Paper 2

Mechanical model of muscle contraction 2. Kinematic and dynamic aspects of a myosin II head during the working stroke

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Abstract

The condition of a myosin II head during which force and movement are generated is commonly referred to as Working Stroke (WS). During the WS, the myosin head is mechanically modelled by 3 two by two articulated segments, the motor domain (S1a) strongly fixed to an actin molecule, the lever (S1b) on which a motor moment is exerted, and the rod (S2) pulling the myosin filament (Mfil). When the half-sarcomere (hs) is shortened or lengthened by a few nanometers, it is assumed that the lever of a myosin head in WS state moves in a fixed plane including the longitudinal axis of the actin filament (Afil). As a result, the 5 rigid segments, i.e. Afil, S1a, S1b, S2 and Mfil, follow deterministic and configurable trajectories. The orientation of S1b in the fixed plane is characterized by the angle θ . After deriving the geometric equations singularizing the WS state, we obtain an analytical relationship between the hs shortening velocity (u) and the angular velocity of the lever ($\dot{\theta}$). The principles of classical mechanics applied to the 3 solids, S1a, S1b and S2, lead to a relationship between the motor moment exerted on the lever (M_B) and the tangential force dragging the actin filament (T_A). We distinguish θ_{up} and θ_{down} , the two boundaries framing the angle θ during the WS, relating to *up* and *down* conformations. With the usual data assigned to the cross-bridge elements, a linearization procedure of the relationships between u and $\dot{\theta}$, on the one hand, and between M_B and T_A , on the other hand, is performed. This algorithmic optimization leads to theoretical values of θ_{up} and θ_{down} equal to $+28^\circ$ (-28°) and -42° ($+42^\circ$) respectively with a variability of $\pm 5^\circ$ in a hs on the right (left), data in accordance with the commonly accepted experimental values for vertebrate muscle fibers.

Introduction

The mechanical study of human movement requires modelling the body as a deformable material set composed of articulated rigid segments. In this context, the calculation of the powers of the internal actions, i.e. muscular, is similar to that of the powers of the articular moments where only the rotational movements are important. For example, to simulate the walking movement, rotational motors are positioned at the joints of the members of a humanoid robot and the combination of their actions ultimately reproduce a translation movement of the robot's centre of gravity. In 1993, I Rayment and his co-authors [1,2] established that the dynamics of a myosin head is associated with the rotational movement of lever S1b, indicating that the linear shortening of a hs results from the collective rotational movements of the levers. The analogy present in the phrases "*lever arm theory*" or "*model of swinging lever arm*" suggests studying muscle fiber as a deformable material set to which the general principles of classical mechanics are applied.

Our model assumes that the movement of lever S1b belonging to a WS myosin head is carried out in a fixed plane during the entire WS state. This fourth hypothesis leads to the emblematic values of θ_{up} and θ_{down} and justifies the impossibility given to the two heads of a myosin molecule to be simultaneously in WS state. The hypothesis n° 4 is demonstrated in paragraph F.4 of Supplement S2.F because it proves to be the necessary and sufficient condition for the the linear moment principle and the work-energy theorem applied to the muscle fiber to provide identical formulations, a key tenet of classical mechanics. This paper is the first step that leads to the calculation of the tension after isometric tetanization and after phase 1 of a length step (Paper 4), to the expression of the tension increase during the last 3 phases of a length step (Paper 5), to the determination of the tension after a succession of length steps (Paper 6) and finally to the Force/Velocity relationship examined in Paper 1.

Methods

When the myosin head is strongly bound to actin, the 5 segments, Afil, S1a, S1b, S2 and Mfil, form a poly-articulated chain usually called cross-bridge (Fig 1a). The 4 joints of the chain are represented by the 4 points A, B, C and D (Fig 1d). The $O_{Afil}X$ axis is the longitudinal axis of the actin filament and the $O_{Afil}Y^o$ axis is the axis perpendicular to $O_{Afil}X$ passing through the centers of the adjacent actin and myosin filaments (Fig 1b).

