



the
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international centre for theoretical physics

ICTP 40th Anniversary

SMR 1564 - 21

SPRING COLLEGE ON SCIENCE AT THE NANOSCALE
(24 May - 11 June 2004)

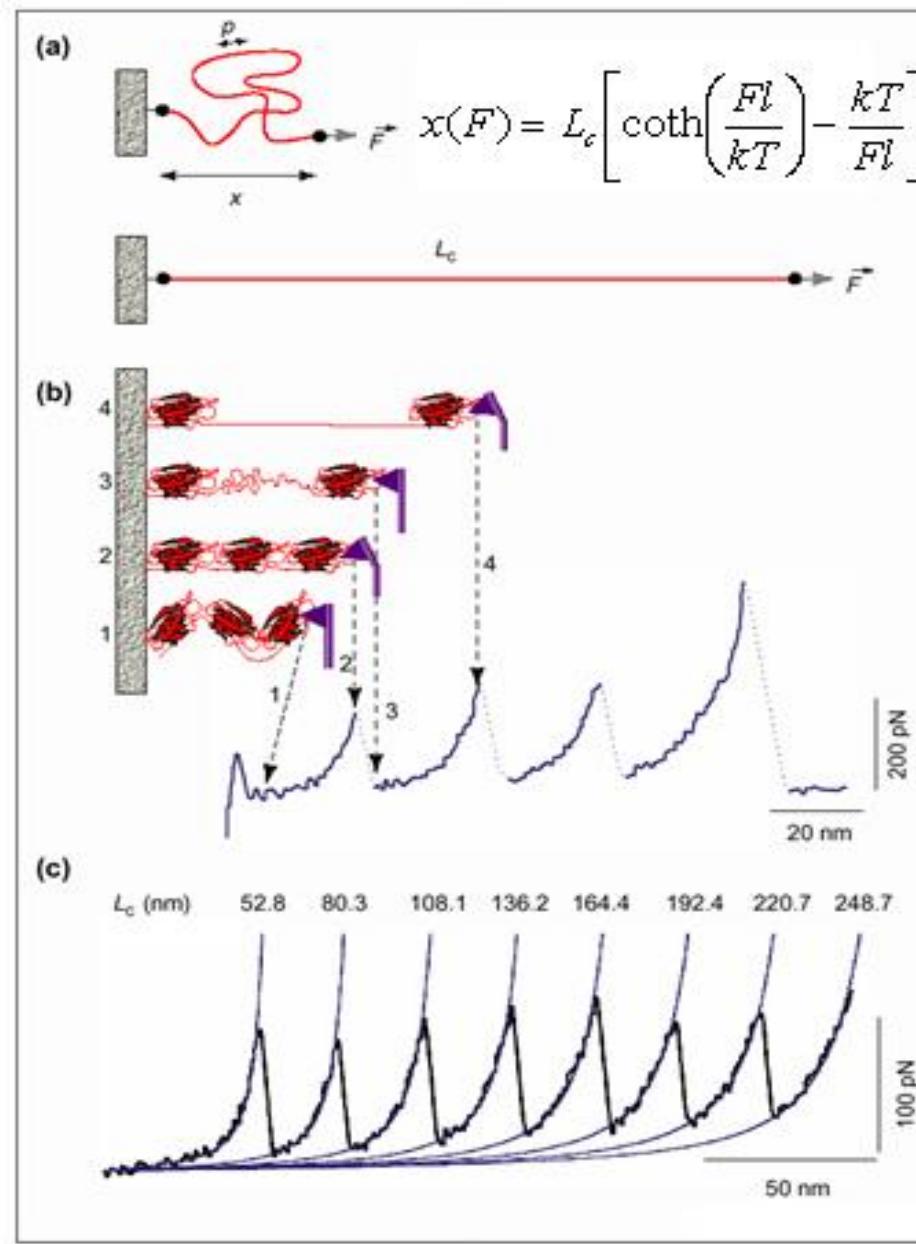
SINGLE MOLECULE BIOPHYSICS - Part II

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Fernandez Laboratory
New York, U.S.A.

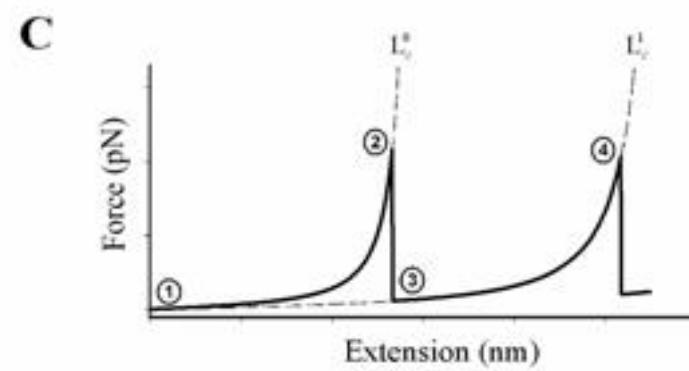
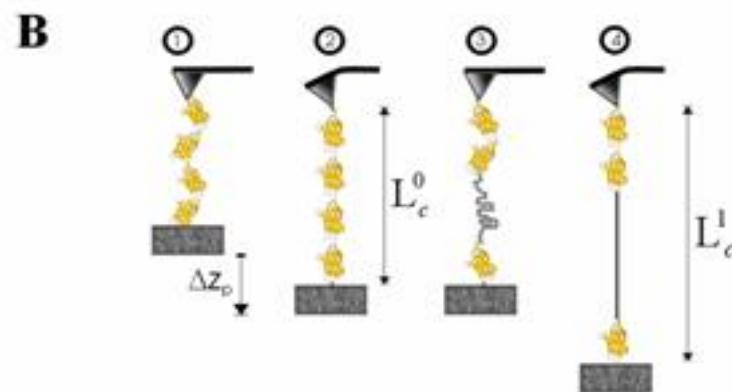
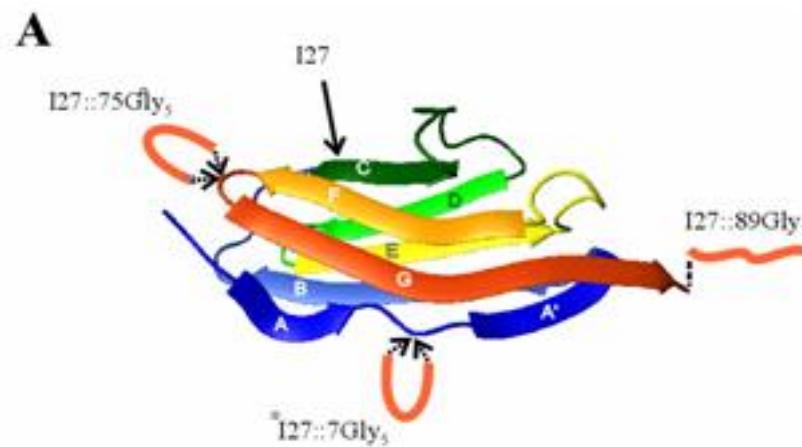
These are preliminary lecture notes, intended only for distribution to participants.

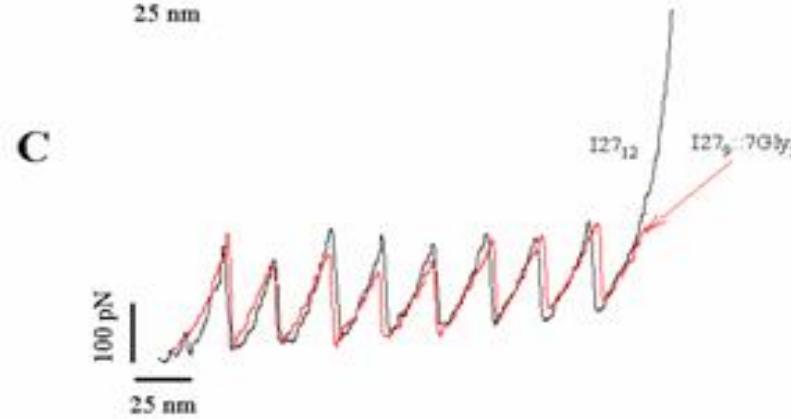
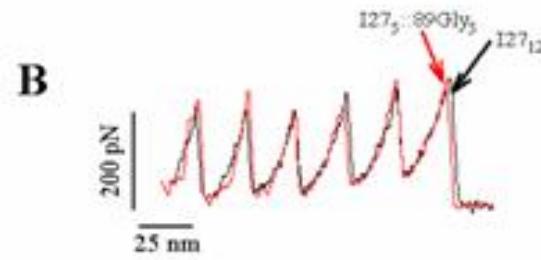
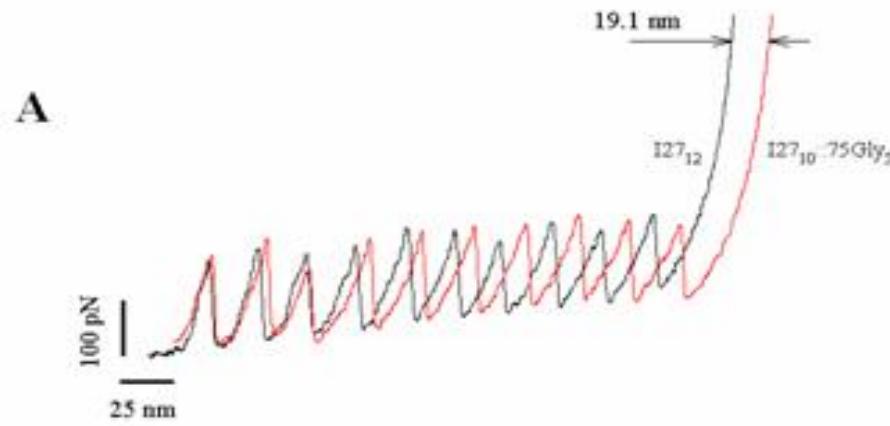
Mechanics of single molecules

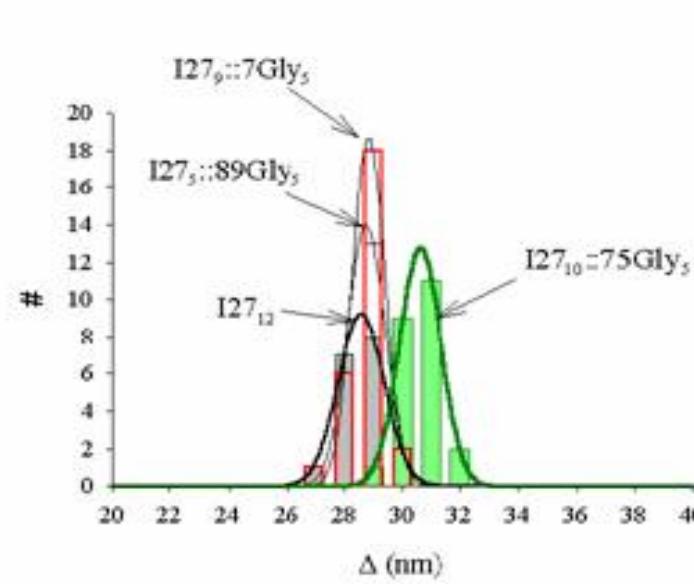
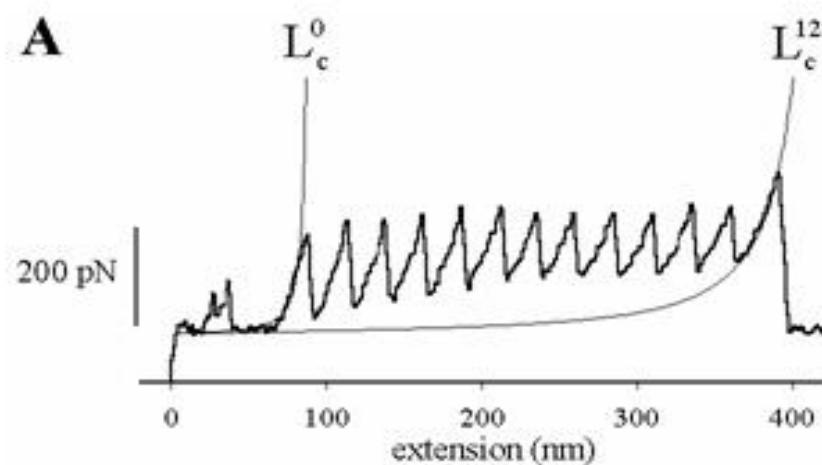
A comparison of the mechanical properties of proteins,
polysaccharides and gold nanowires

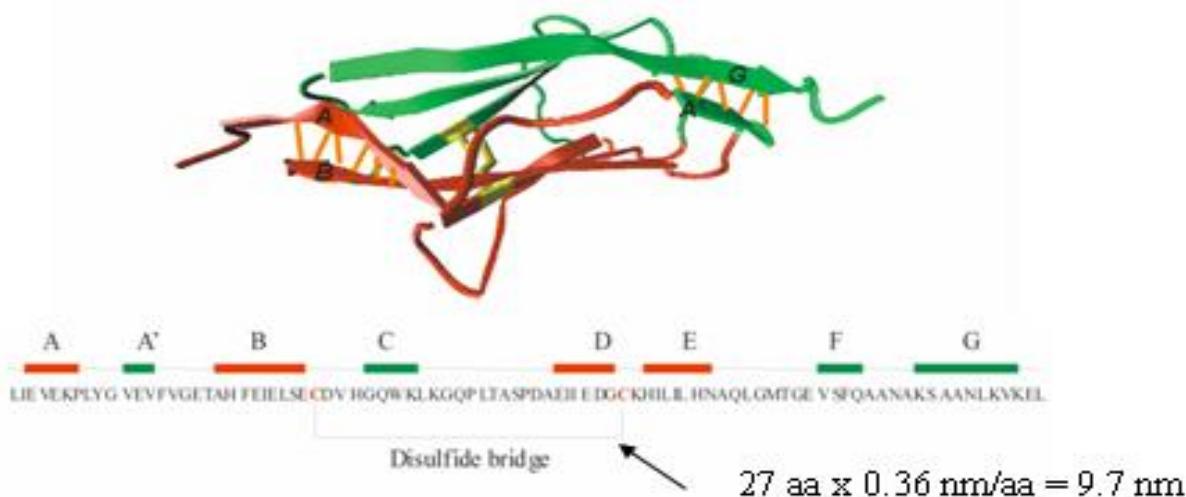


Igor Demonstration of actual data and its analysis with models of polymer elasticity



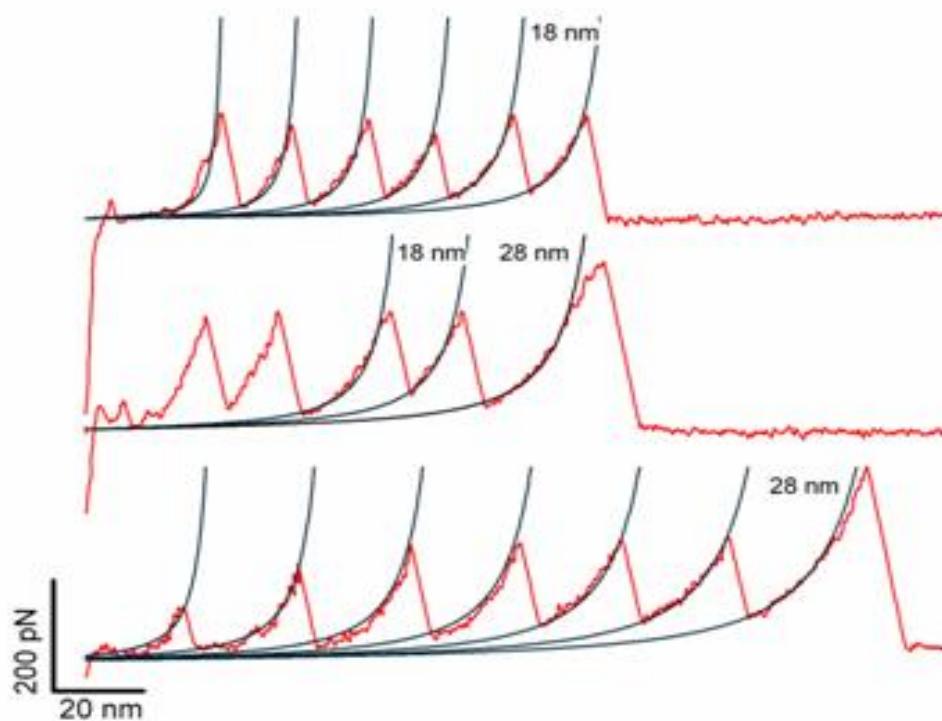






10 mM DTT

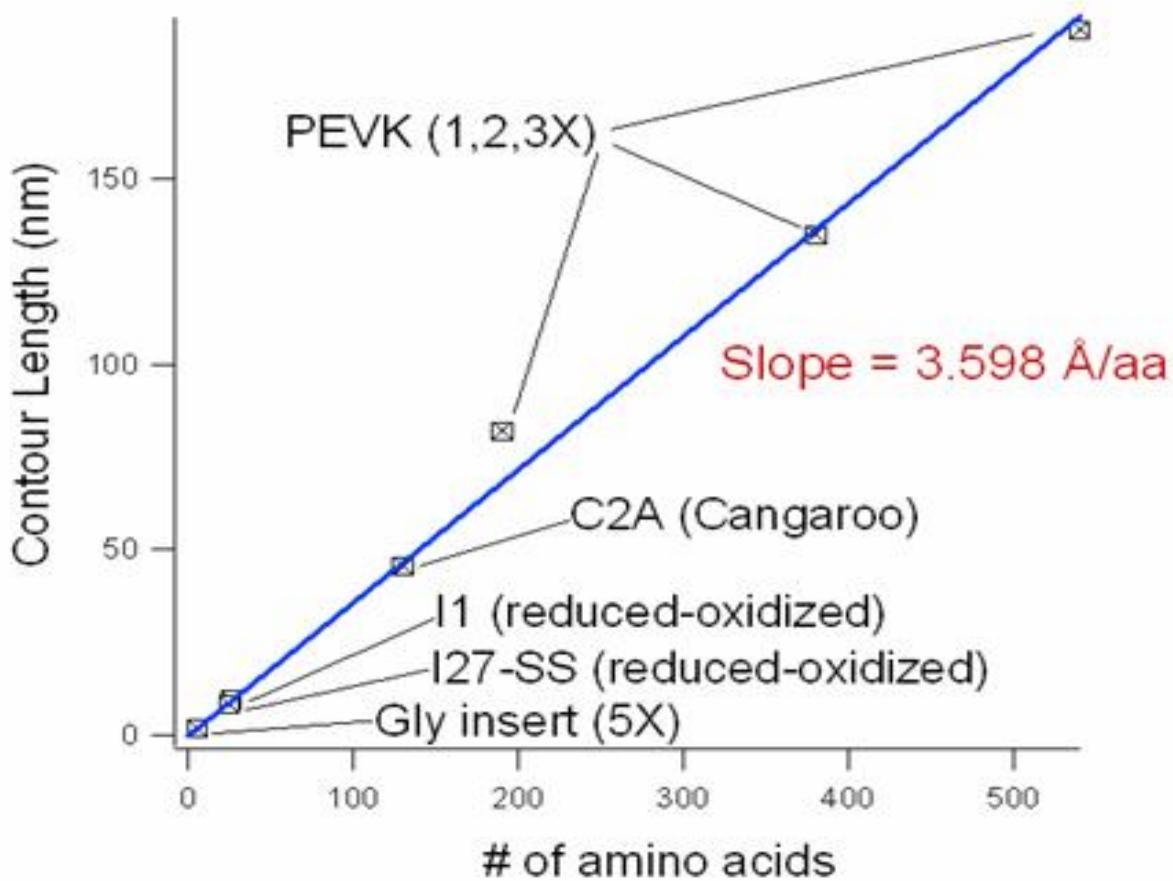
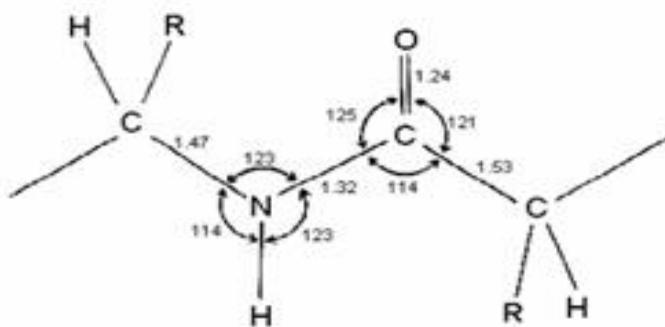
t=0 min



$(\text{I27-C}_28\text{C}_{54})_8$

t=120 min

T> 12 hrs.

