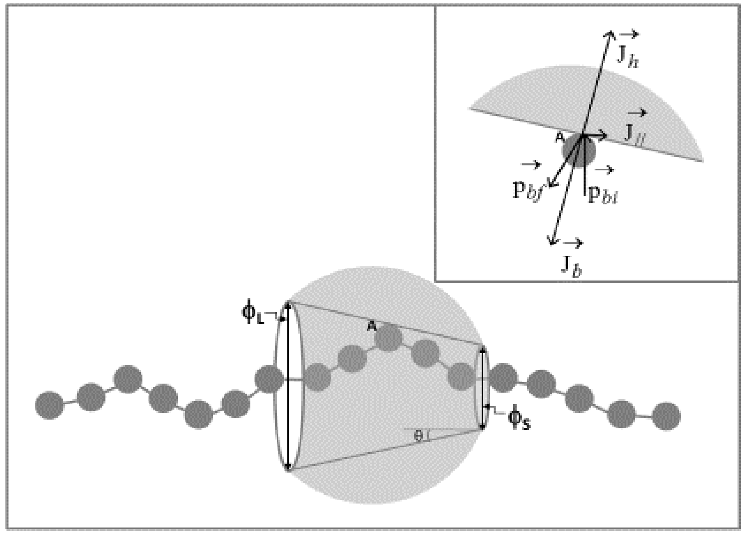
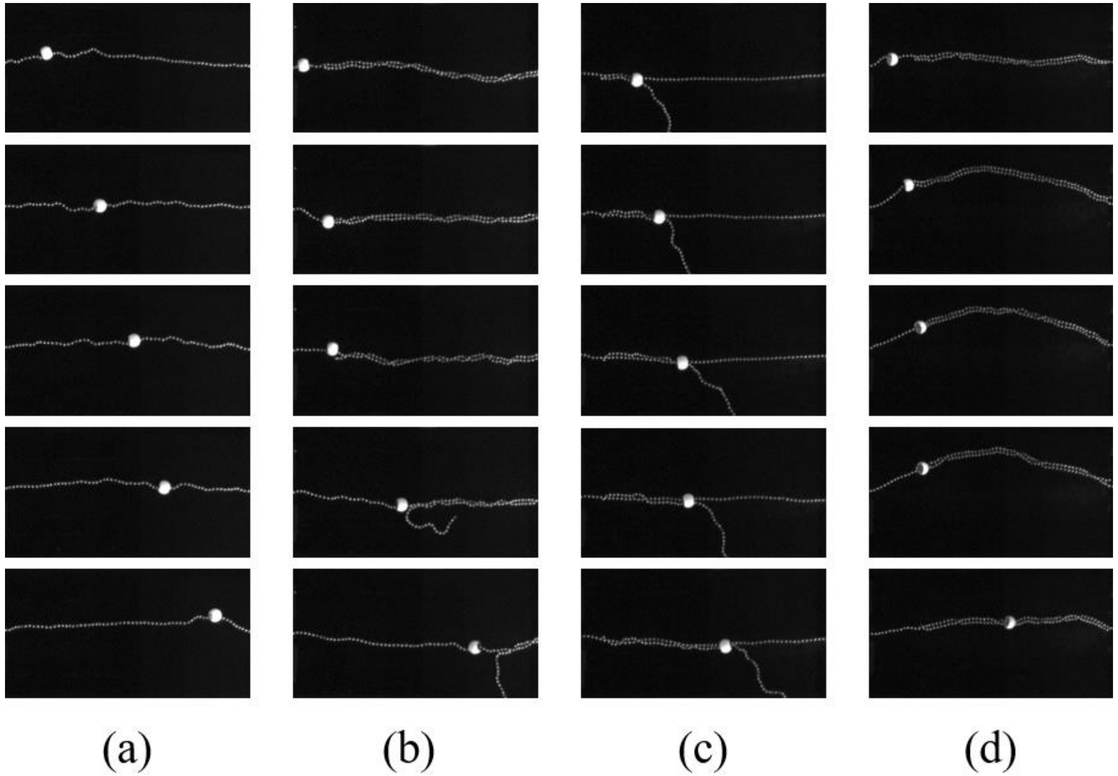
A mechanical mechanism for translocation of hexameric and nonstructured helicases

Ya-chang Chou*

Department of Physics, National Tsing-Hua University, Hsinchu, Taiwan, Republic of China

E-mail: ycchou@phys.nthu.edu.tw





The basic concepts of the existing chemomechanical mechanisms of translocation of helicases on DNA

(1) Helicase has at least two independent binding sites on DNA.
(2) The sequence of DNA binding and releasing depends on NTP hydrolysis.
(3) A power stroke from conformation change of helicase push it moving.