Classically the WS state presented by I. Rayment [1] is based on 3 conditions: (1) the segments S1a, S1b and S2 are rigid, (2) S1a is strongly or "stereo-specifically" attached to an actin molecule of Afil, (3) a motor-moment is exerted on S1b and consequently a tensile force is applied to the Mfil via S2.

Fig 1. Geometric characteristics of a WS myosin head.

(a) Myosin molecule, one of whose 2 heads is in WS forming a cross-bridge between the myosin filament (Mfil) and the actin filament (Afil). (b) Definition of the angle β in the $O_{Afil} Y^\circ Z^\circ$ plane. (c) Definition of the θ angle in the IXY plane where point I is the projection of C on $O_{Afil} X$ according to $O_{Afil} Y$. (d) Cross-section in the $O_{Afil} Y^\circ Z^\circ$ plane where A°, B°, C° and D° are the orthogonal projections of A, B, C and D in the $O_{Afil} XY^\circ$ plane. (e) Orthogonal projection of a schematized sarcomere in the $O_{Afil} XY^\circ$ plane.

We propose a fourth condition which assumes that during the WS, the lever S1b represented by the segment BC moves in the fixed plane $O_{Afil}XY$ forming the angle β with the plane $O_{Afil}XY$ (Figs 1b and 1d), the orientation of the lever S1b in the plane $O_{Afil}XY$ being characterized by the angle θ (Fig 1c).

The four supplements associated with the article and cited in the text are entitled S2.C, S2.D, S2.E and S2.F.

Kinematics of a myosin head in WS

Our assumption allows the calculation of the positions of the 3 segments S1a, S1b and S2 (see paragraph D.1 of Supplement S2.D). By temporal derivation, we obtain a relationship between the relative hs shortening velocity (u) and the angular velocity of S1b ($\dot{\theta}$):

$$u = \dot{\theta} \cdot L_{S1b} \cdot [\cos\theta + \sin\theta \cdot \tan\varphi^\circ \cdot \cos\beta + \text{res}] \quad (1)$$

where $\dot{\theta} = d\theta/dt$; L_{S1b} is the S1b length with $L_{S1b} = |BC|$; φ° is the instantaneous angle between $D^\circ Y$ and $D^\circ C^\circ$ in the $O_{Mfil}XY^\circ$ plane (Fig 1e), points C° and D° are the orthogonal projections of C and D on the $O_{Afil}XY^\circ$ plane (Fig 1d); res is a "residual" function taking instantaneous values close to 0, whose formula is explained in (D10) in the Supplement S2.D.

Since φ° depends on θ , α and β according to the equality (D3) of Supplement S2.D, we introduce the analytical function:

$$R(\theta, \alpha, \beta) = \cos\theta + \sin\theta \cdot \tan\varphi^\circ \cdot \cos\beta + \text{res} \quad (2)$$

With (2), equality (1) is rewritten:

$$u = \dot{\theta} \cdot [L_{S1b} \cdot R(\theta, \alpha, \beta)] \quad (3)$$

Dynamics of a WS head located in a hs that shortens at constant speed

Our model is applied to a hs of the muscle fiber in isometric conditions or shortening at steady slow speed. In this case, it is attested with the calculations developed in Supplement S1.C that the only mechanical actions present in the hs are the linking forces and moments of the poly-articulated chains (Afil + S1a + S1b + S2 + Mfil) where S1a, S1b and S2 belong to the heads in WS state (Fig 2). A motor-moment ($\mathcal{M}_B$) is enforced to point B symbolizing the pivot joint between S1a and S1b during the WS. The moments in C and D are zero.

Among the forces exerted on S1a, S1b and S2, only the tangential components T_A and T_D relating to points A and D and the $\mathcal{M}_B$ moment exerted at point B are shown in Fig 2; see Fig D2 of Supplement S2.D for a complete representation of the actions involved.