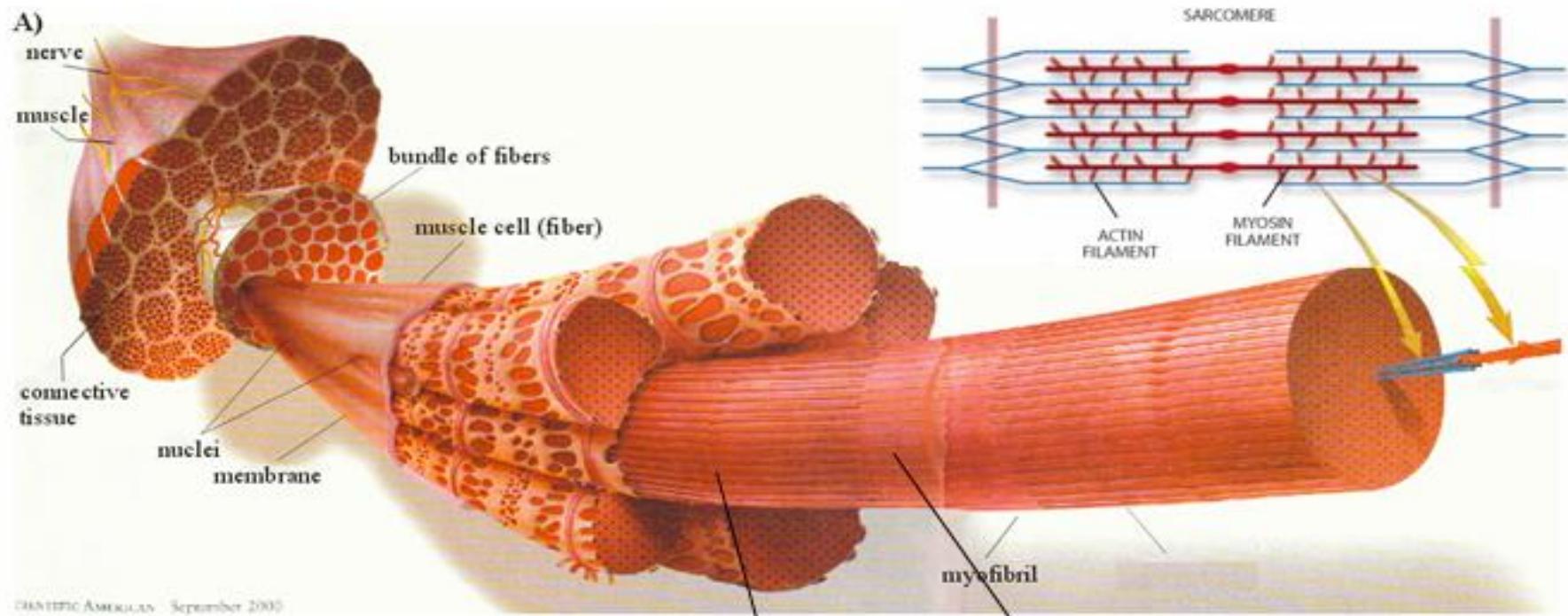


Reverse Engineering of Titin

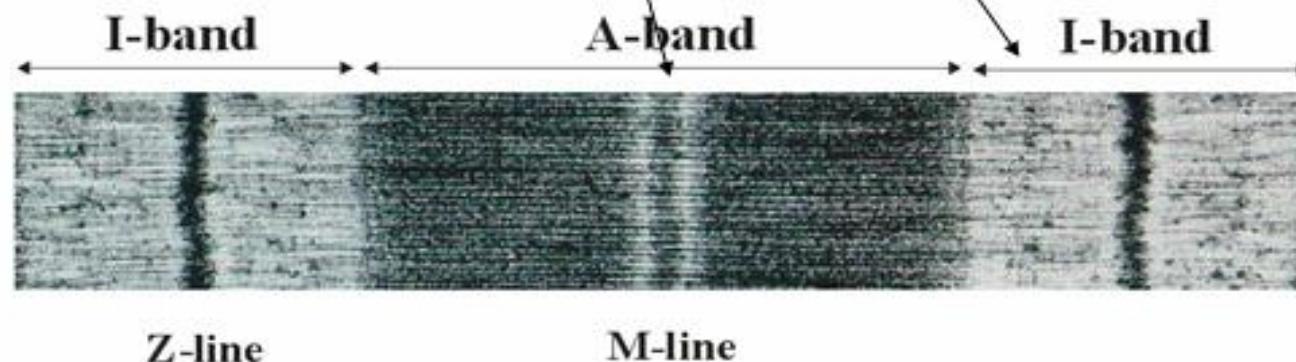
Hypothesis: Muscle elasticity results from the nano-mechanics of titin

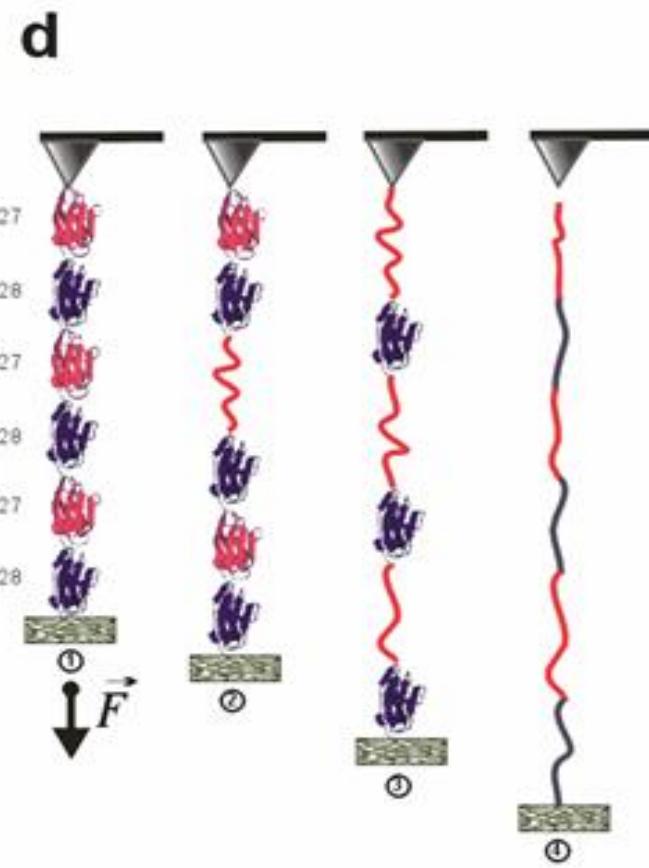
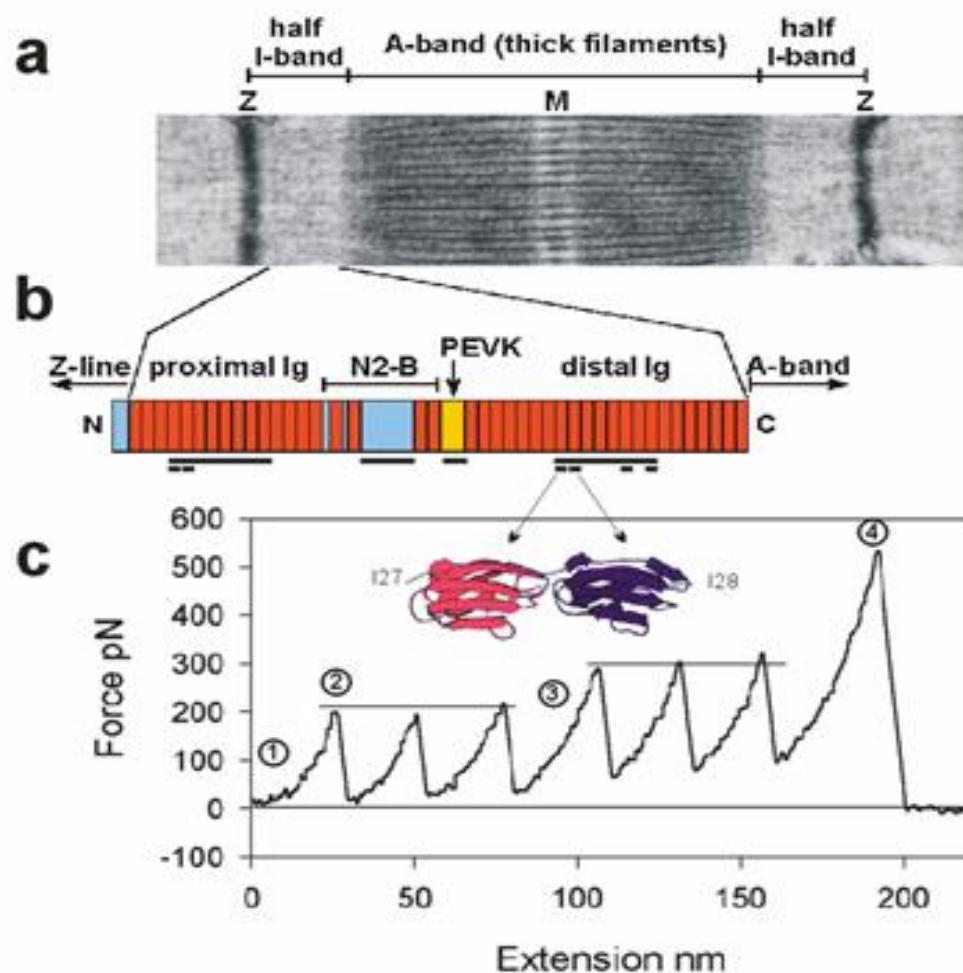
Experimental design: examine the mechanical architecture of individual titin modules, add up their extensibility and scale to whole tissue.

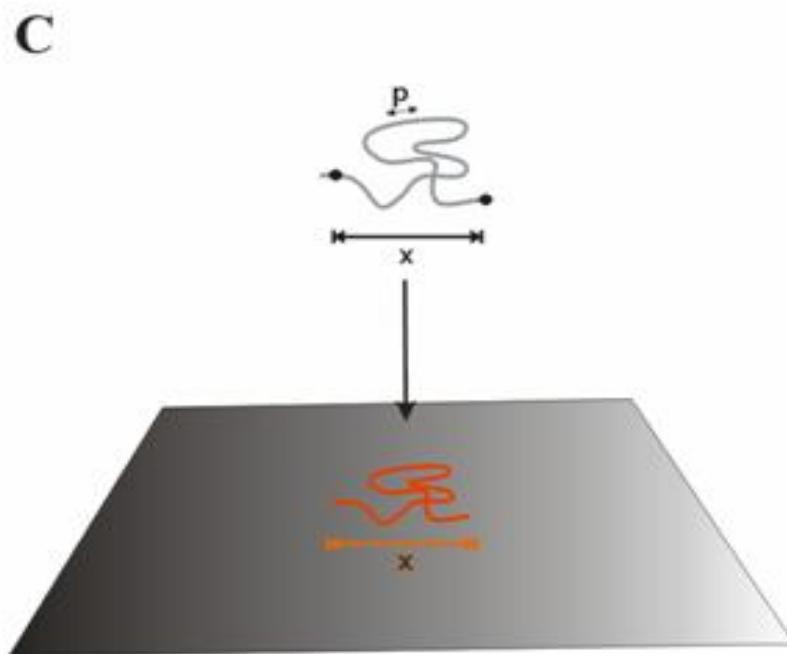
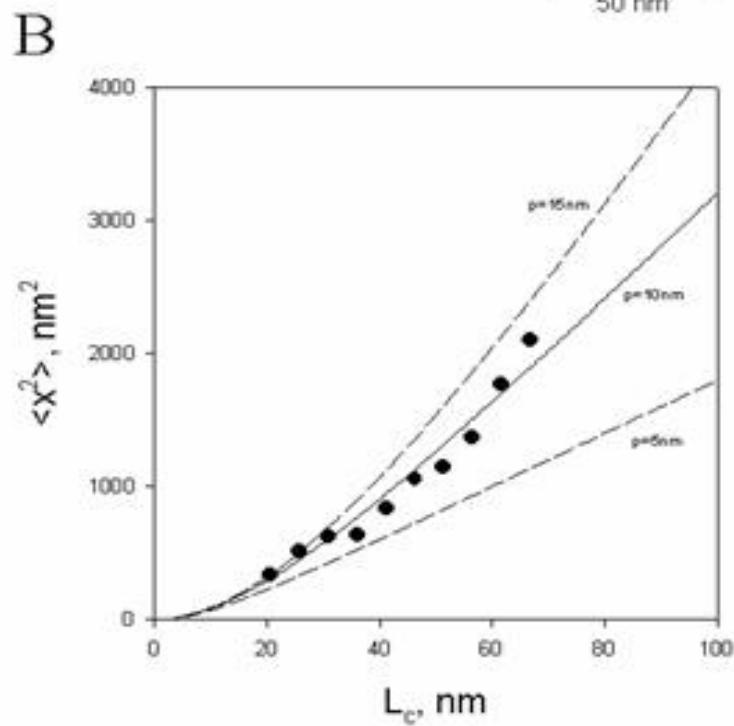
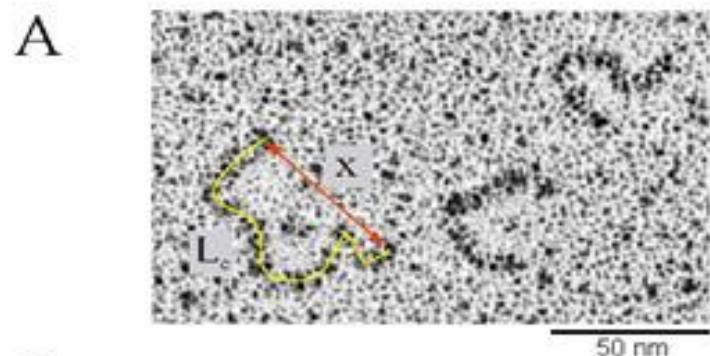
Muscle can contract and also can extend elastically



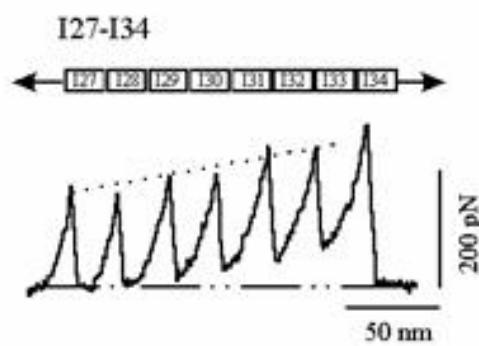
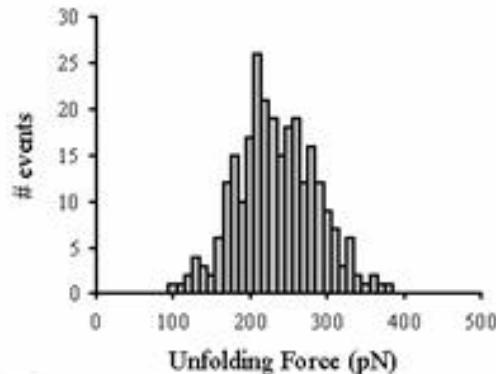
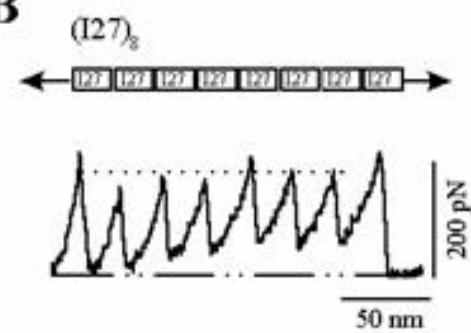
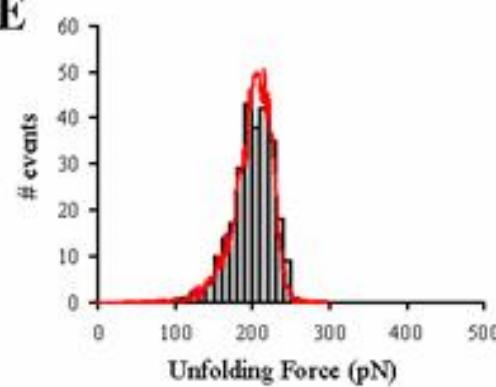
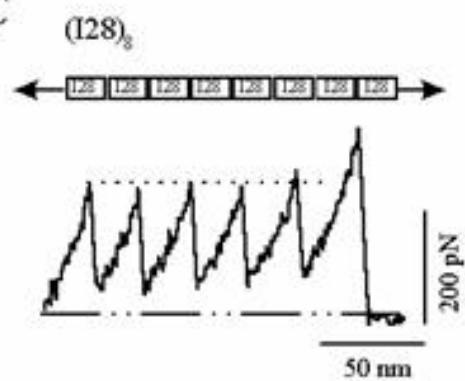
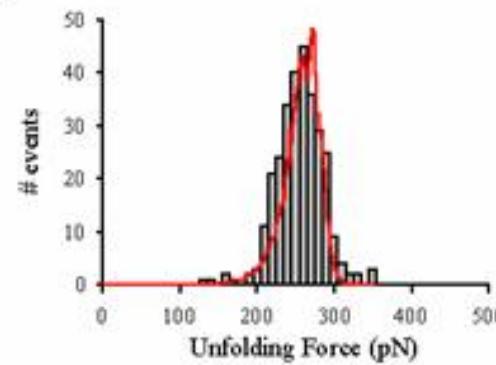
CARTERIC AMERICAN September 2000

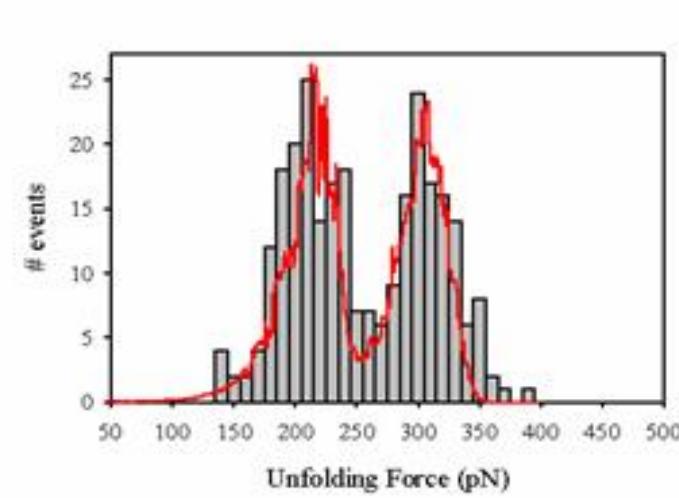
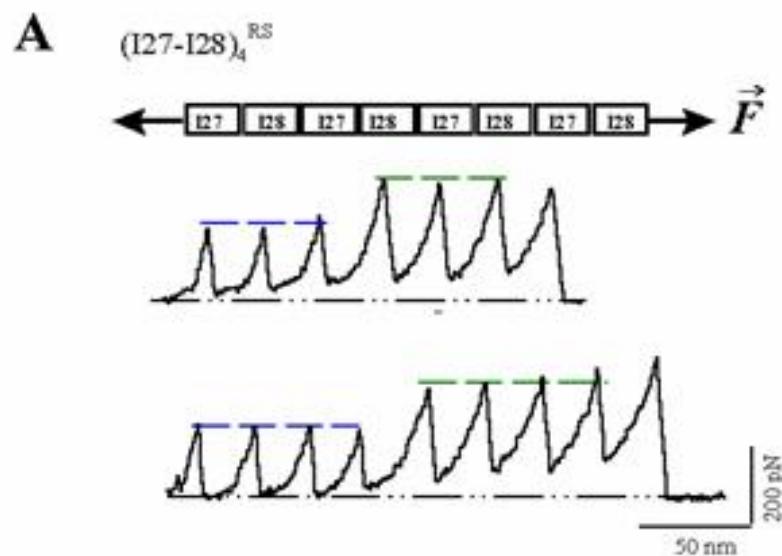




