, divided by the time needed to complete the loop.

'Bob J' himself is the first to insist that he did not develop the work loop technique *de novo*, but rather added phasic stimulation to advance and popularize Machin and Pringle's work on the asynchronous flight muscle of an insect (Machin and Pringle, 1959; Machin and Pringle, 1960). Characterized by the ability to contract multiple times in response to a single pulse of stimulation, asynchronous muscle is found only in the insect flight system. By contrast, most muscles are synchronous, i.e. each pulse of stimulation produces a single contraction. Because of this coupling, the mechanical output of synchronous muscle depends strongly on the timing and pattern of stimulation (Josephson, 1985). By examining synchronous muscle, Josephson alluded to the tremendous importance of the nervous system for the mechanical output of muscle. Countless studies have shown that changes in any of the stimulation parameters considerably affect muscle work and power. Even very slight changes to the stimuli such as replacing a single pulse in a burst of three pulses by a doublet can increase muscle power output by over 50% (Stevens, 1996).

In addition to quantifying the work and power of muscle, the direction of a work loop indicates the muscle's mechanical function. Prior to work loops, muscle power was calculated from maximally stimulated muscle while shortening with a constant load, which always resulted in power production (Josephson, 1993). We now know that muscles have a much wider variety of functions. Although flight and swimming muscles generate mechanical power (Josephson, 1985; Marsh et al., 1992; Rome and Lindstedt, 1997; Biewener et al., 1998; Altringham and Ellerby, 1999), some muscles function to dampen motion, stabilize a system, or absorb energy, such as those in a fish tail or roach leg (Rome and Lindstedt, 1997; Dickinson et al., 2000). To represent these muscles, negative work
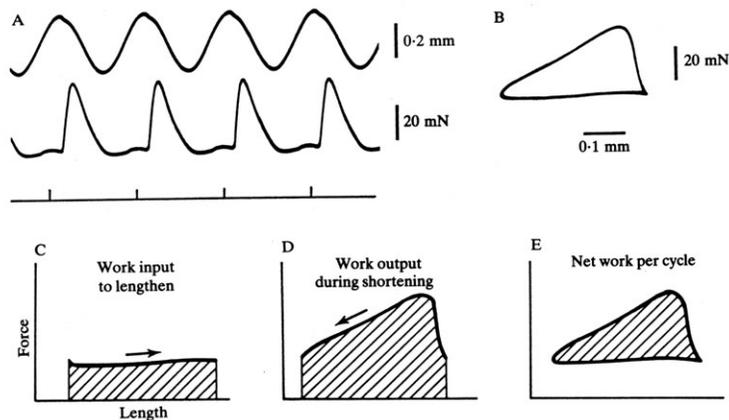
Fig. 1. The method for measuring work output. (A) A metathoracic first tergocoxal muscle is stimulated while it is subjected to sinusoidal length change. The upper trace monitors muscle length, the middle trace muscle tension, and the lower trace time of stimulation. (B) Muscle force plotted against length. The area of the resulting loop is the work done per cycle (C–E). Reproduced from Josephson (Josephson, 1985).

loops rotate clockwise as muscle force production peaks during lengthening. Energy absorption by muscle, for example in the quadriceps of people landing from a jump, had never before been quantified.

Alternatively, work loops may not be simple positive or negative loops, but rather shaped like an 'L', a line or even a figure-eight. In such cases, these muscles neither produce nor absorb energy over a cycle. For a muscle that generates force without changing length, its tendon can stretch and recoil as represented by an L-shaped work loop, such as in the calf muscles of hopping wallabies, running turkeys and, presumably, walking humans (Griffiths, 1989; Roberts et al., 1997; Fukunaga et al., 2001). These muscles function to generate and transmit forces without producing or absorbing energy. Muscle function and work loop shape can be modulated by slight changes in input parameters such as cycle frequency, muscle length change, mode of locomotion, or even anatomical position within the animal. As we continue to explore non-steady behaviours such as maneuvering and stabilization, more muscles will likely be shown to perform a variety of roles, such as dampers to stabilize, and not necessarily to function as power generators.

Two of the major determinants of work loop shape in muscle include the kinetics of activation and deactivation, or how quickly the muscle generates force and relaxes, respectively. For maximal power production, for example, a muscle would hypothetically generate a counterclockwise box-shaped work loop (Rome and Lindstedt, 1997). To maximize the area inside the loop, the muscle would activate instantly at the beginning of shortening and deactivate instantly at the beginning of lengthening. However, activation and deactivation kinetics vary greatly with

strain conditions (Josephson and Stokes, 1989; Josephson, 1999; Caiozzo and Baldwin, 1997; Askew and Marsh, 1998). Further, theoretical instantaneous shortening activation and stretch deactivation conflict with the reality of history-dependent properties such as shortening deactivation and stretch activation (Edman, 1975; Pringle, 1978). These highly variable activation and deactivation kinetics constrain possible shapes of work loops and influence whether muscles function like a motor, a brake, a spring or otherwise.

Since Josephson's study of insect flight muscle, the work loop technique has been used to study muscles across all animal taxa and many levels of organization. When possible, force and length measurements are made *in vivo* with tools and techniques such as tendon buckles, strain gauges, optic fibres, sonomicrometry and ultrasonography. However, such *in vivo* methods are most easily used on larger animals, such as birds and mammals. Alternatively, muscle length and activation patterns can be determined *in vivo*, then imposed on the muscles *in vitro*. The work loop technique has even been extended beyond biological tissues to determine the mechanical power output of artificial muscle, providing a basis of comparison to biological muscle (Full and Meijer, 2002).

All muscles can be modulated to produce or absorb energy and everything in between, depending on the input parameters and the muscles' inherent rates of force generation and relaxation. Unfortunately for experimental biology, Bob Josephson now spends his days cycling across foreign countries rather than building his own computers, writing his own software or publishing yet another potential classic in JEB. But fortunately, we have the work loop technique to quantify the difference

between the capacity or potential of a muscle and its realized function under *in vivo* conditions. Given the body of work produced (pun intended) and inspired since 1985, the work loop technique has clearly paved its own way within muscle physiology and altered how we measure, study and understand muscle function in animals.

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