The linear and angular moment principles are implemented to a WS myosin head located in a hs on the right; see paragraph D.2 of Supplement S2.D. They provide the following relationships:

$$T_A = T_D \quad (4)$$

$$\mathcal{M}_B = T_A \cdot L_{S1b} \cdot \left(\cos \theta + \frac{\sin \theta \cdot \tan \varphi^\circ}{\cos \beta} \right) \quad (5)$$

It is posed:

$$S(\theta, \alpha, \beta) = \cos \theta + \frac{\sin \theta \cdot \tan \varphi^\circ}{\cos \beta} \quad (6)$$

With (6), equality (5) is reformulated:

$$\mathcal{M}_B = T_A \cdot L_{S1b} \cdot S(\theta, \alpha, \beta) \quad (7)$$

Calculation of θ_{up}

The purpose of this work is to specify the values of θ_{down} and θ_{up} which optimize the linearization of the relationship (3), which is equivalent to seeking the constancy of the function $R(\theta, \alpha, \beta)$ between these 2 limits. The maximum variation of the θ angle during the WS ($\delta\theta_{Max}$) is given classically equal to 70° [2,3,4,5,6]. This value is recorded in Table 1 and only θ_{down} remains to be determined because:

$$\theta_{up} = \theta_{down} + \delta\theta_{Max} = \theta_{down} + 70^\circ \quad (8)$$

Determination of $R_0(\theta)$ and $S_0(\theta)$

When both α and β angles are zero, functions $R(\theta, 0, 0)$ and $S(\theta, 0, 0)$ are noted as $R_0(\theta)$ and $S_0(\theta)$, respectively. With the formula given in (D10) in Supplement S2.D, we note that the residual function (res) present in (1) and (2) is cancelled if $\beta=0$. Under these conditions, according to equations (2) and (6), the following relations are verified:

$$R_0(\theta) = S_0(\theta) = \cos \theta + \sin \theta \cdot \tan \varphi^\circ \quad (9)$$

Table 1. Geometric characteristics of a myosin II head in WS in a vertebrate half-sarcomere on the right.

Acronym	Definition	Value	Variability range
AB_X	Distance between A and B according to OX	2 nm	[0 nm ; 5 nm]
AB_Y	Distance between A and B according to OY	1.5 nm	[0.5 nm ; 3 nm]
L_{S1b}	Length of the lever S1b	10 nm	[8 nm; 11 nm]
L_{S2}	Length of the rod S2	50 nm	[30 nm ; 65 nm]
$d_{2Mfil}^{(1)}$	Distance between the centers of 2 adjacent Mfil	46 nm	[40 nm ; 55 nm]
$d_{AMfi}^{(1)}$	Distance between the centers of adjacent Afil and Mfil	26.6 nm	[23 nm ; 32 nm]
δX_{Max}	Stroke size or maximum step during the WS	11.5 nm	[10 nm; 12 nm]
$\delta \theta_{Max}^{(2)}$	Maximum variation of θ during the WS	70°	[60° ; 80°]

$$^{(1)} d_{AMfi} = d_{2Mfil} \cdot \sqrt{3}/3$$

$$^{(2)} \delta \theta_{Max} = |\theta_{up} - \theta_{down}|$$

Fig 2. Actions of the inter-segmentary links of a myosin head in Working Stroke.

Algorithmic methods

The algorithms work as follows: the θ_{down} angle is incremented from -90° to 0° with a pitch of 0.5° , i.e. a total of 181 θ_{down} values tested. At each pitch, the angle θ_{up} associated with θ_{down} is determined using equality (8).

1/ Minimization of deviations

At each iteration of θ_{down} the variable R_0 is evaluated according to (9) for θ varying between θ_{down} and θ_{up} with a pitch of 0.5° . Then the average (R_{WS}) of these 141 values of R_0 is calculated. Finally, the 141 deviations between R_{WS} and the 141 values of R_0 are characterized and summed. The value of θ_{down} for which the sum of differences is minimal is chosen.

2/ Zero slope

At each iteration of θ_{down} the slope of the regression line between the 2 variables R_0 and θ is calculated, θ being incremented between θ_{down} and θ_{up} with a pitch of 0.5° . The program searches for the value of θ_{down} for which the slope cancels out or is closest to zero, i.e. the value for which R_0 becomes independent of θ .