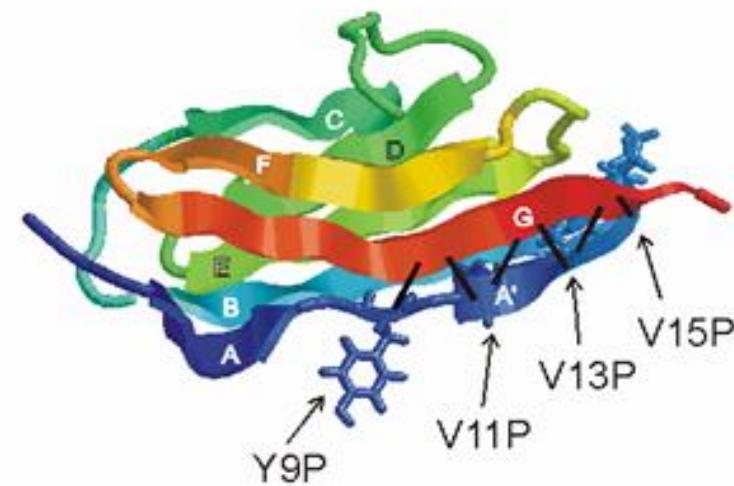


$$\langle x^2 \rangle_{2D} = 4pL_c \left(1 - \frac{2p}{L_c} \left(1 - e^{-\frac{L_c}{2p}} \right) \right)$$

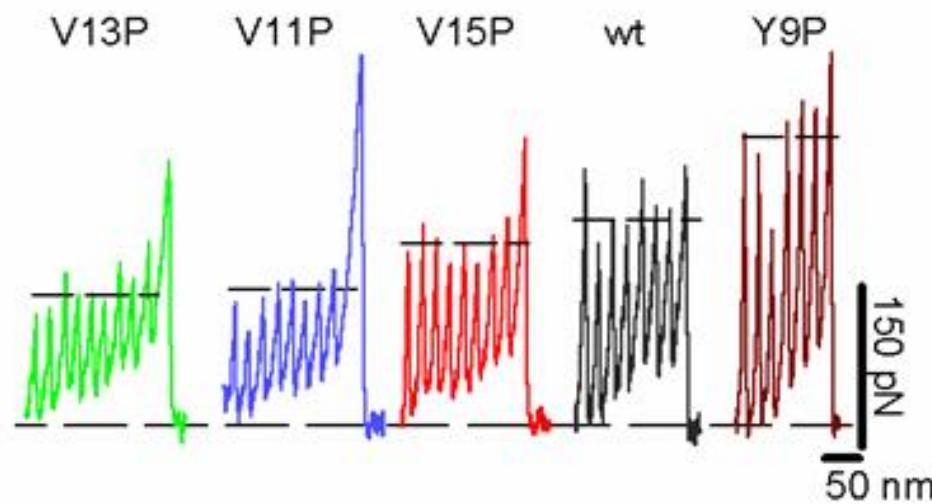
A**D****B****E****C****F**

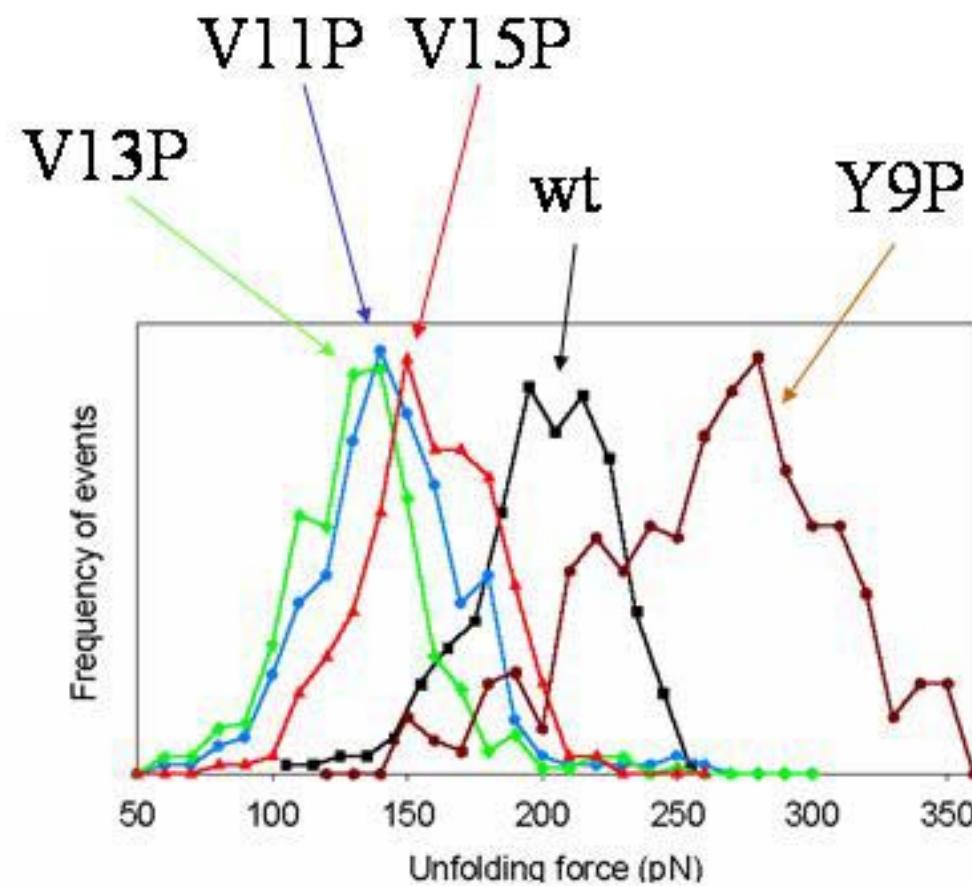


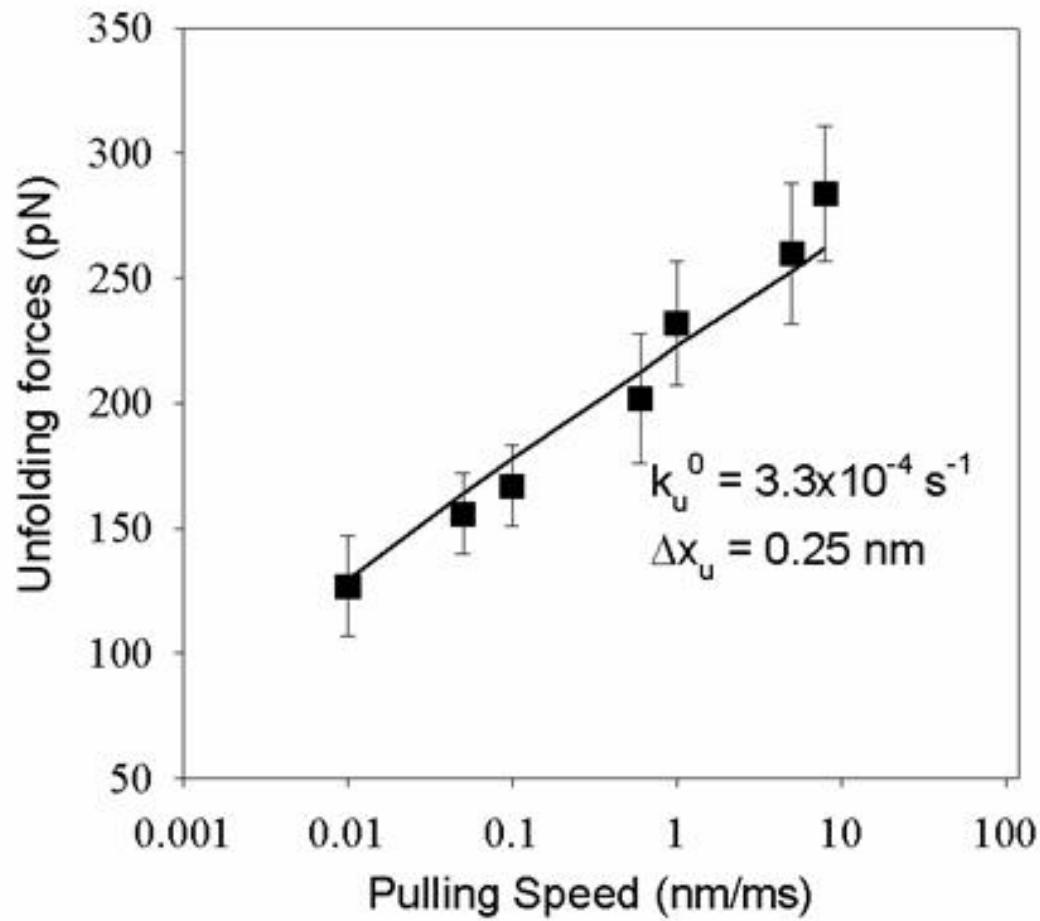
a

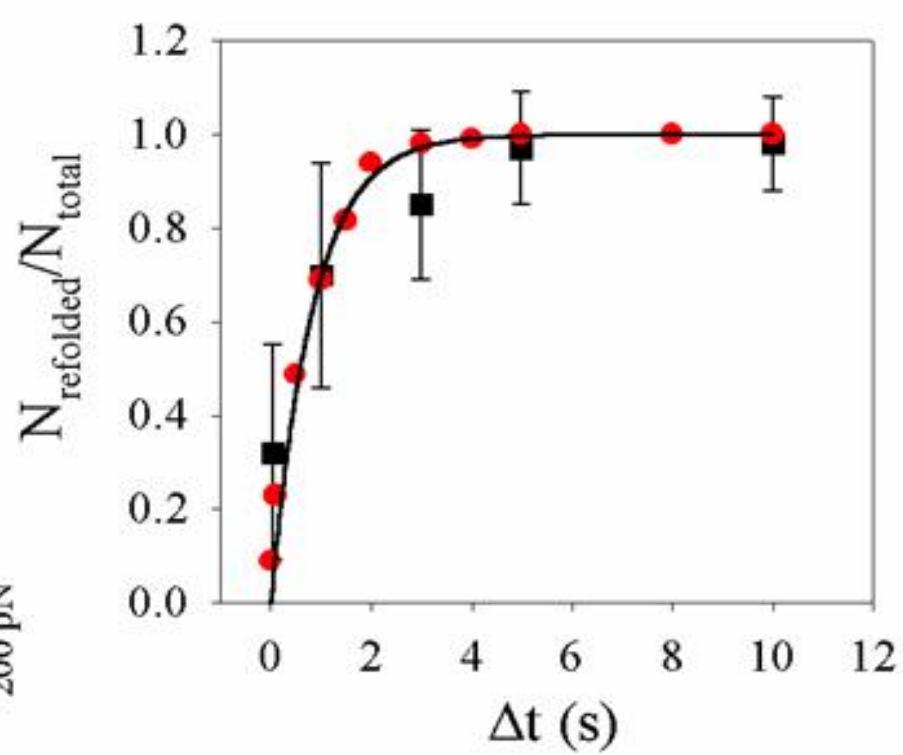
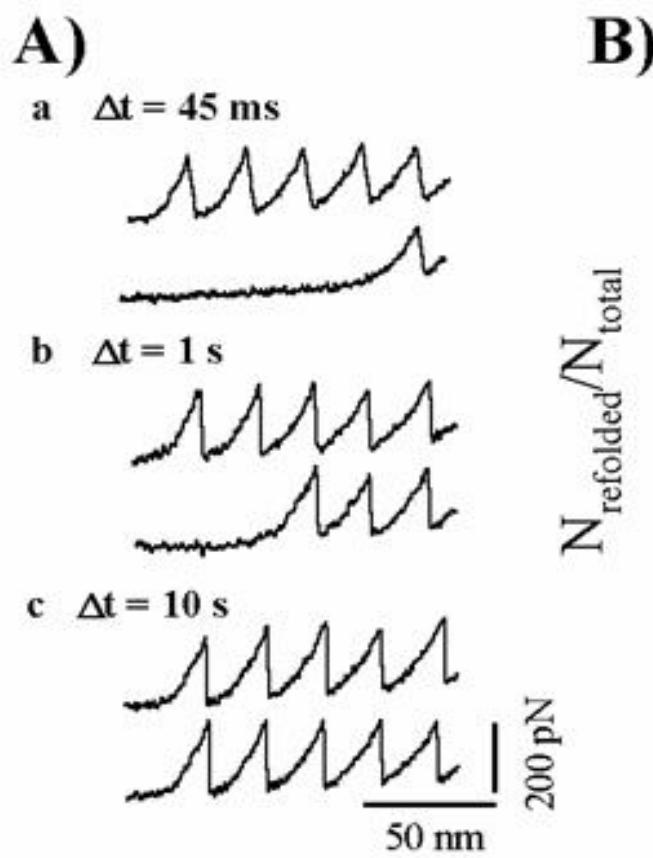


b

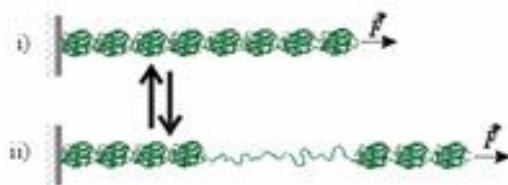




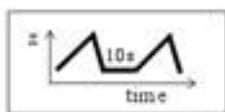




a



b



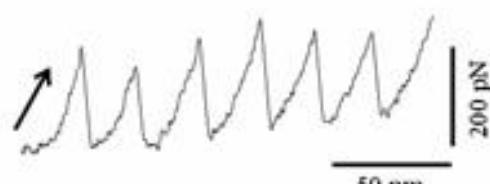
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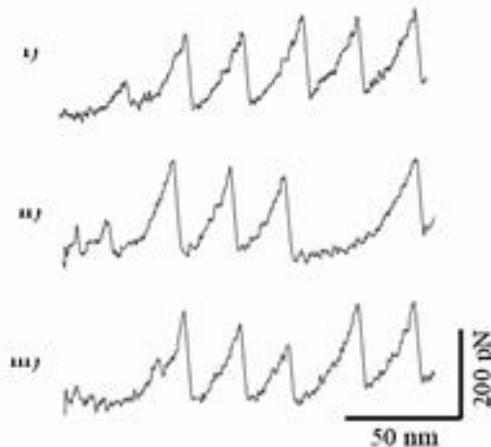
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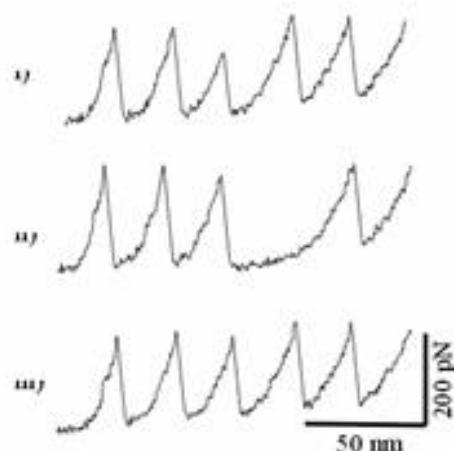
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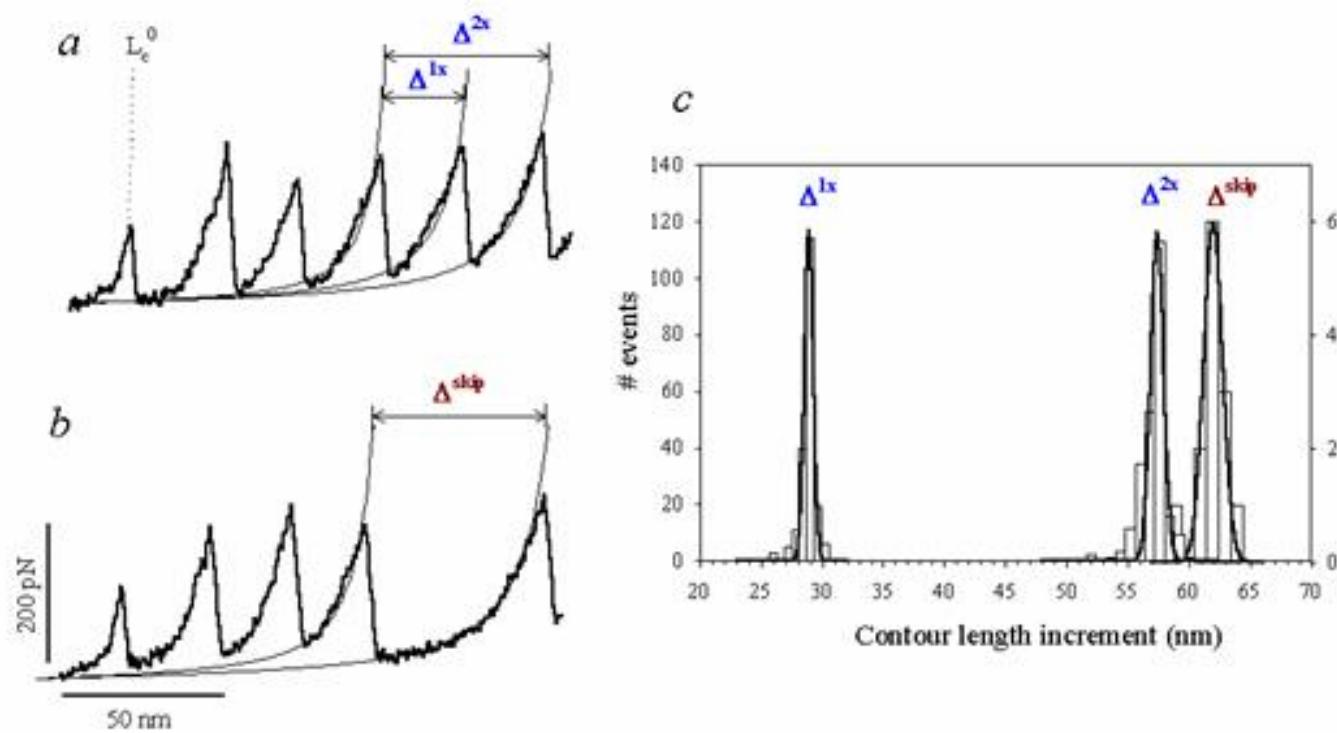


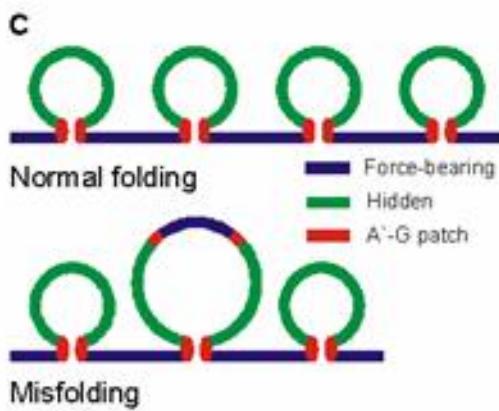
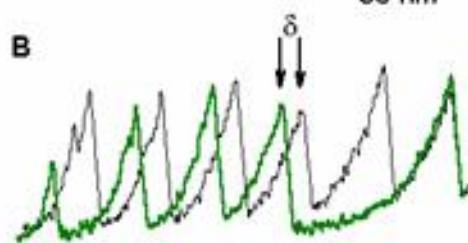
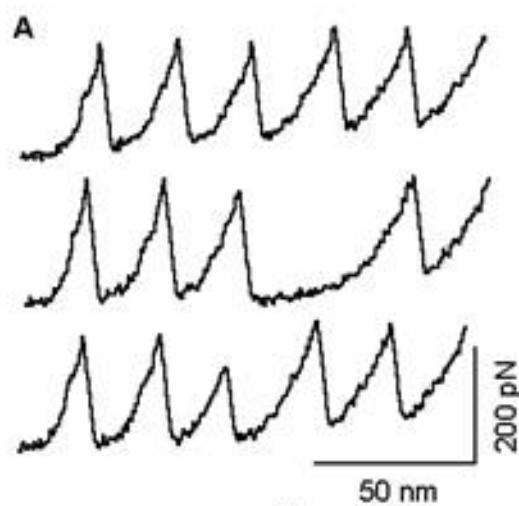
c

