

# Friction of F-actin knots

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## Abstract

We use existing data of force-extension experiments on F-actin molecules tied into knots to compute a value of 0.15 for the static friction coefficient for contact between different parts of the same molecule with itself. This estimate for protein-protein friction is relevant for the stabilization of the 273 known proteins with knots, one percent of the structures deposited in the Protein Data Bank.

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## 1. Introduction

There are 273 examples of proteins with knots, which constitutes about 1% of the structures deposited in the Protein Data Bank (Virnau et al., 2006). Hitherto the biological function of these, mostly trefoil, knots is not known. They are supposed to be mobile along the amino acid chain (Sulkowska et al., 2008), and thermal motion might even undo them (Kirmizialtin and Makarov, 2008). But these knots, as all knots, must be stabilized by friction, and the question is then how strong is the friction between two segments of the same protein? In the literature we found but one example where a non-natural knot is tied on a protein: in Arai et al. (1999) optical tweezers were used to tie a trefoil knot on a F-actin filament and force-extension measurements were carried out.

## 2. Methods

The effect of friction on knot stability has been known for a long time, but has been analyzed quantitatively only recently (Audoly et al., 2007). The

bending energy of an elastic ring of radius  $R$  is  $(1/2)(\kappa/R^2) 2\pi R$ , where  $\kappa$  is the flexural rigidity of the filament. Macroscopic beam theory identifies it with the product of Young's modulus  $E$  and the second moment of area  $I$  of the cross section,  $\kappa = EI$ , while on the microscopic scale the flexural rigidity is related to the persistence length  $L_p$  via the relation  $\kappa = L_p k_B \Theta$  ( $k_B$  being the Boltzmann constant and  $\Theta$  the absolute temperature). The potential energy associated with the external tension  $T$  applied on the ring is  $(2\pi R)T$ . Minimization of the total energy with respect to the radius  $R$  gives the equilibrium condition  $T = (1/2)(\kappa/R^2)$ , which is the left hand side of Eq. (1). In the braid part of the knot (see Fig. 1), each strand, of thickness  $r$ , exerts a normal contact force  $P$  on the other one. By definition of the static friction coefficient  $\mu$ , a horizontal force  $\mu P$  has to be added to  $T$  if the contact is to be unblocked, i.e. a force smaller than  $\mu P$ , applied in either direction has no effect. The normal pressure in the braid part of an elastic trefoil knot is  $P = 0.49 \kappa R^{-3/2} r^{-1/2}$ , see Audoly et al. (2007) for a derivation (the exponents  $-3/2$  and  $-1/2$  can be found from similarity arguments and the coefficient 0.49 was derived numerically). Altogether this results in the following relation between the pulling force  $T$  and the radius  $R$  of a loose trefoil knot (see Fig. 1) :

$$\left| \frac{Tr^2}{\kappa} - \frac{1}{2} \left( \frac{r}{R} \right)^2 \right| \leq 0.49 \mu \left( \frac{r}{R} \right)^{3/2}, \quad (1)$$

where  $r$  is the radius of the circular cross-section of the filament.

### 3. Results

According to Eq. (1), in the absence of friction the equilibrium radius of a trefoil knot under tension  $T$  is  $R = \sqrt{\kappa/(2T)}$ . By fitting their data to this expression, Arai et al. (1999) obtained an estimate for the flexural rigidity of F-actin,  $\kappa = 5.5 \pm 3.6 \times 10^{-26} \text{ Nm}^2$ , which is in reasonable agreement with the persistence length  $L_p = 1800 \pm 300 \text{ nm}$  reported in Käs et al. (1996). The scatter of the 359 points of Fig. 2-top, plotted from Fig. 2 of Arai et al. (1999), is due to the friction term in the right-hand side of Eq. (1), unknown by the time of the experiments. We extracted the data from the PDF file of Arai et al. (1999) and we now analyze it in light of this new term. In Fig. 2-bottom we plot  $\left| \frac{Tr^2}{\kappa} - \frac{1}{2} \left( \frac{r}{R} \right)^2 \right|$  as a function of  $R/r$ , using parameter values reported in Arai et al. (1999) ( $r = 5 \text{ nm}$  and  $\kappa = 5.5 \times 10^{-26} \text{ Nm}^2$ ).