Disadvantage:

The mechanical nature of the power stroke is not clear.

The physical mechanical mechanism

Basic concepts:

(1) The thermal motions of DNA and helicase are ubiquitous and vigorous in the nano-meter scale.

(2) The isotropic random thermal motion can be rectified by the asymmetric structures of helicases to generate directional motion.

(3) The asymmetries in the central holes of the two-layered ring structure of the hexameric helicases and the cleft of the non-structured helicases are essential.

(4) The random collisions between the DNA strand and the helicase in the central channel (or cleft) generate impulsive forces on helicase toward the small end (as shown in the Graphic Abstract).

(5) The small end leads the translocation.

(6) Entropic consideration gives the same conclusion.

Estimation of the average force generated (from Graphic Abstract (GA)):

$$F = mv_i^2 \sin 2\theta / l \sim (3k_BT \sin 2\theta)/l,$$ l is the average channel width.

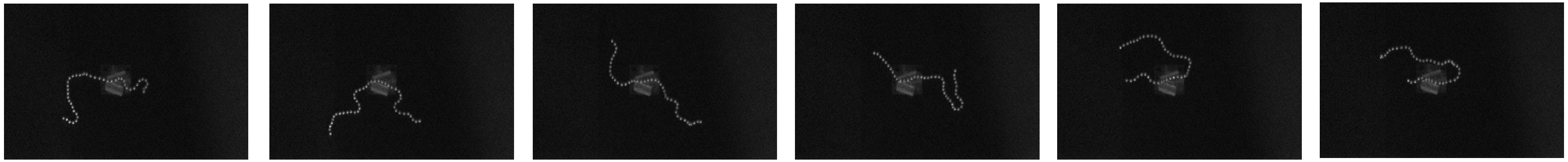
With $k_BT = 4$ nm.pN, taking $l = 4$ nm, $\theta \approx 45^\circ$,

$F \approx 3$ pN, which is close to the stall force of the molecular motors.

Demonstrations of functions of helicases according to mechanical mechanism in simulation experiments:

1. Translocation on single strand chain: (Shown in column (a) of GA).
2. Unwinding of double-strand chain: (column (b) of GA).
3. Rewinding of two separated single-stranded chains: (column (c) of GA).
4. Strand switching: (column (d) of GA).

Demonstration of the translocation of non-structured helicases



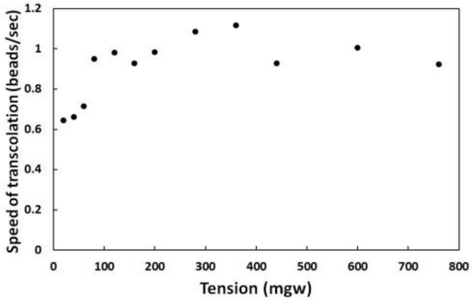
The mechanical mechanism explains the reported behaviors of helicases well.

Dependence on physical parameters: (common to all helicases, only mechanical mechanism can explain.)

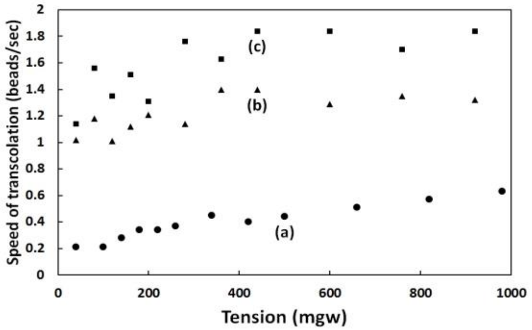
(a) For hexameric helicases, translocation is led by the small end.

	Helicase	Domain ahead	Small end ahead?
Eukaryotic	E1	NTD	Yes
	CMG	NTD	Yes
Bacterial	DnaB	CTD	Yes
	T7	CTD	Yes
	Rho	CTD	Yes

(b) Effect of applied tension on chain.



(c) Effect of stiffness of chain



stiffness: (a)<(b)<(c)

Summary:

(a) The mechanical mechanism is generally applicable to the two major categories of helicases: hexameric and non-structured helicases.

(b) The role of hydrolysis of ATP is to indirectly provide energy for the translocation of helicases, through locally enhancing the random motion of DNA and helicases.

(c) Applicability of the mechanism can be extended to other molecular motors having the similar asymmetric structures, such as packaging motor of phages, claw-shaped motors of polymerase and Hsp70 chaperones.