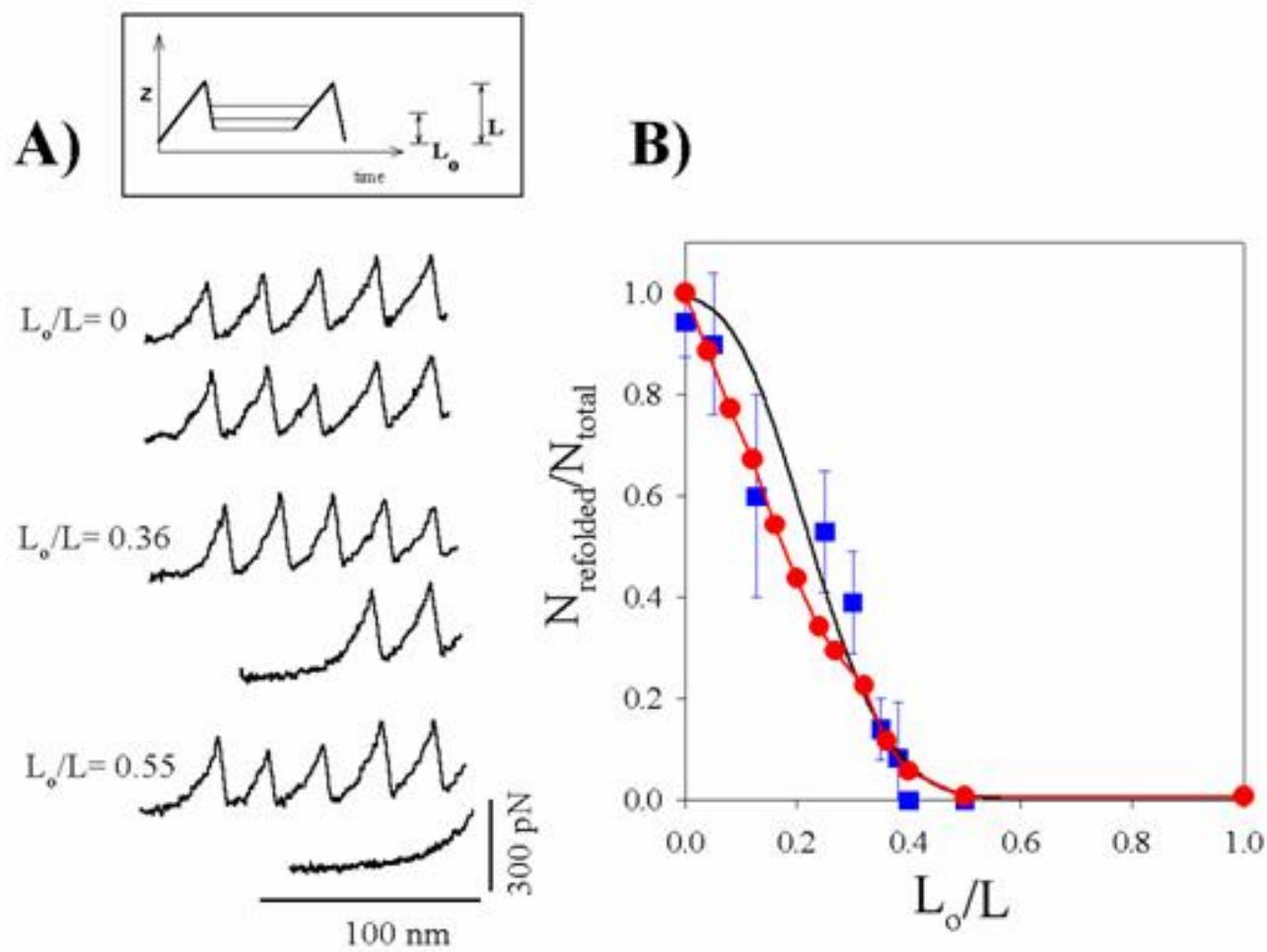


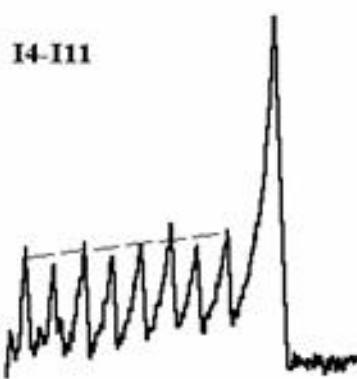
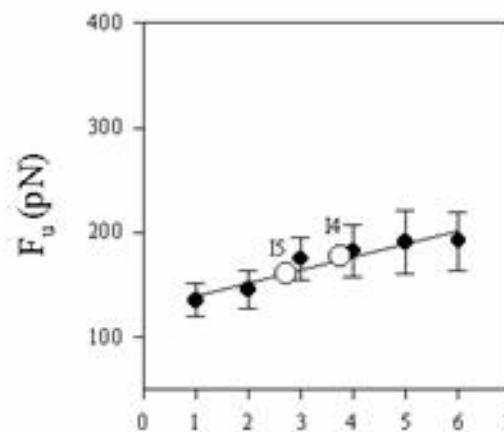
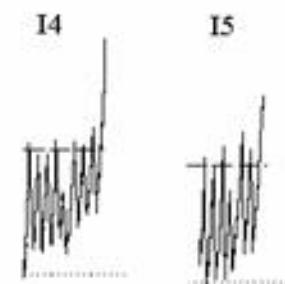
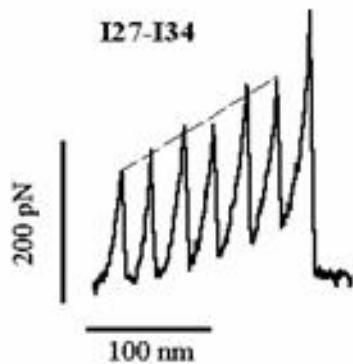
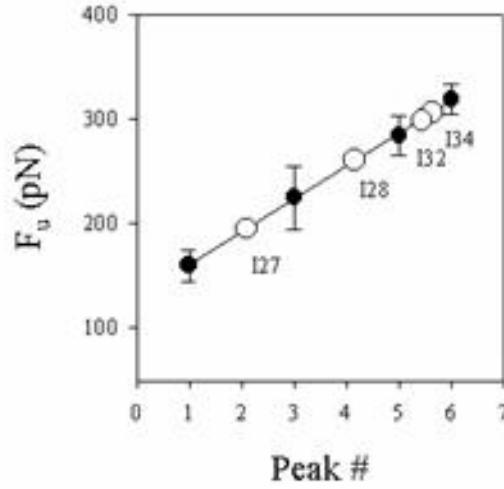
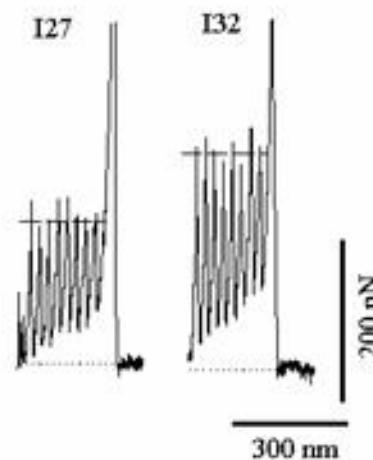
d

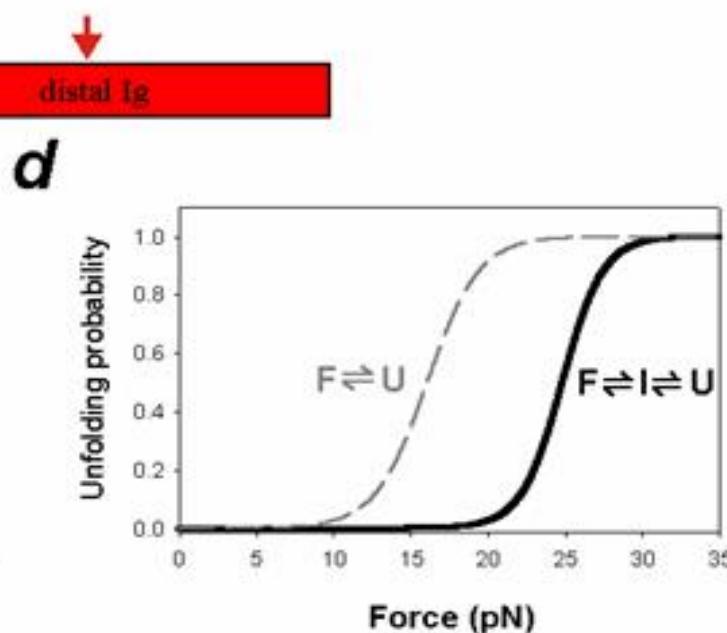
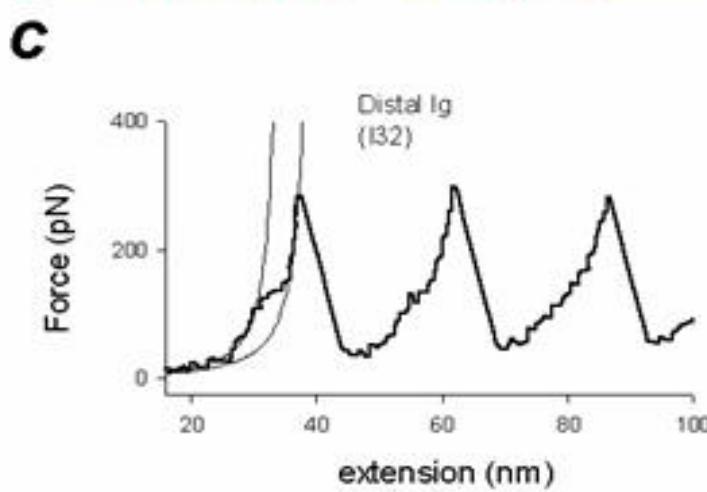
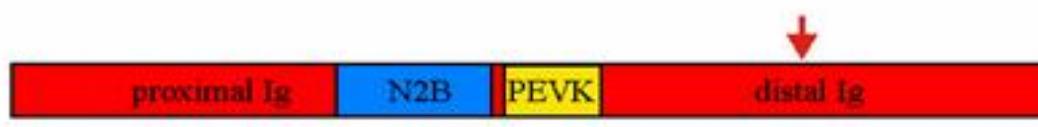
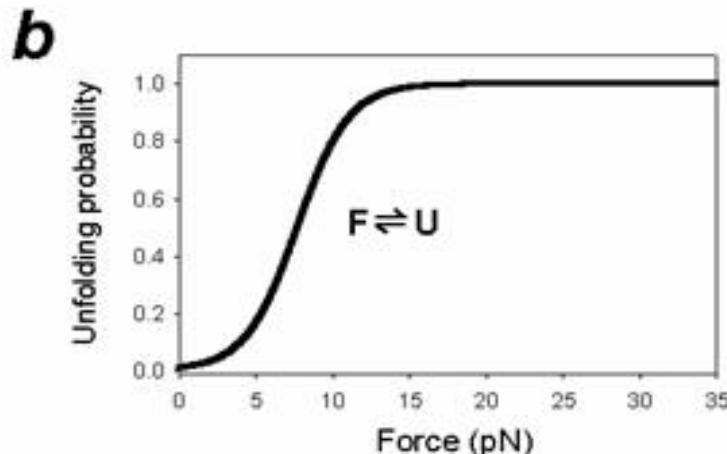
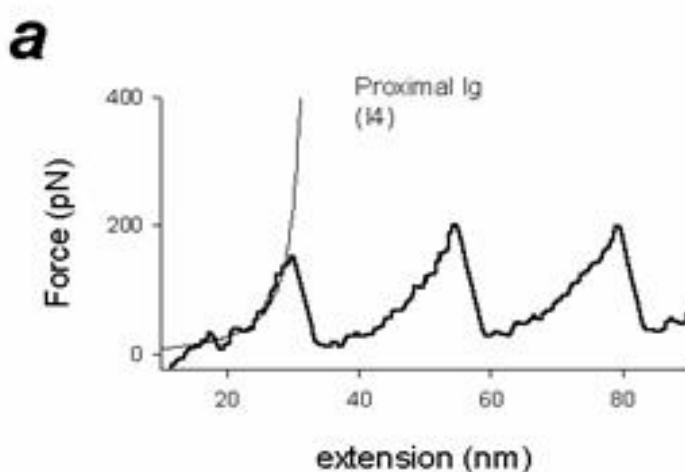




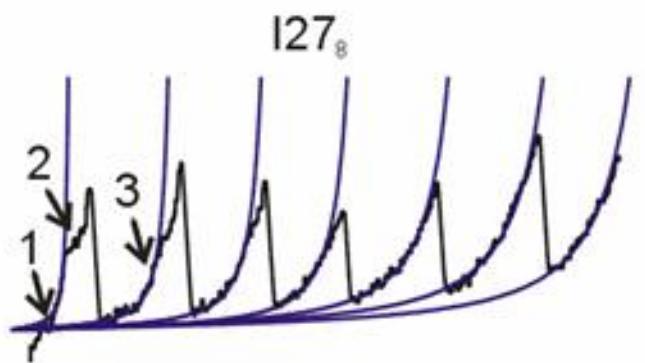




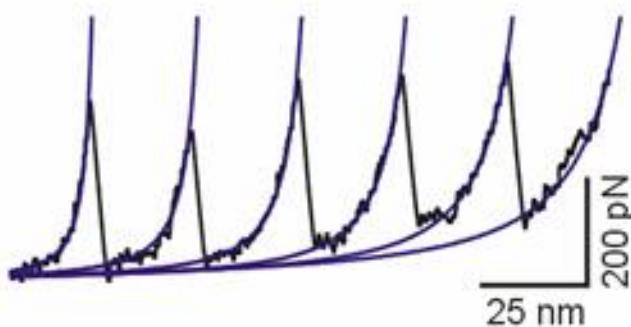
**a****b****c****d****e****f**



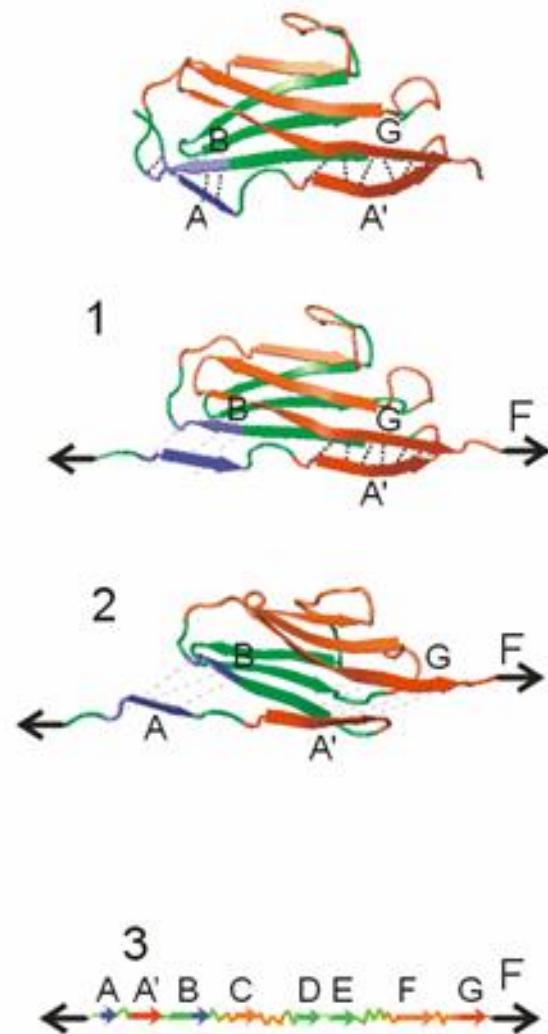
a



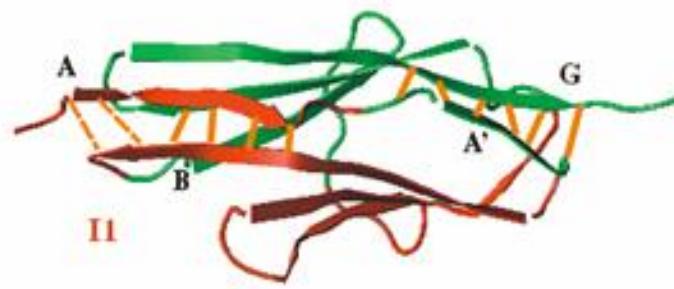
I27₉ K6P



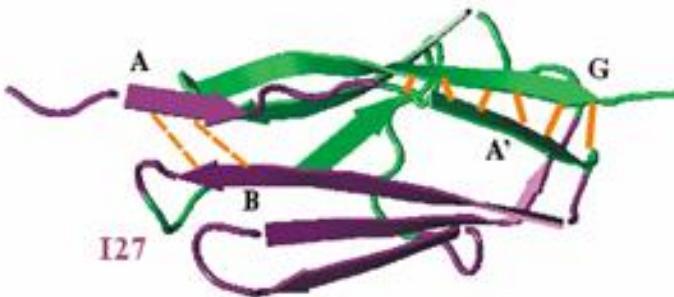
b



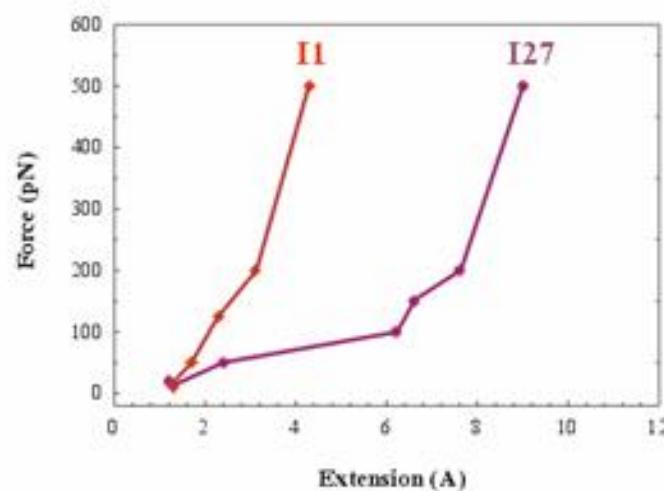
A)