With respect to both methods, all calculations are performed using reference data [7.8] that are reported in the "Value" column of Table 1. In both cases, it must be ensured a posteriori that the calculation carried out between the limits θ_{down} and θ_{up} provides the value planned for δX_{Max} defined as following:

$$\delta X_{\text{Max,eq}} = | X_{\text{eq}}(\theta_{\text{up}}) - X_{\text{eq}}(\theta_{\text{down}}) | \quad (10)$$

where X_{eq} is the exact calculation of the abscissa X according to equation (D5) of Supplement S2.D, equation reproduced below :

$$X_{\text{eq}}(\theta) = L_{\text{S1b}} \cdot \sin \theta + L_{\text{S2}}^0(\theta) \cdot \cos[\varphi^\circ(\theta)] - L_{\text{S2}}^0(\theta = 0) \cdot \cos[\varphi^\circ(\theta = 0)] \quad (11)$$

where the different terms present in the right member of (11) are explained in Supplement S2.D.

All calculation algorithms have been developed with Visual Basic 6 software.

Statistics

Application of the linear regression is described in Methods section of Paper 1.

Results

Determination of θ_{down}

The plot of the R_0 function defined in (9) appears with a red line on Fig 3a. The deviation minimization algorithm applied to R_0 described in the Methods section provides the value of θ_{down} in a hs on the right:

$$\theta_{\text{down}} = -42^\circ \quad (12a)$$

The *down* position of lever S1b at the end of the WS is also called as post-powerstroke, prerecovery, like-rigor or M^* . Its angular value is given equal to 45° in modulus [9,10,11,12,13,14], which is close to the value found in (12a).

The *up* position of lever S1b at the beginning of the WS, also called as pre-powerstroke, postrecovery or M^{**} , takes for orientation according to the relations (8) and (12a):

$$\theta_{\text{up}} = -42^\circ + 70^\circ = +28^\circ \quad (12b)$$

In a half-sarcomere on the left, the boundaries θ_{down} and θ_{up} are identical in module and opposite as a sign.

Linearization of equations between θ_{down} and θ_{up}

The averages of the two functions R_0 and S_0 between the two limits θ_{down} and θ_{up} determined by (12a) and (12b) are called R_{WS} and S_{WS} , respectively. With the equality (9), the algorithmic calculations of R_{WS} and S_{WS} give (line $\beta=0^\circ$ of Table E1 of Supplement S2.E):

$$R_{\text{WS}} = \overline{R_0(\theta)} = \overline{S_0(\theta)} = 0.945 \quad (13)$$

Between θ_{down} and θ_{up} , equations (3) and (7) are approximated by the 2 respective constants R_{WS} and S_{WS} , (Figs 3a, 3b, 3c and 3d; thick black line) such that:

$$\forall \theta \in [\theta_{\text{down}} ; \theta_{\text{up}}], \quad R(\theta, \alpha, \beta) \approx S(\theta, \alpha, \beta) \approx R_{\text{WS}} = S_{\text{WS}} \quad (14)$$

Using the equalities presented in (14), we proceed between θ_{down} and θ_{up} to the linearization of equations (3) and (7), respectively:

$$u \approx \dot{\theta} \cdot L_{\text{S1b}} \cdot R_{\text{WS}} \quad (15)$$

$$\mathcal{M}_B \approx T_A \cdot L_{\text{S1b}} \cdot S_{\text{WS}} \quad (16)$$

Fig 3. Evolutions of $R(\theta, \alpha, \beta)$, $S(\theta, \alpha, \beta)$ and $res(\theta, \alpha, \beta)$ in function of θ varying between -70° and $+60^\circ$ according to 4 values from β with $\alpha=0^\circ$.
(a) $\beta = 0^\circ$; (b) $\beta = 20^\circ$; (c) $\beta = 40^\circ$; (d) $\beta = 60^\circ$.

Scope of validity of the linearization according to β

The angle β varies between -60° and $+60^\circ$; see expression (G9) of Supplement S3.G of accompanying Paper 3. In equations (2), (3), (6), (7) and (9), only the cosine of β is involved, so the study of the positive values of β is sufficient. The functions $R(\theta,0,\beta)$, $R(\theta,0,\beta)$ and $res(\theta,0,\beta)$ are represented as a function of θ by red, blue and green lines, respectively, in Figs 3b, 3c and 3d for 3 β values (20° , 40° and 60°).