The figure shows the predicted decrease of the friction effect with increasing knot size  $R$ . Due to the blocking nature of friction, the parameter  $\mu$  should not be computed by averaging the data points, but rather as an upper limit to the scatter. The upper continuous line, that lies above 95% of the data points, is drawn using the value  $\mu = 0.15$  (the lower curve is drawn with  $\mu = 0.15$  for comparison). We attribute the presence of 5% of the points above the  $\mu = 0.15$  curve to unknown experimental circumstances and to the fact that contact between different parts of the F-actin molecule might not be uniform, with occasional strong self-interactions yielding an effective friction coefficient above 0.15.

#### 4. Discussion

How blocking and unblocking occur is not known (reptation being a possibility), but the friction coefficient determined here is the macroscopic expression of the hindrance opposed to thermal motion and undoing of knots (Kirmizialtin and Makarov, 2008). Friction phenomena between macroscopic surfaces (metal/metal, metal/isolator, isolator/isolator) are beginning to be understood only now. AFM experiments brings the question down to molecular levels (Socoliuc et al., 2004, 2006). In biology, particularly in cytokinesis (where F-actin plays an important role (Canman et al., 2008)), friction is certainly relevant but has not yet been quantified. The value of 0.15 for the self-friction coefficient of F-actin filaments that we report here might be of general significance and might help quantifying the role of friction in the stabilization of protein configurations.

Similarly the self friction coefficient of a macroscopic elastic rod can be estimated in the following way. A trefoil knot is to be tied on the rod and the knot tightened. Then releasing the applied tension ( $T \rightarrow 0$ ) will enable the knot to re-open, though not entirely as friction will eventually hold it locked in a configuration where  $\mu = \sqrt{r/R}/(2 \times 0.49) \simeq \sqrt{r/R}$ .

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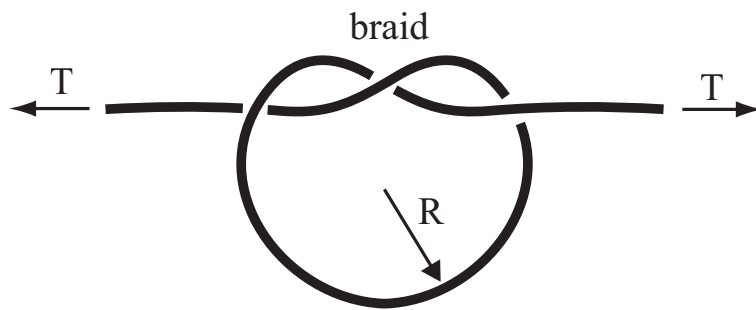


Figure 1: An open trefoil knot tied on an elastic filament. As the pulling tension  $T$  is increased the loop radius  $R$  decreases. Friction takes place in the braid region, where the two strands contact.

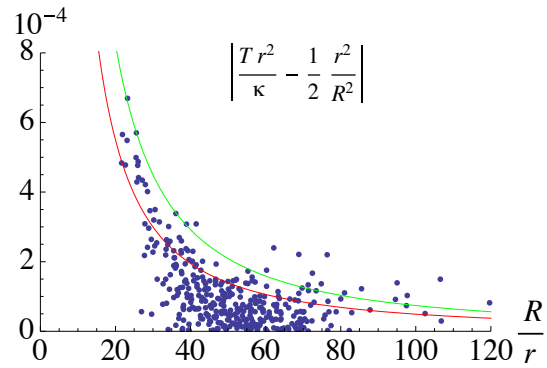
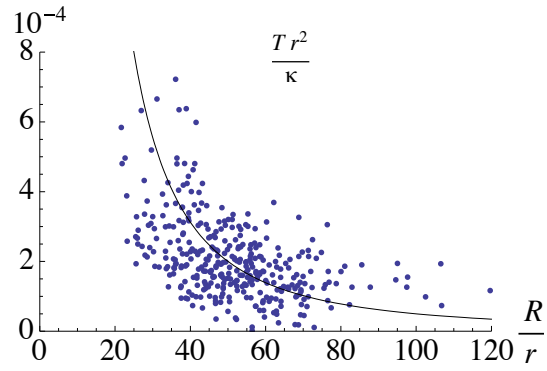


Figure 2: Experimental data from Arai et al. (1999), re-plotted in a way to illustrate Eq. (1). (top) Tension as function of the loop radius  $R$ . The continuous line is from Eq. 1 with  $\mu = 0$ . (bottom) The continuous lines are for  $\mu = 0.1$  (lower, red),  $\mu = 0.15$  (upper, green). Most of the data points lies under the latter one, yielding an estimate for the parallel-self-friction coefficient of the F-actin molecule.