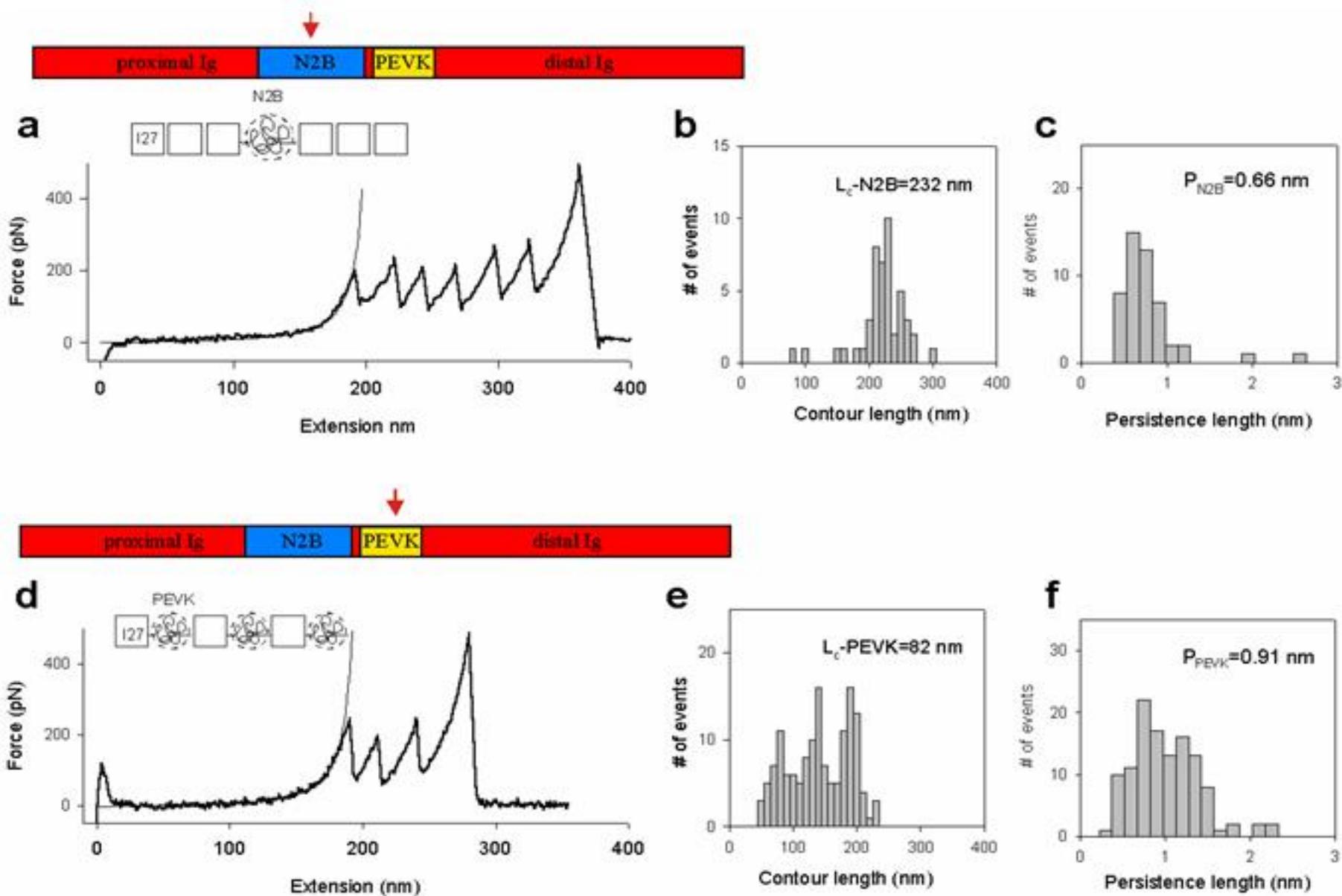


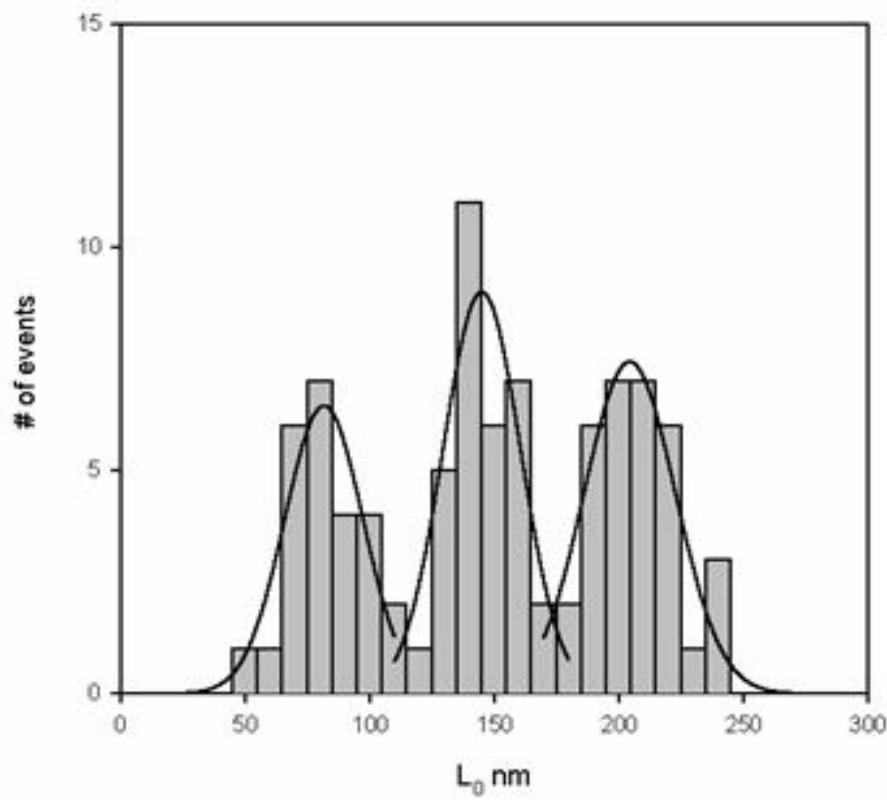
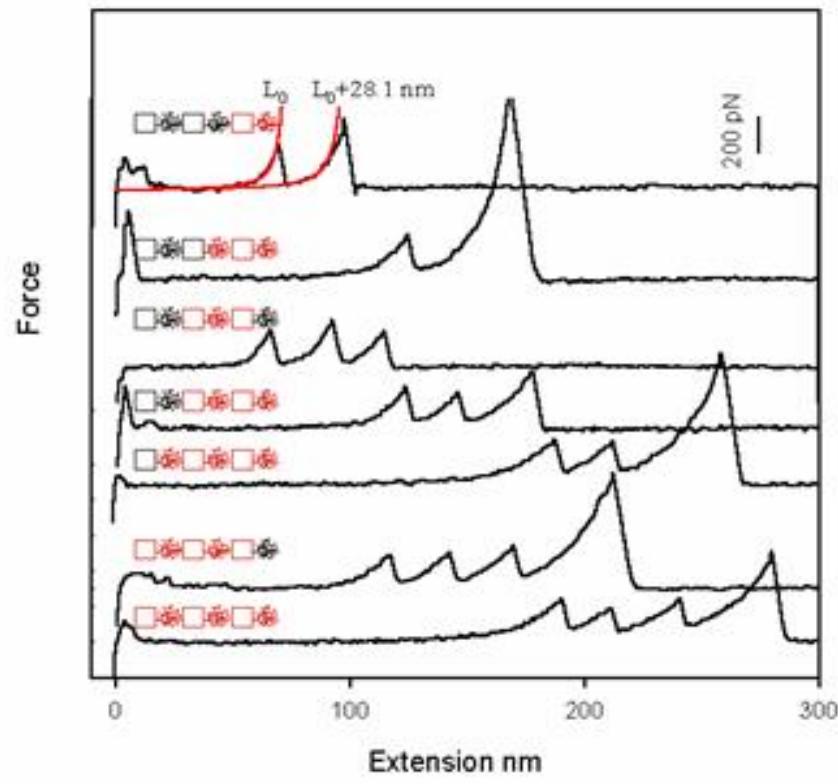
B)



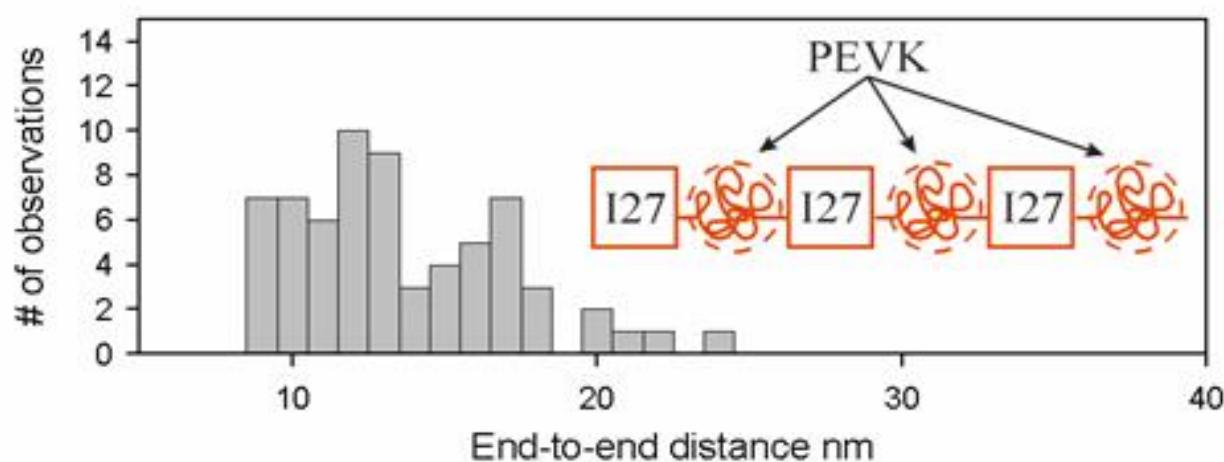
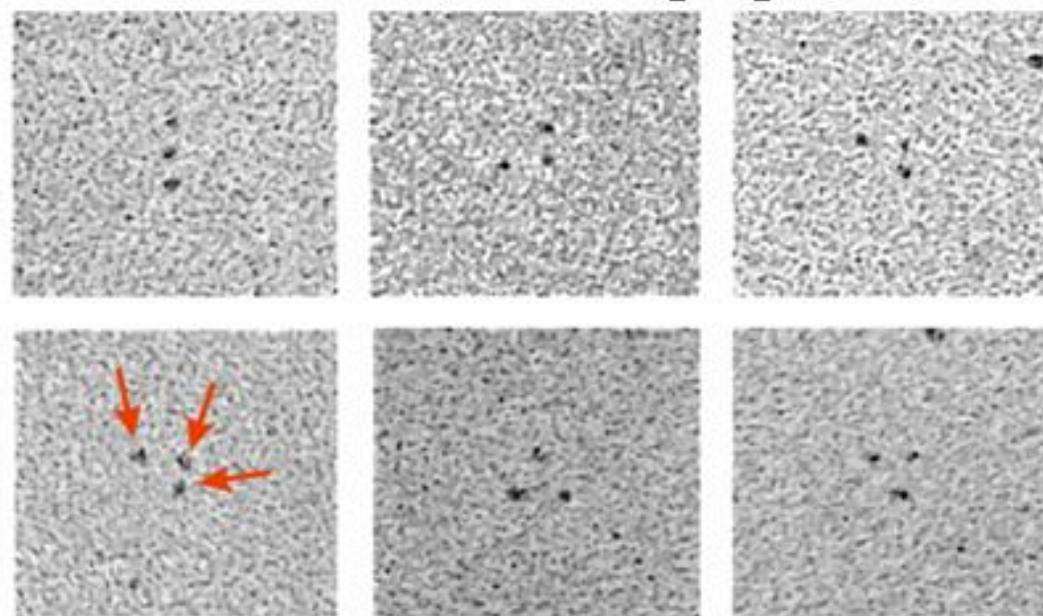
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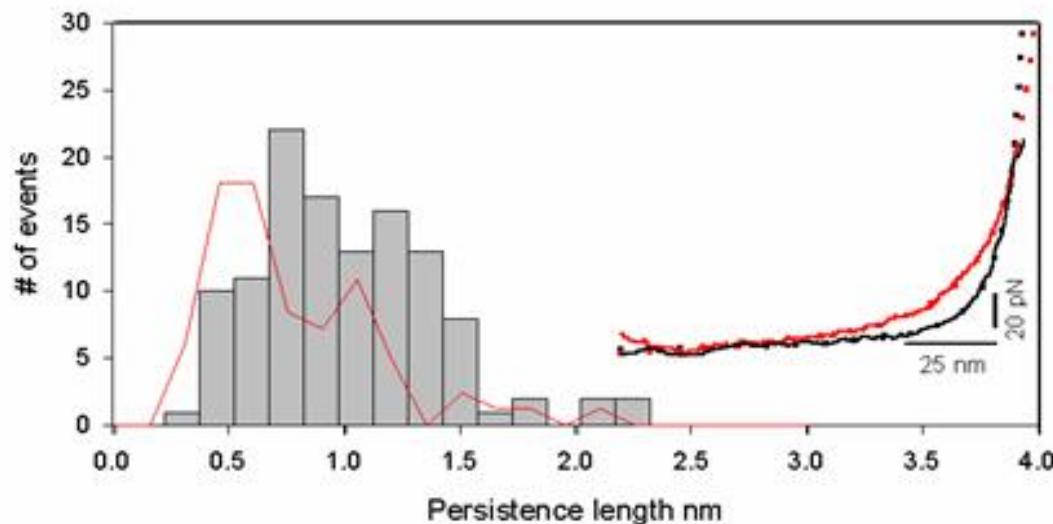
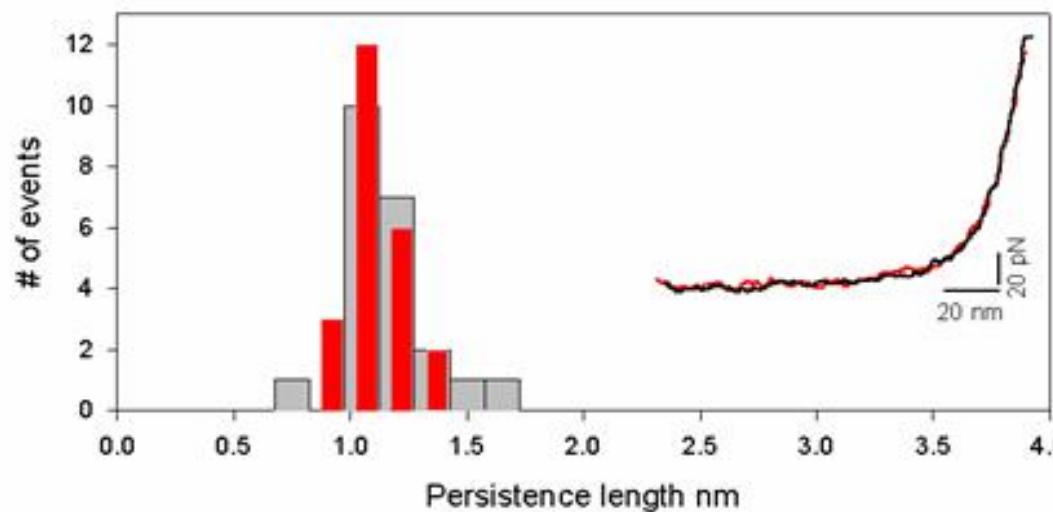






An I27 chimera reveals the mechanical properties of the PEVK region



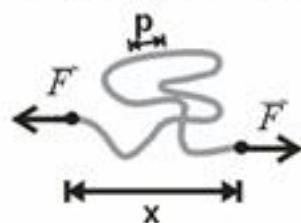
A**B**

Summary of elastic properties of I band titin



	Unfolding rate (s ⁻¹)	Folding rate (s ⁻¹)	Kuhn length (nm)	Unfolding distance (nm)	Folding distance (nm)
Proximal Ig domains	3.3×10^{-3}	0.33	20 (folded) 0.7(unfolded)	0.25	2.2
N2B unique sequence	—	—	1.2 (random coil)	—	—
PEVK segment	—	—	1.8 (random coil)	—	—
Distal Ig domains	8×10^{-5}	1.2	20 (folded) 0.7(unfolded)	0.25	2.2
Unfolding intermediate of distal Ig domains	1.0×10^{-2}	10^2	—	0.33	0.33

1.- Use the FJC model to calculate the extension of titin segments



$$x_{FJC}(F) = L_c \cdot u\left(\frac{Fl_k}{k_b T}\right)$$

where L_c is the contour length, $u(Fl_k/k_b T)$ is the Langevin function and where the Kuhn length $l_k = 2p$.

2.- For a given constant force, calculate the extension of each segment

$$x(F)_{proximal} = L_c^{folded}(F) \cdot u\left(\frac{Fl_k^f}{k_b T}\right) + L_c^{unfolded}(F) \cdot u\left(\frac{Fl_k^u}{k_b T}\right)$$

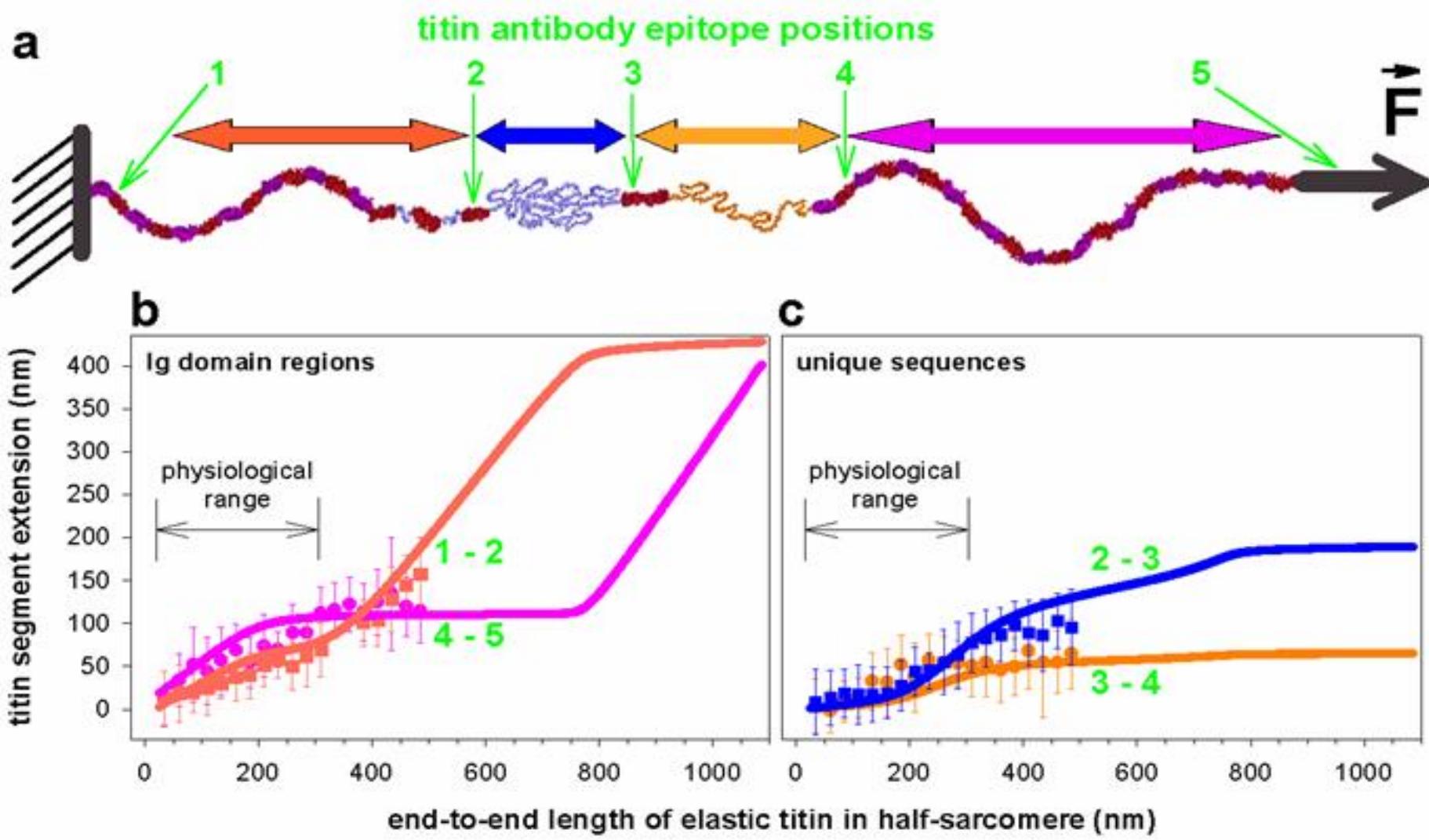
$$L_c^{folded}(F) = N(1 - P_u(F)) \cdot 4.4 \text{ nm}$$