With 2% tolerance for R_{WS} , the calculations presented in Table E1 of supplement S2.E indicate that the approximations established in formulae (13) to (16) remain valid under the following condition:

$$-45^\circ \leq \beta \leq +45^\circ \quad (17)$$

This specification will be required for the realization of a WS with the modalities determined by the data in Table 1.

Linear relationship between the displacement of a hs and the rotation of the lever belonging to a head in working stroke

By arbitrarily matching the zero of the abscissa X with the zero of the angular positions θ and after integrating equation (15), the relationship between the abscissa (X_{lin} ; lin for *linear*) and θ is written:

$$X_{lin} \approx (L_{Sib} \cdot R_{WS} \cdot \theta) \cdot \mathbf{1}_{[\theta_{down}; \theta_{up}]}(\theta) \quad (18)$$

where $\mathbf{1}$ is the indicator function defined in (A2b) in Supplement S1.A of Paper 1.

With the values of θ_{down} and θ_{up} fixed in (12a) and (12b) and by respecting the conditions dictated in (17), the adequacy between the X_{eq} and X_{lin} abscissa formulated according to (11) and (18) is verified by linear regression for the 141 values of θ varying between θ_{down} and θ_{up} with a 0.5° pitch. The determination coefficient is higher than 99.9% in all cases; see Figs 4a, 4b and 4c where the X_{eq} and X_{lin} abscissa are represented as a function of θ by a pink and black line, respectively, for 3 values of the angle β .

From (18) we derive the linear relationship between the algebraic displacement of the hs (ΔX) and the corresponding rotation of the lever ($\Delta\theta$) defined as:

$$\Delta X \approx (R_{WS} \cdot L_{Sib} \cdot \Delta\theta) \cdot \mathbf{1}_{[\theta_{down}; \theta_{up}]}(\theta) \quad (19)$$

Fig 4. Evolutions of X_{eq} and X_{lin} abscissa in function of θ varying between -70 and $+60^\circ$ according to 3 values of β with $\alpha=0^\circ$. The determination coefficient (r^2) is calculated by linear regression of X_{eq} as a function of X_{lin} between θ_{down} and θ_{up} .

(a) $\beta = 0^\circ$. (b) $\beta = 30^\circ$. (c) $\beta = 45^\circ$.

Maximum step of one myosin head during WS (stroke size)

The maximum shortening of the hs (δX_{Max}) corresponding to $\delta \theta_{\text{Max}}$ is called "stroke size". It is calculated according to the linear approximation provided in (19):

$$\delta X_{\text{Max,lin}} \approx (R_{\text{WS}} \cdot L_{\text{S1b}}) \cdot \delta \theta_{\text{Max}} \quad (20)$$

Note that the lever arm is not equal to L_{S1b} but to $(R_{\text{WS}} \cdot L_{\text{S1b}})$.

For work on intact vertebrate fibers, the stroke size generally varies between 10 and 12 nm [4,5,15,16,17,18,19]. The mean value of 11.5 nm is used for δX_{Max} confirmed by numerical application with the R_{WS} value determined in (13) and the data from Table 1:

$$\delta X_{\text{Max,lin}} \approx 0.945 \cdot 10 \text{ nm} \cdot (70^\circ \cdot \pi / 180^\circ) \approx 11.5 \text{ nm} \quad (21)$$

All tables in Supplement S2.E display in columns 4 and 5 the maximum steps $\delta X_{\text{Max,eq}}$ and $\delta X_{\text{Max,lin}}$ calculated according to relations (10) and (20), respectively. In all cases with the condition imposed in (17), the difference between the calculations of the 2 steps does not exceed 2%.

From now on, the stroke size (δX_{Max}) will be calculated according to (20).

Influence of the algorithmic method

With the zero slope method (see Methods section) used in paragraph E.2 of Supplement S2.E, there is a $+1^\circ$ difference compared to the values determined in (12a) and (12b) with the deviation minimization method. The data in Table E2 lead to conclusions similar to those in the previous paragraph. For all cases tested under identical conditions, the zero slope method provides similar results to the minimization of deviations, the difference for the values of θ_{down} and θ_{up} never exceeding 1° .