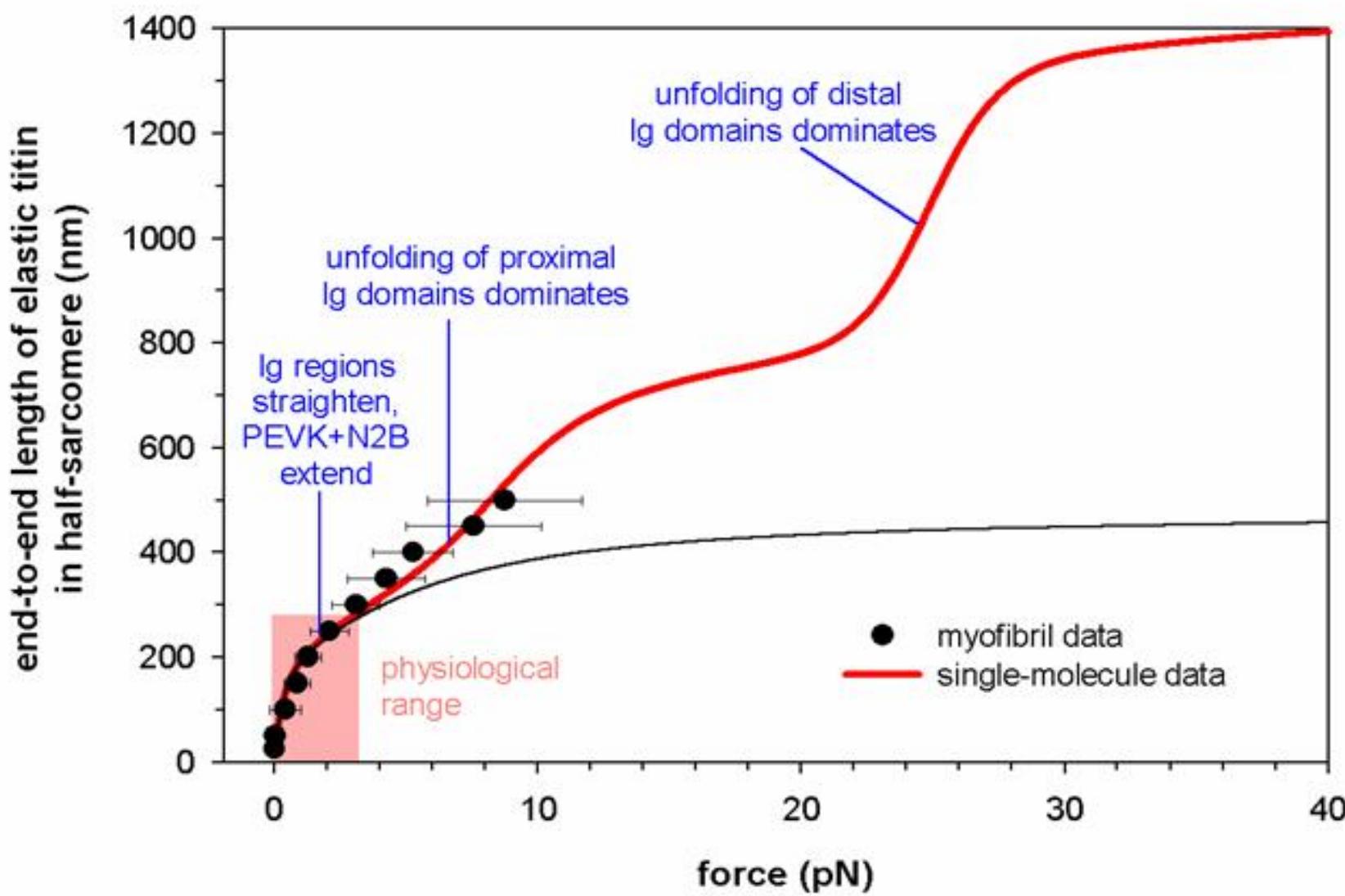
$$L_c^{unfolded}(F) = N P_u(F) \cdot 32.5 \text{ nm}$$

$$x_{N2B}(F) = L_{N2B} \cdot u\left(\frac{Fl_k^{N2B}}{k_b T}\right)$$

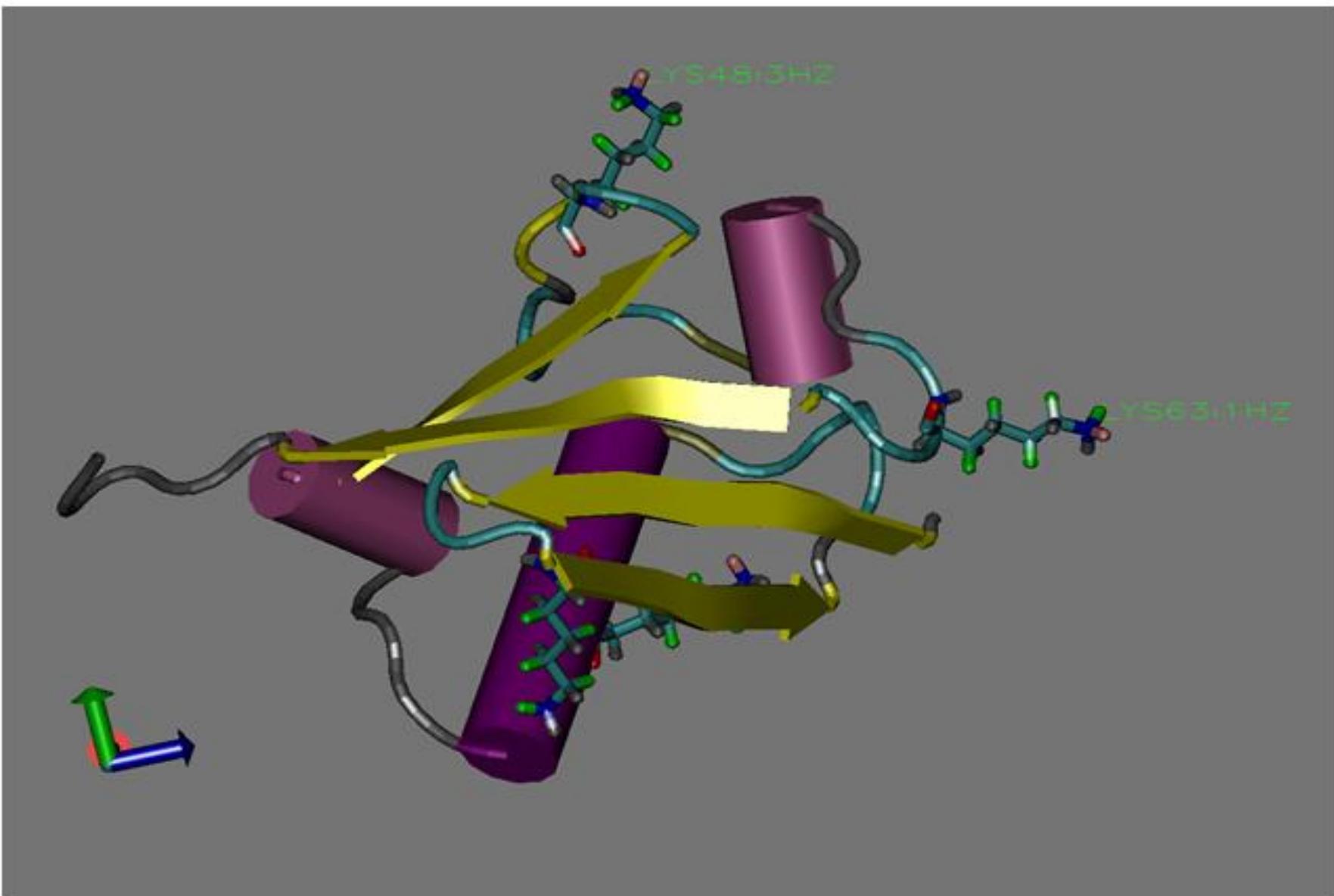
3.- Add up the extension of all four segments

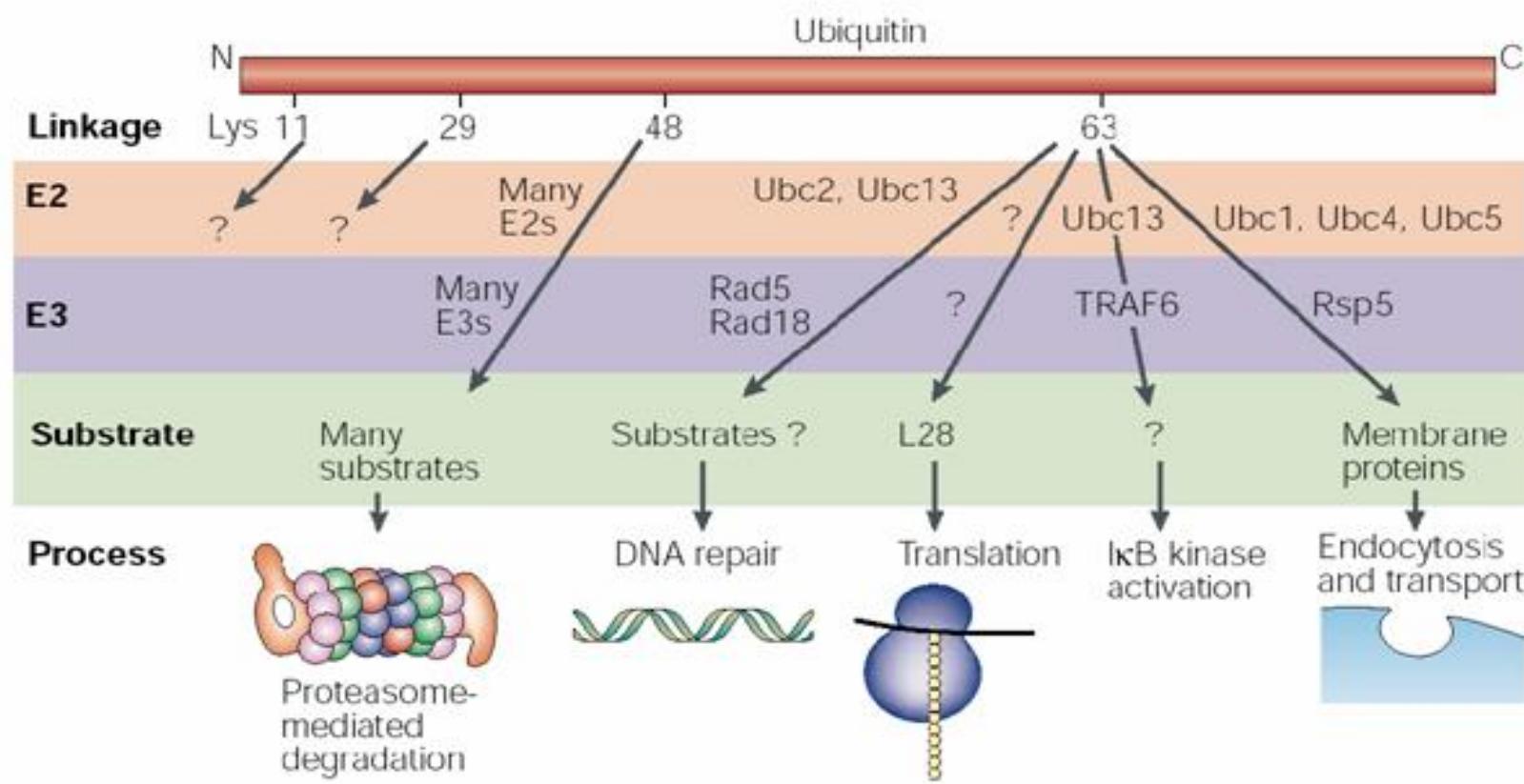
$$x(F)_{I-band} = x(F)_{proximal} + x(F)_{N2B} + x(F)_{PEVK} + x(F)_{distal}$$





Mechanical stability is
topology dependent





From Weissman, Nature Reviews, 2001, 2:169-178

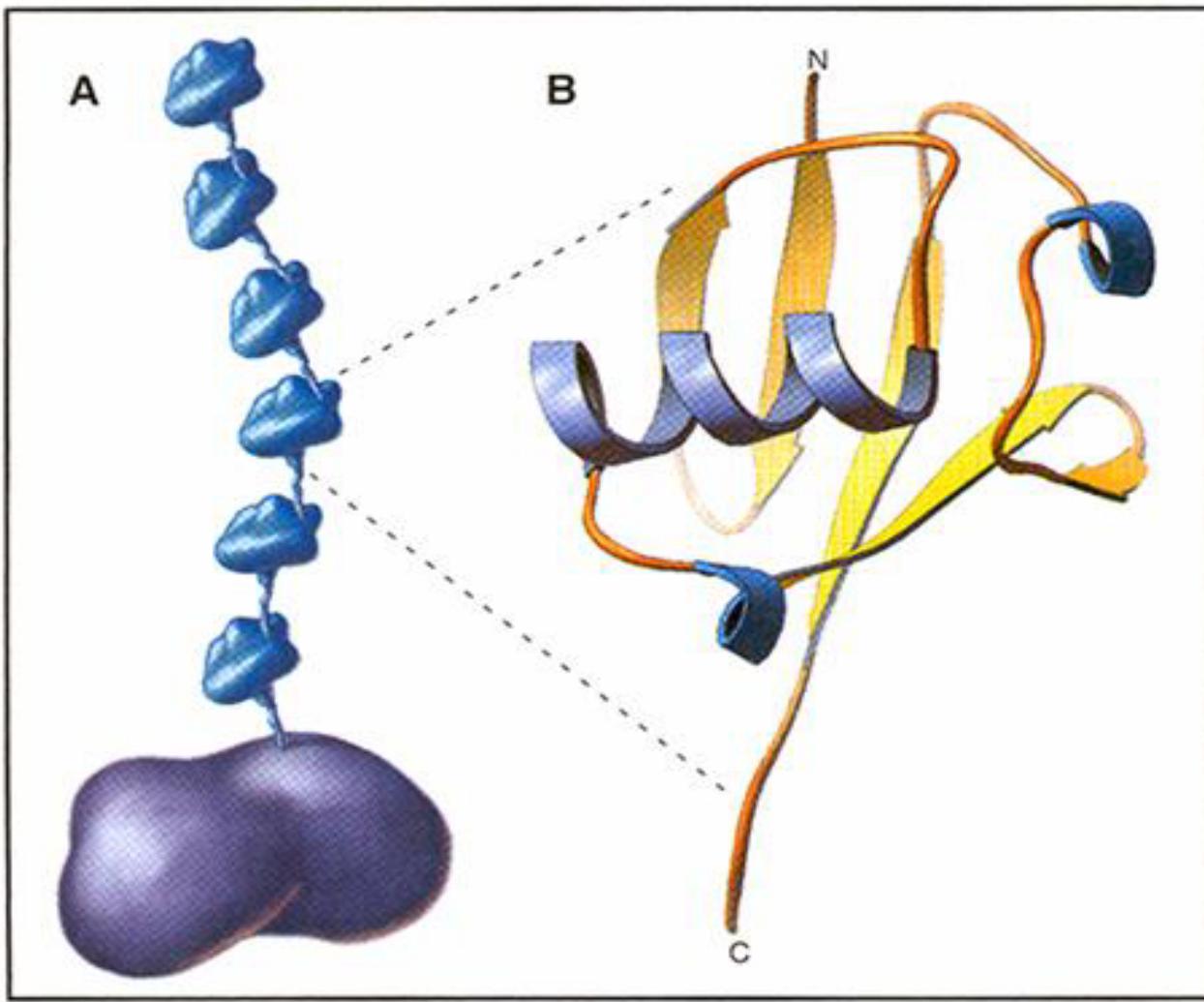
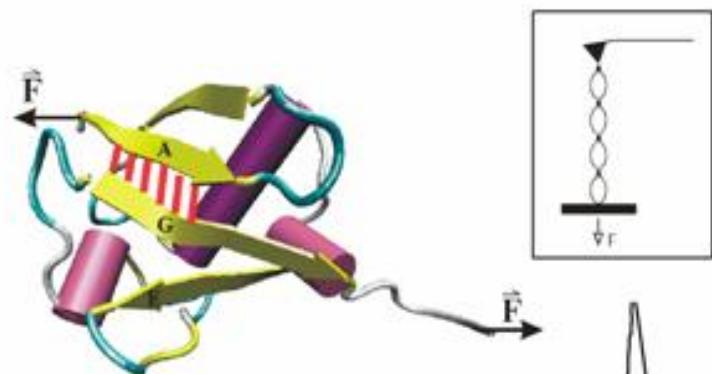
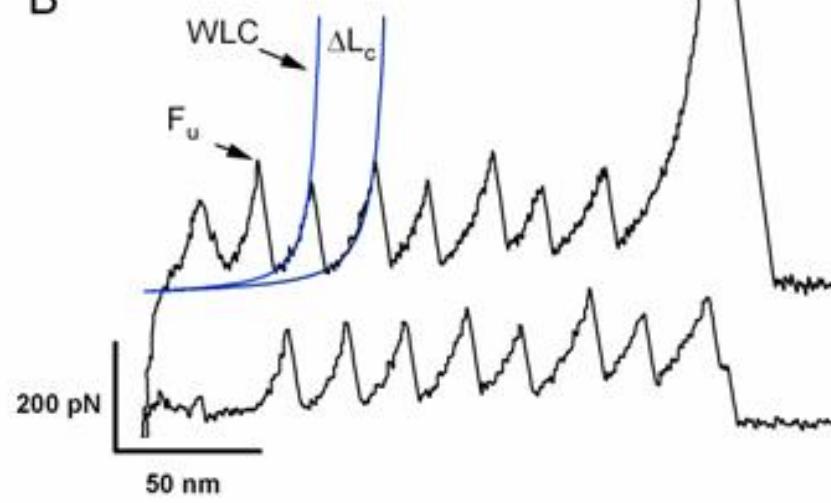


Figure 24-7 A polyubiquitin chain (*A*) is generated on a protein to target it for degradation in the proteasome by sequential conjugation of ubiquitin (*B*), shown in ribbon diagram.

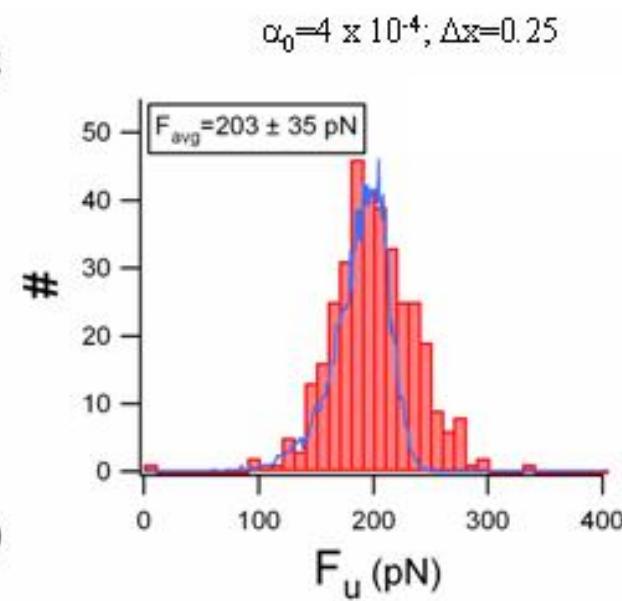
A



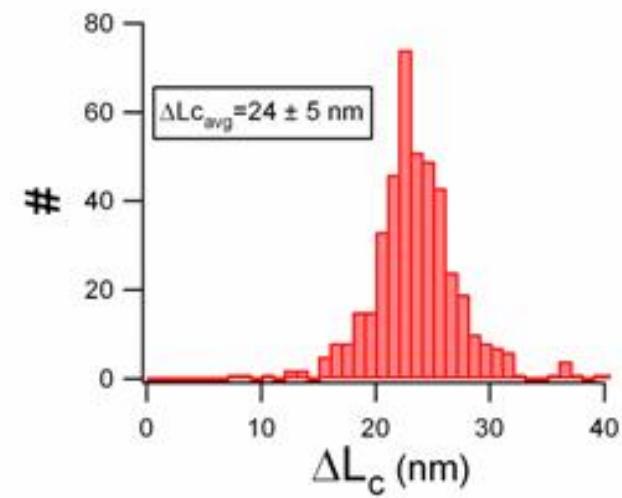
B

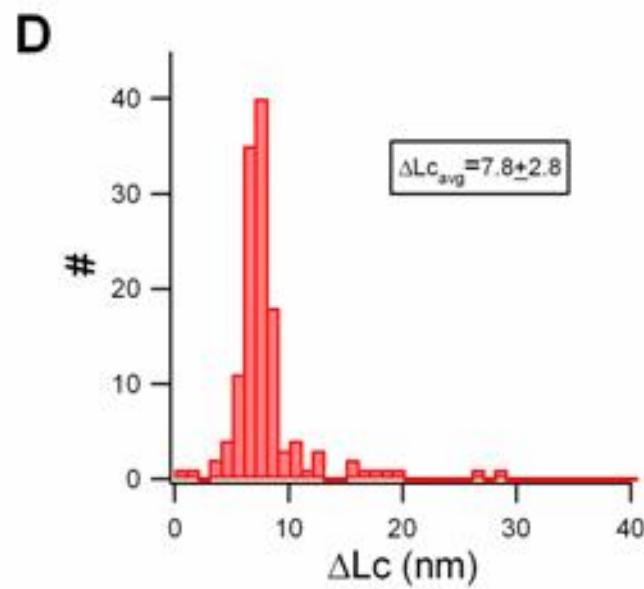
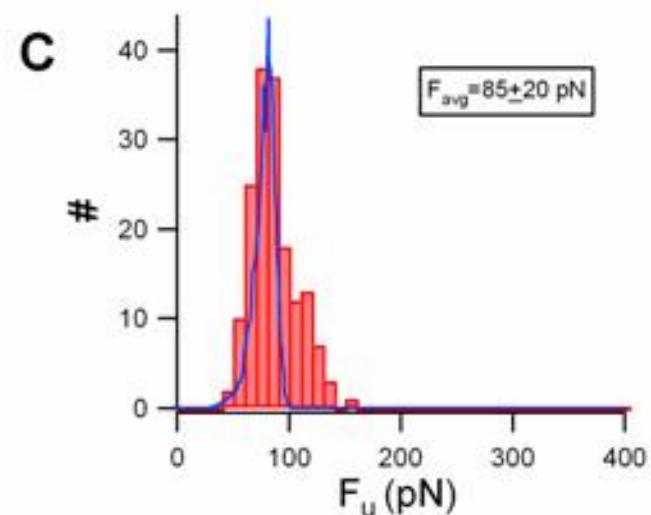
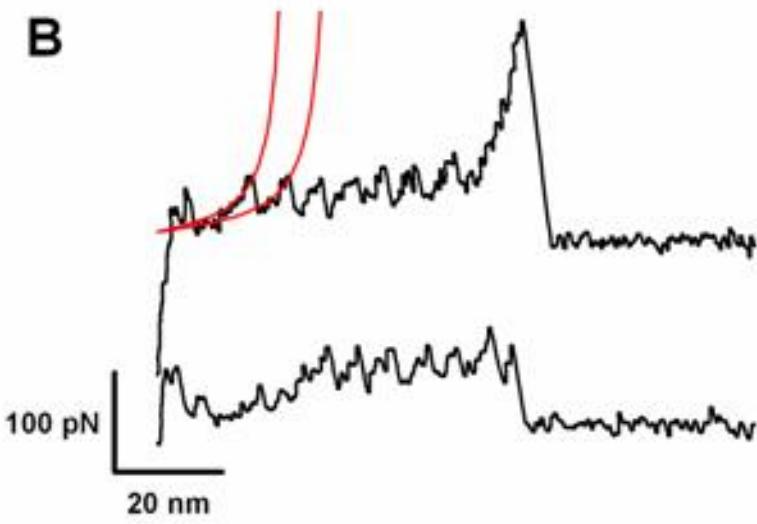
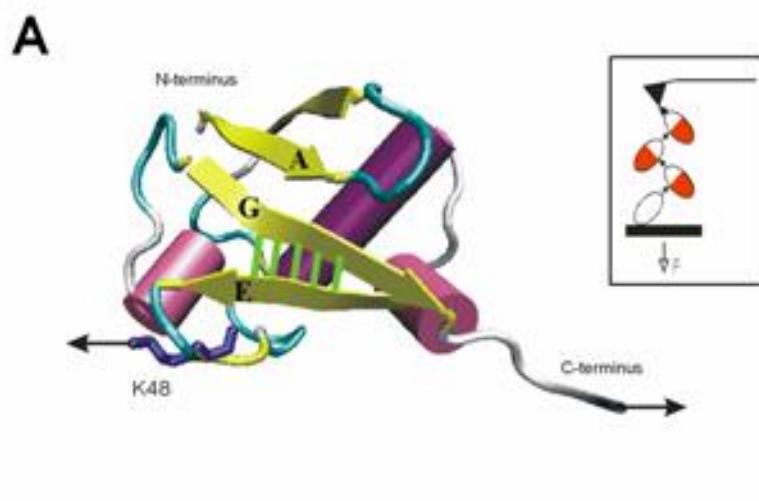


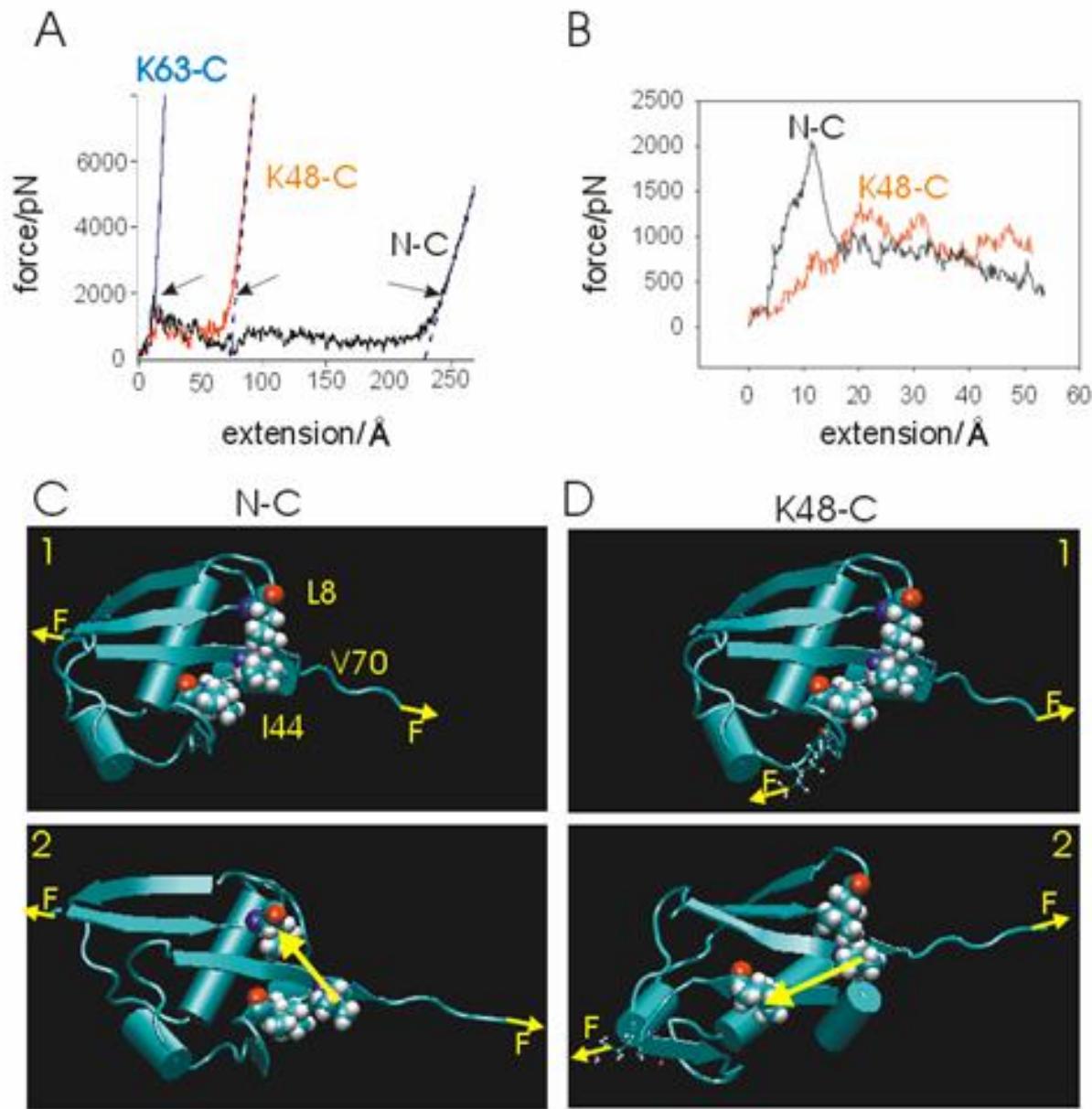
C



D







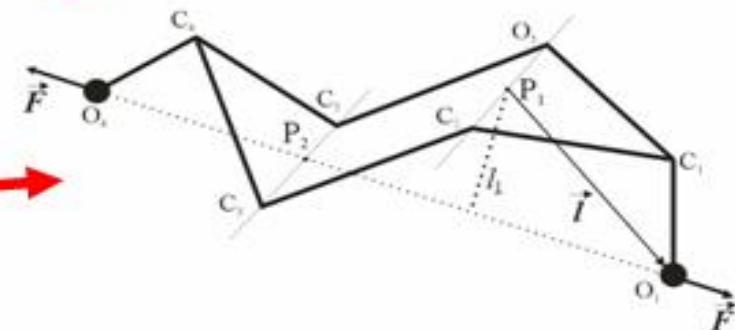
The mechanical design of polysaccharides



Trees are also elastic

have you seen a tree in a storm?

Trees are made of
polysaccharides



A single sugar ring

A sugar ring has two stable conformations

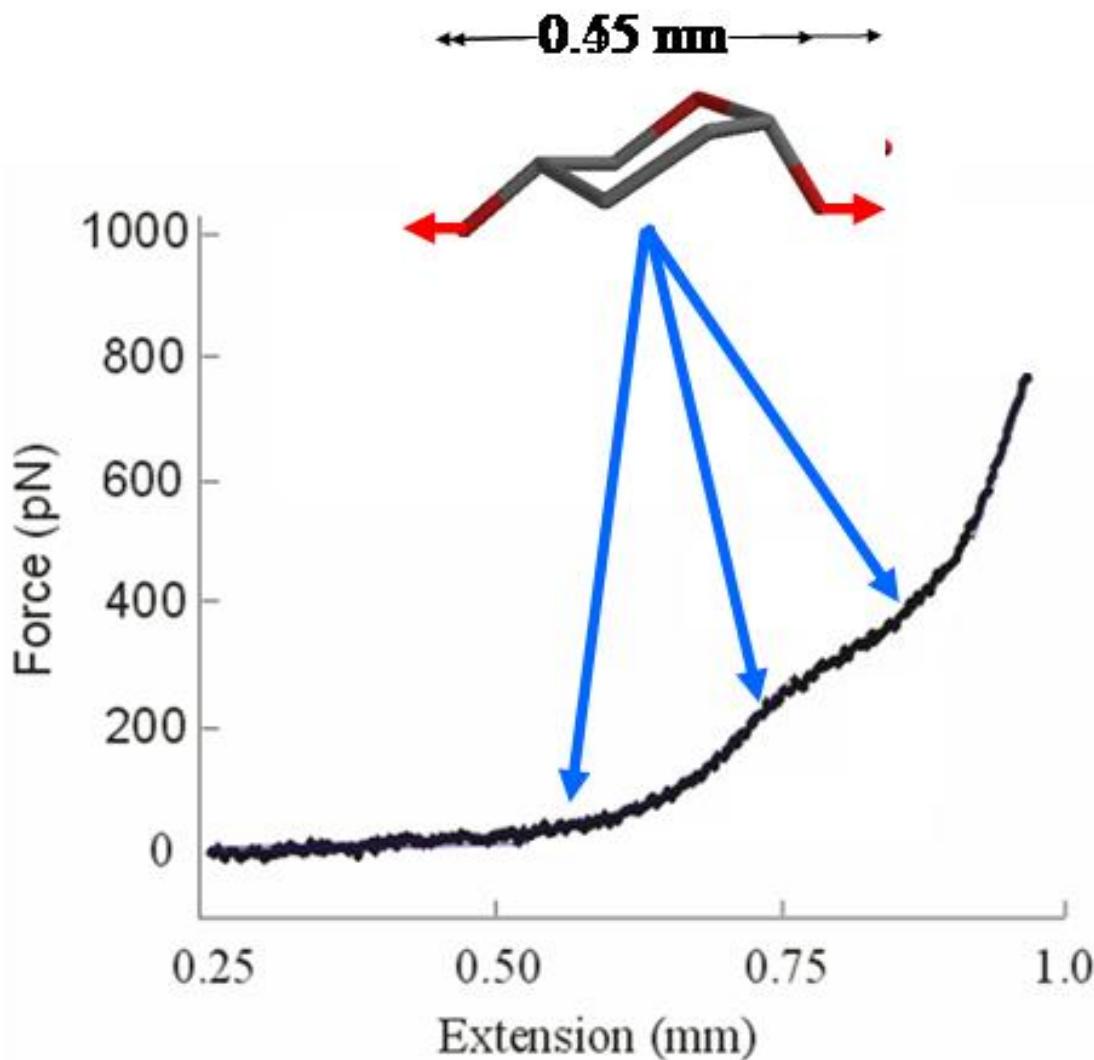
Chair conformation

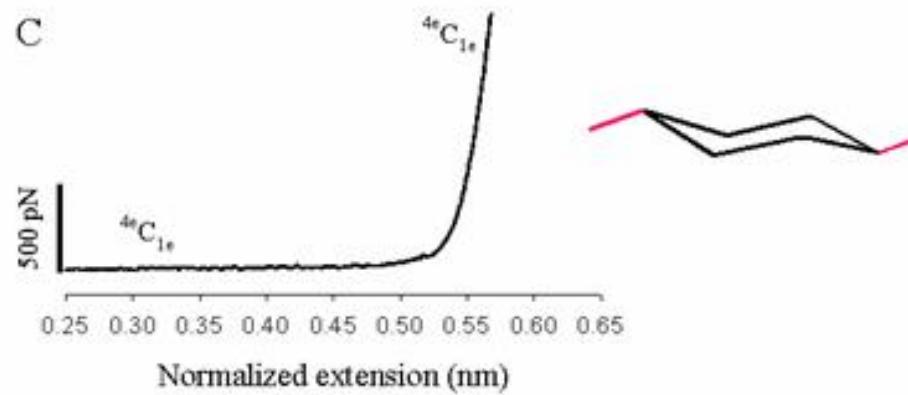
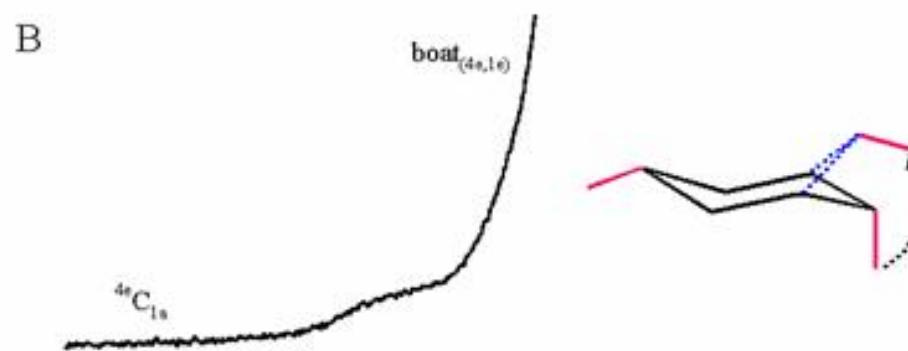
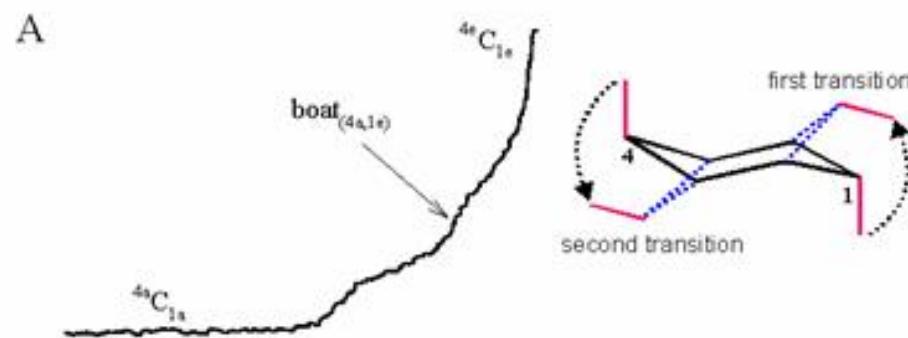


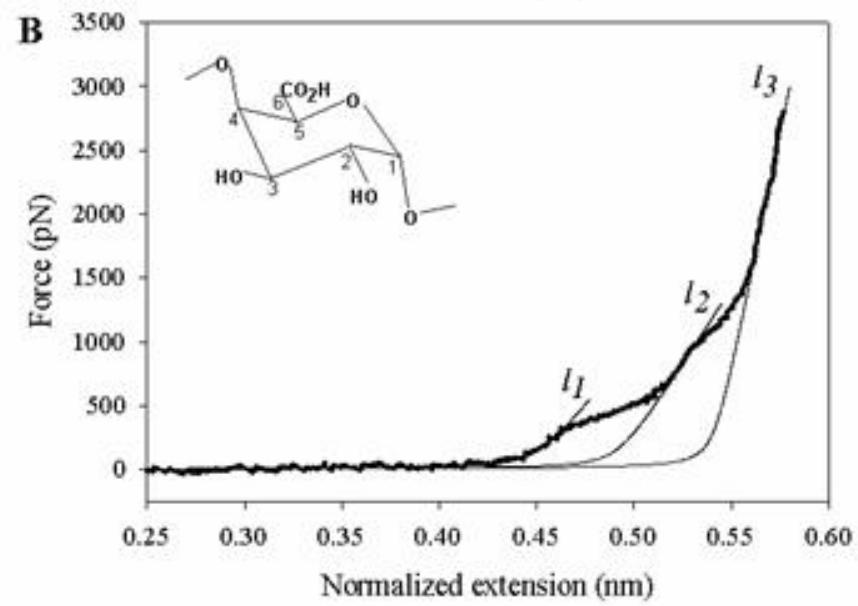
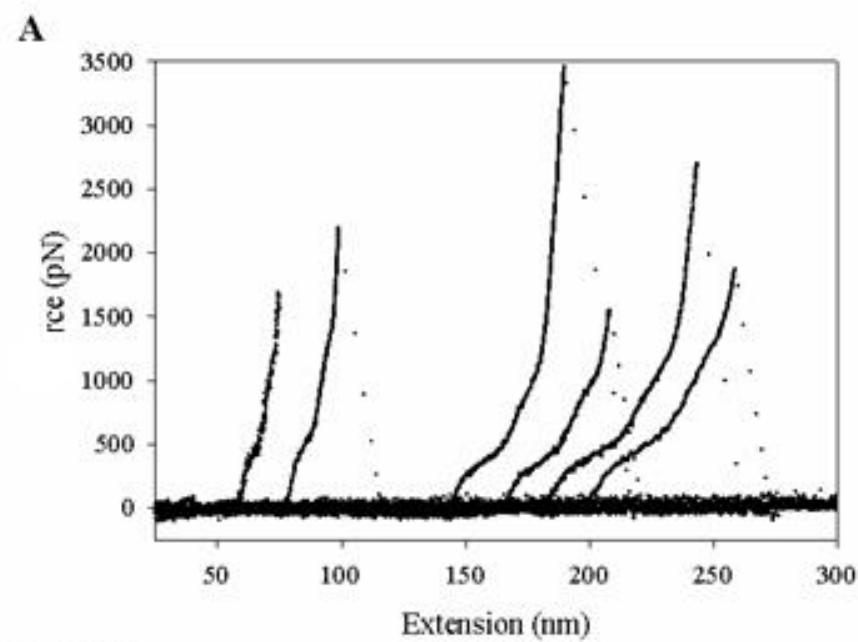
Boat conformation

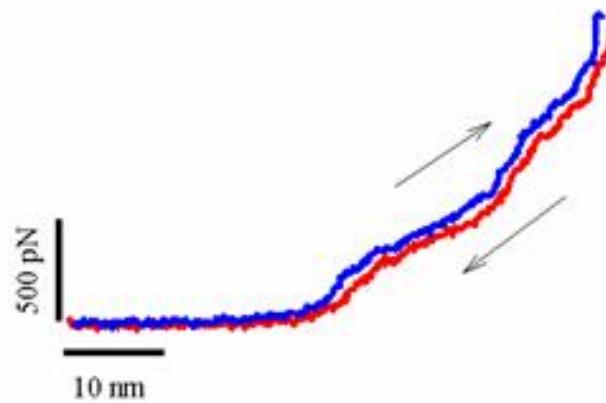
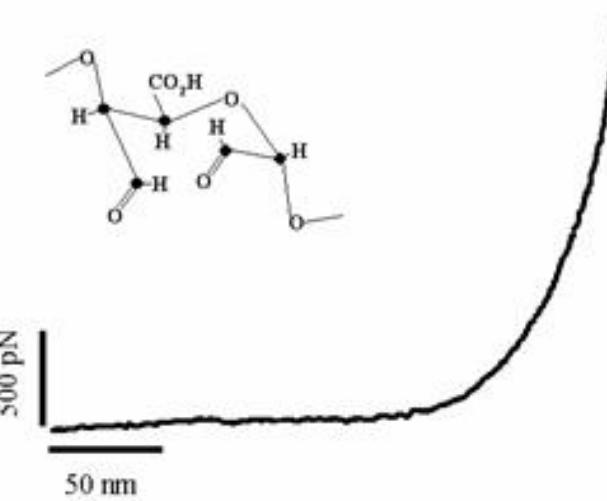


If we mechanically stretch a sugar ring, it gets longer by switching from a chair to a boat conformation