Negligible influence of α

The angle α varies between -30° and $+30^\circ$; see expression (G5) of Supplement S3.G of accompanying Paper 3. The calculations made in Tables E3a and E3b of section E.3 in Supplement S2.E show that the value of α does not modify the conclusions indicated previously.

Influence of lever length

The angles θ_{down} and θ_{up} are estimated with a standard L_{S1b} value equal to 10 nm [20,21]. In paragraph E.4 of Supplement S2.E, two other L_{S1b} values are tested: calculations with these 2 data yield deviations of $\pm 0.5^\circ$ for θ_{down} and θ_{up} . The reckonings exposed in Tables E4a and E4b induce conclusions consistent with those obtained when L_{S1b} is equal to 10 nm. The main difference is in the stroke size (δX_{Max}) assessed at 11 and 12 nm for L_{S1b} equal to 9.5 and 10.4 nm, respectively. These results are logically ensued from the equality (20).

Significant influence of inter-filament spacing (lattice)

In the previous calculations, the distance between 2 myosin filaments (d_{2Mfil}) is equal to 46 nm (Table 1) as provided for the standard value in a skeletal fiber [7.8]. In paragraph E.5 of Supplement S2.E, two other d_{2Mfil} values were tested, 42 and 50 nm, for which respective deviations of $+3^\circ$ and -3° are noted with respect to the data seen in (11) and (12) for θ_{down} and θ_{up} . There is a marked influence of the lattice on the θ angle in accordance with experimental observations: see Fig 8 in [22] and Fig 4 in [23] where the temperature rise increases the inter-filament spacing.

In conclusion, to take into account the variability of the data and methods of calculations, the values of θ_{down} and θ_{up} are specified with a common variability of $\pm 5^\circ$.

Discussion

Hypothesis of the lever moving in a fixed plane during the Working Stroke

Extensive crystallographic and electron microscopy observations of the movement of the myosin head carried out *in situ* will reveal the validity of this assumption. However, there are concrete elements to support this hypothesis.

The idea that the movement of the myosin head is achieved in the same plane and therefore in a single direction is suggested on page 63 of the article princeps from I. Rayment [1] :

« However, the structure of the myosin head suggests that the power stroke arises from the reversal of domain movement in the myosin heavy chain induced by nucleotide binding ... An immediate suggestion is that myosin forms a tight interaction with actin in only one orientation. »

The article by A. Houdusse [11] evokes this point : *« The converter rotates about 65° between the transition and nucleotide-free states of scallop S1 and leads to a movement of the lever arm between these states that has a very small azimuthal component. »*

S. Hopkins' work [24] reinforces the hypothesis, as an excerpt from the abstract indicates:

« We applied rapid length steps to perturb the orientations of the population of myosin heads that are attached to actin, and thereby characterized the motions of these force bearing myosin heads. During active contraction, this population is a small fraction of the total. When the filaments slide in the shortening direction in active contraction, the long axis of LCD tilts towards its nucleotide-free orientation with no significant twisting around this axis. In contrast, filament sliding in rigor produces coordinated tilting and twisting motions. »

Or Arakelian's [25] as suggested by an excerpt from the summary:

« We hypothesized that an azimuthal reorientation of the myosin motor domain on actin during the weak-binding to strong-binding transition could explain the lever arm slew provided that myosin's α -helical coiled-coil subfragment 2 (S2) domain emerged from the thick filament backbone at a particular location. »

If in our model the point A of fixing S1a on the surface of the actin molecule is unique, S1a is in reality strongly linked at several points [26,27,28,29], i.e. a precise and identical orientation for each S1a of a WS head towards the longitudinal axis of the Afil. Several studies [27,28] indicate a rotation of the mechanically guided lever S1b within the converter belonging to the motor domain, which again implies a single orientation.

In paragraph F.4 of Supplement S2.F, a mechanical study relating to the set of the WS myosin heads in a muscle fiber leads to two formulations of the force exerted at the ends of a myofibril, one by applying the linear and angular moment principles, the other according to the work-energy theorem. The equality between the 2 terms R_{WS} and S_{WS} delivered in (14) and the collinearity along the Oz axis of the vectors "moment" and "S1b angular rotation speed" for each moving WS head are essential so that the 2 expressions are equal. Precisely the hypothesis 4 of the lever moving in a fixed plane during the WS brings these 2 conditions.

Corollaries of the hypothesis

The double helix structure of the Afil (see Supplement S3.G to Paper 3) prevents the two heads of a myosin molecule from being simultaneously in WS state. Indeed the two heads being attached to two distinct actin molecules, their respective levers would each evolve with a different angle β . However, S2 being the common rod linking at the Mfil, it is geometrically impossible that the two angles β remain constant when the Afil moves relative to the Mfil along the longitudinal axis OX. The corollary is documented by several researchers [30,31].

The equality (20) indicates a proportionality relationship between the stroke size (δX_{Max}) and the length of the lever (L_{S1b}), a relationship observed experimentally [21,32]. Equality (20) is another relationship of proportionality between δX_{Max} and $\delta \theta_{Max}$, also interpreted [33].

Conclusion

With the knowledge of the angles α , β and θ , the hypothesis of the lever displacement in a fixed plane allows the complete geometrization of the cross-bridge formed by a WS myosin head. Consequently, the relative position of the Mfil with respect to the Afil makes it possible to check if the WS state is feasible or not and in the confirmed case, to calculate the orientation θ of the lever. By applying this rule to an idealized half-sarcomere, it becomes possible to know the statistical distribution of θ . This is the subject of the study proposed in accompanying Paper 3.

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Supporting information

S2.C Supplementary Chapter. Forces and energies involved in the working stroke of a myosin II head.

- C.1 Units at the scale of a myosin head
- C.2 Brownian displacements and thermal shocks
- C.3 Hydrolysis of an ATP molecule and maximum tensile force of a myosin II head
- C.4 Strong binding (SB)
- C.5 Weak binding (WB)
- C.6 Acceleration quantities of gravitational origin
- C.7 Acceleration quantities of inertial origin
- C.8 Archimedes' Forces
- C.9 Viscous type friction forces
- C.10 Conclusion

References of Supplement S2.C

S2.D Supplementary Chapter. Kinematics and dynamics of a myosin head in Working Stroke.

- D.1 Calculations relating to the kinematics of a WS myosin head with Fig D1
- D.2 Calculations relating to the dynamics of a WS myosin head in a right hs shortening at constant velocity with Fig D2

S2.E Supplementary Chapter. Influence of various parameters on the 4 variables $\bar{R}$, $\bar{S}$, $\delta X_{Max,eq}$ and $\delta X_{Max,lin}$.

E.1 Influence of β displayed in Table E1

E.2 Influence of the algorithmic method displayed in Table E2

E.3 Influence of the angle α tested with $\alpha = +30^\circ$ (Table E3a) and $\alpha = -30^\circ$ (Table E3b)

E.4 Influence of the lever length with $L_{S1b} = 9.5$ nm (Table E4a) and $L_{S1b} = 10.4$ nm (Table E4b)

E.5 Influence of the inter-filament distance with $d_{2Mfil} = 42$ nm (Table E5a) and $d_{2Mfil} = 50$ nm (Table E5b)

S2.F Supplementary Chapter. Kinematics and dynamics of a stimulated muscle fiber and a myofibril.

F.1 Isolated fiber with Fig F1

F.2 Kinematics of a myofibril in the shortening or lengthening phase

F.3 Dynamics of a myofibril shortening or lengthening at constant speed with Fig F2

F.4 Theorem of work- energy applied to a muscle fiber shortening or lengthening at constant speed

References of Supplement S2.F

CP2 Supplementary Material. Computer Programs for calculating the variables, X_{eq} , X_{lin} , R , S , res, and plotting the 5 variables as a function of θ . Algorithms are written in Visual Basic 6.

DA2 Supplementary Material. Data relating to computer programs used for Paper 2. Access Tables are transferred to Excel sheets.