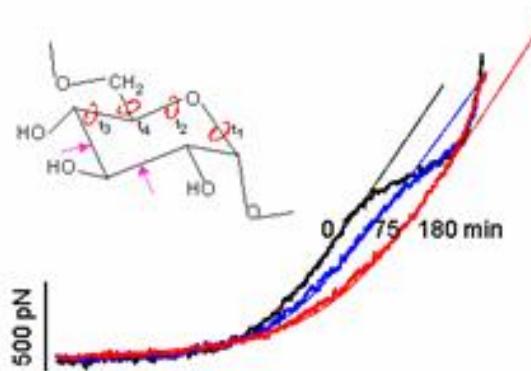




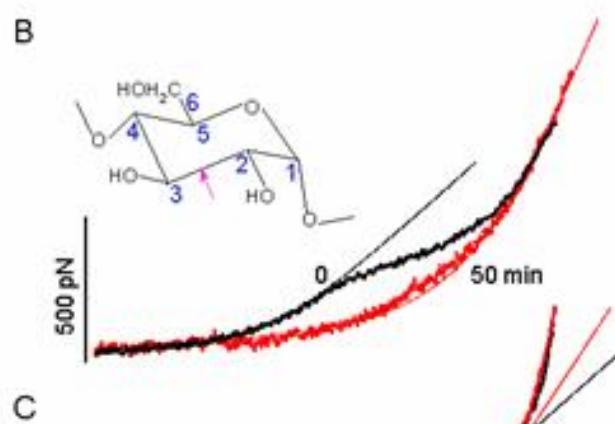


A**B**

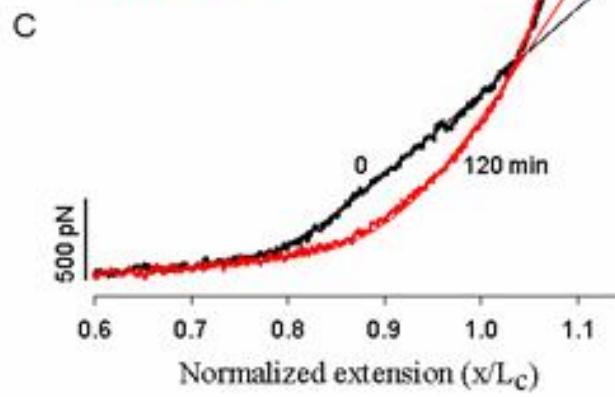
A



B



C



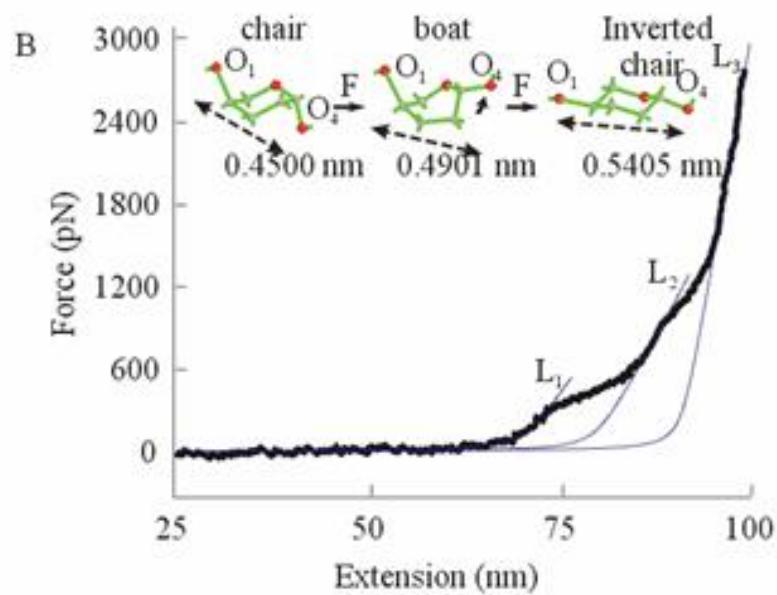
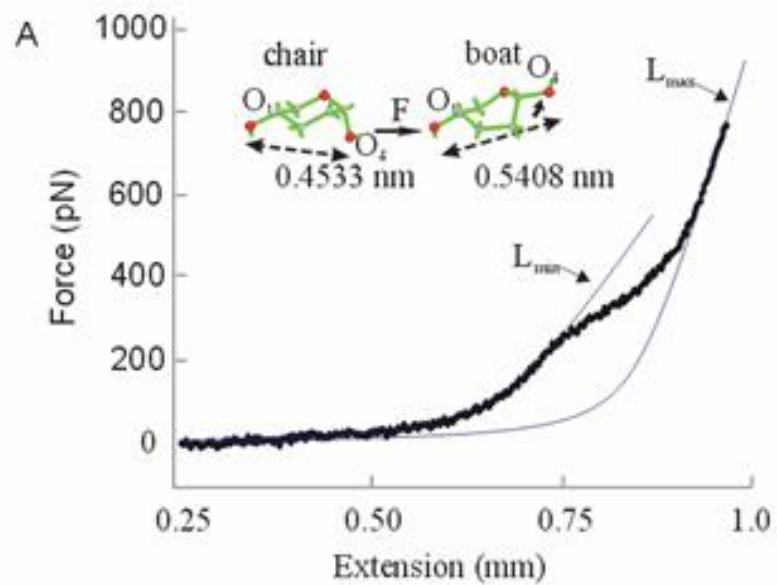


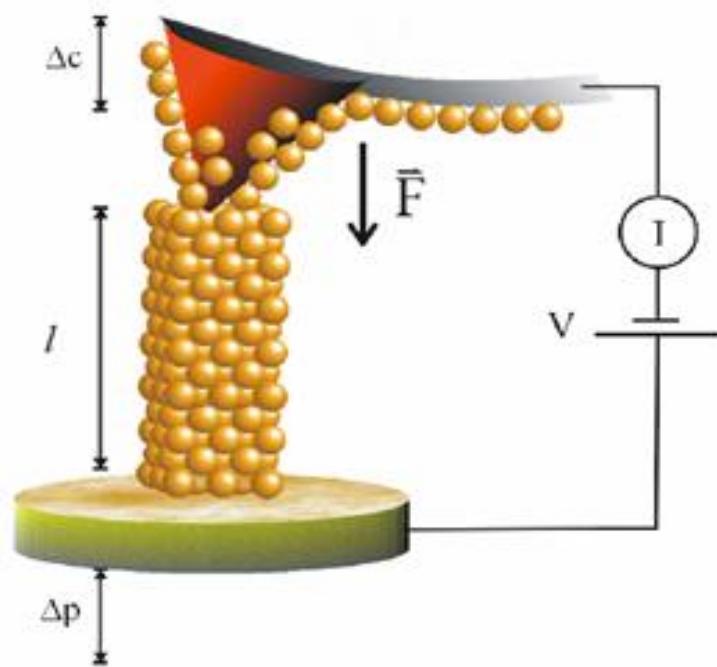
Table 1. *Ab initio* calculation of the separation of glycosidic oxygen atoms during chair-boat transitions.

	Calculated				Experimental*
	$O_iO_j^{F=0}$ (Å)	$O_iO_j^F$ (Å)	Δ (Å)	$\frac{\Delta}{O_iO_j^F} (\%)$	$\frac{L_{\max} - L_{\min}}{L_{\max}} (\%)$
Amylose α-1,4	4.533	5.408	0.875	16.2	16.8 ± 1.8 (n=11)
Dextran α-1,6	4.412	5.696	1.284	22.5	19.5 ± 2.1 (n=23)
Cellulose β-1,4	5.417	5.417	0	0	0 (n=29)

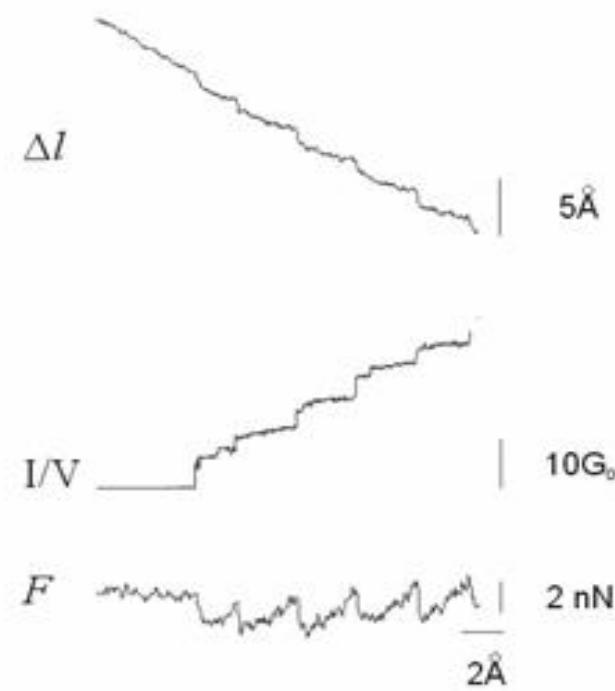
* The table compares the distance between glycosidic oxygen atoms, in the relaxed ($F=0$) and stretched conformations, $(O_iO_j^F - O_iO_j^{F=0}) / O_iO_j^F$, with the experimentally measured extension of the contour length, $(L_{\max} - L_{\min}) / L_{\max}$. The experimental values for L_{\min} and L_{\max} were obtained from the fits of the FJC model to the force-extension curve before and after the plateau region (thin lines in Fig 3B).

Mechanical properties of a gold nanowire

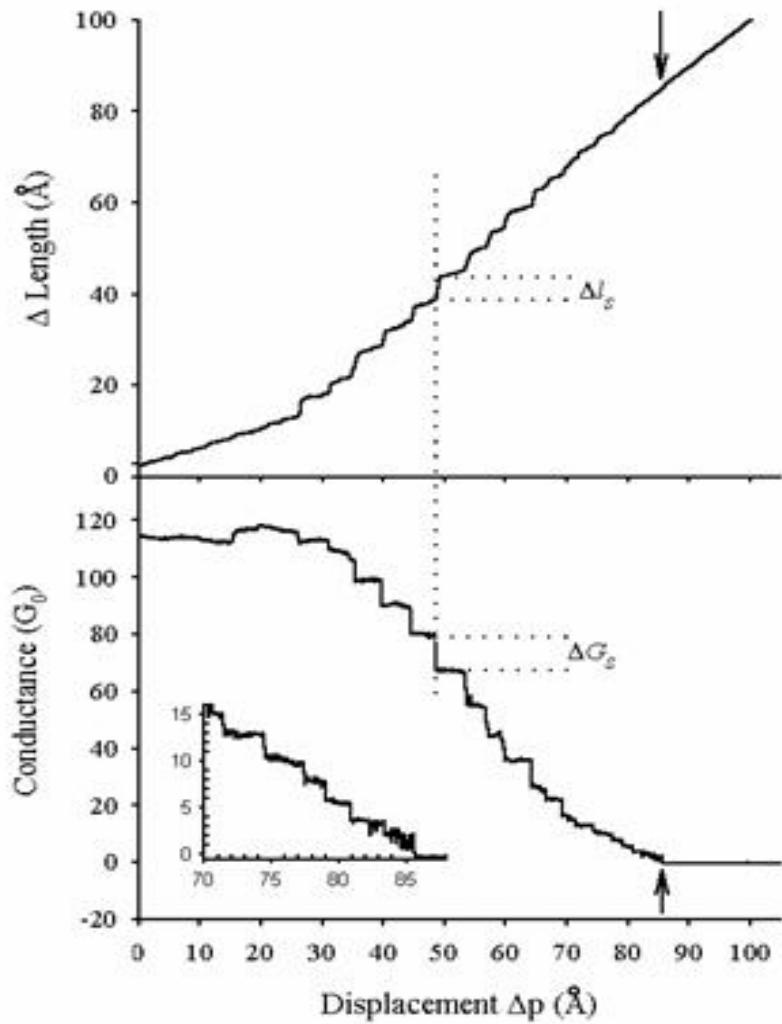
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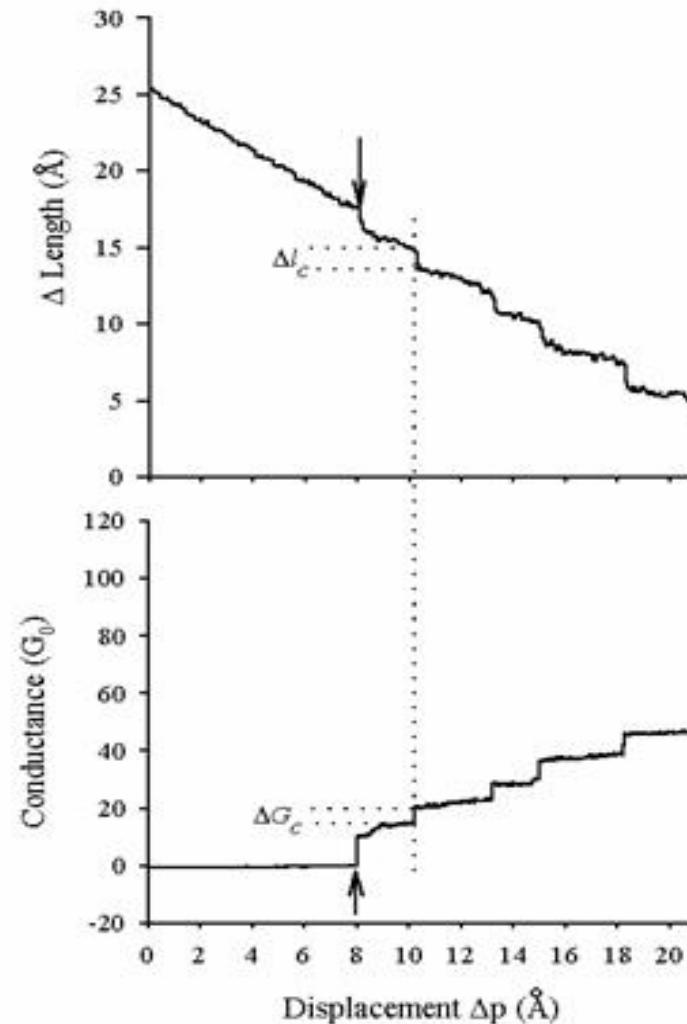
B



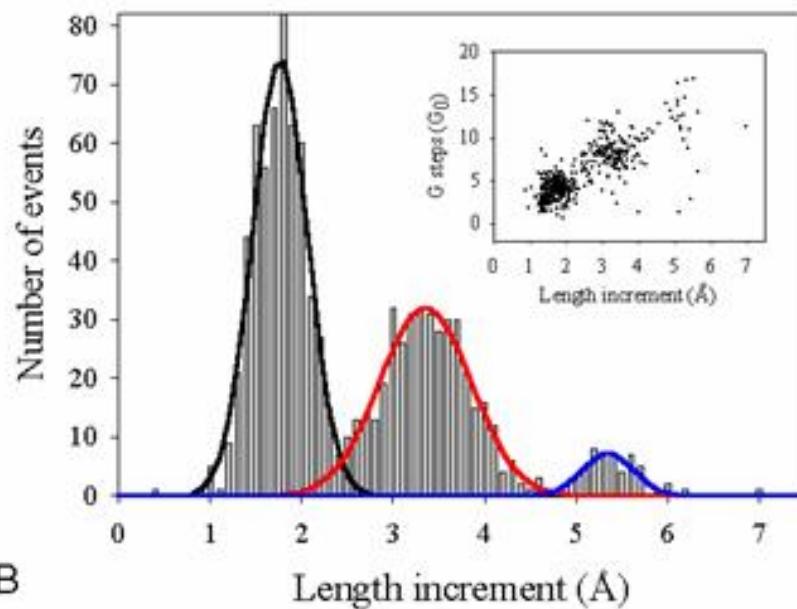
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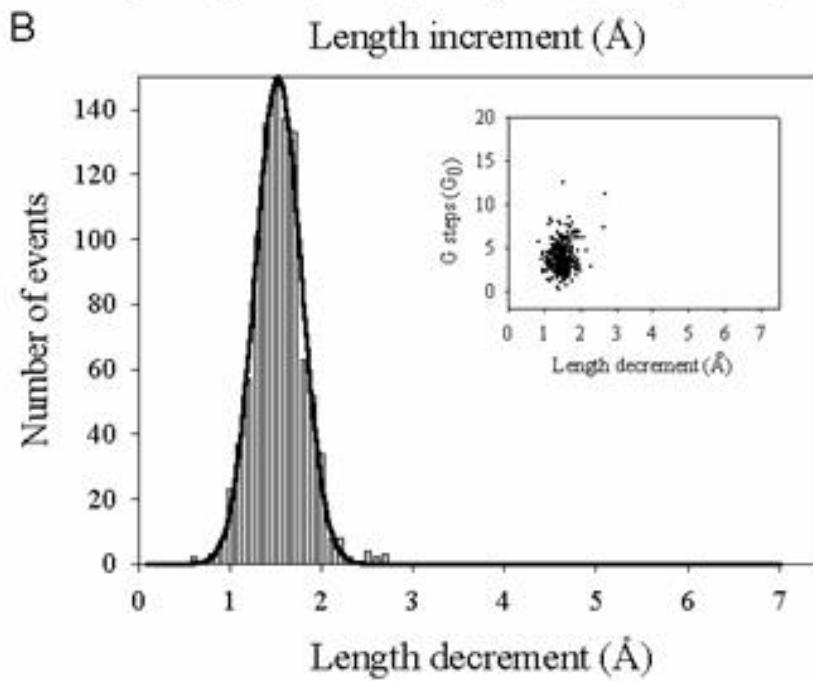
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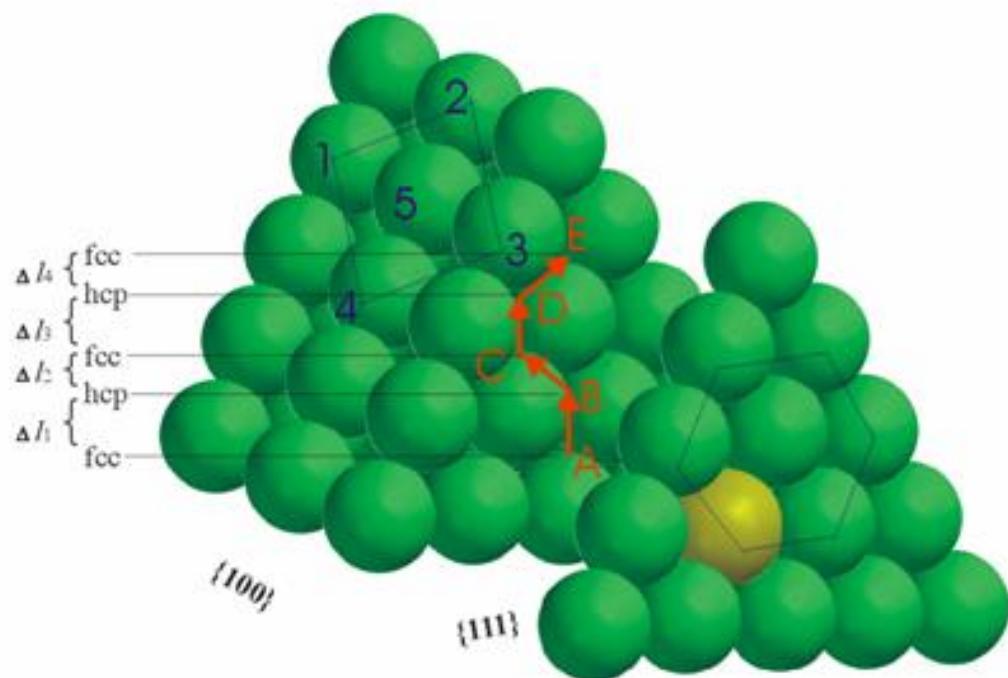
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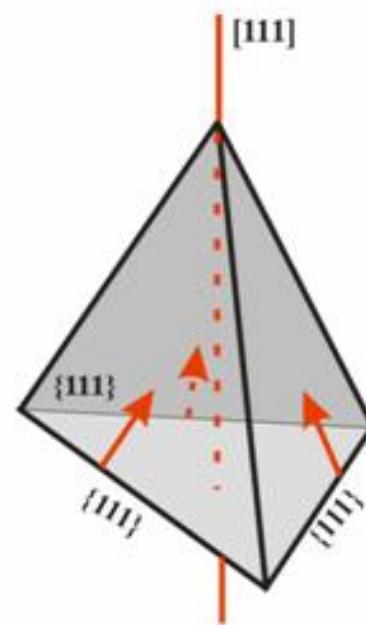
B



A



B



Mesoscopic materials have similar mechanical properties

