Physica A 507 (2018) 398–405

Contents lists available at ScienceDirect

Physica A

journal homepage: www.elsevier.com/locate/physa

Life time of catch bond clusters

Tal Robin [a], Igor M. Sokolov [b], Michael Urbakh [a,*]

[a] *School of Chemistry, Tel-Aviv University, Tel-Aviv 69978, Israel*
[b] *Institute of Physics, Humboldt University Berlin, Newtonstrasse 15, D-12489 Berlin, Germany*

HIGHLIGHTS

- An accurate analytical equation for the lifetime of adhesion clusters is derived.
- A contribution of fluctuation effects to a response of cluster to an external force is elucidated.
- A scaling equation for the variation of the cluster lifetime with the number of bonds has been found.

ARTICLE INFO

Article history:
Received 16 December 2017
Received in revised form 18 March 2018
Available online 16 May 2018

Keywords:
Adhesion cluster
Life time
Catch bond

ABSTRACT

We consider the mean lifetime of adhesion clusters under a constant applied force and discuss in details different approximate solutions of this problem focusing on catch bond clusters. The analytical equation for the lifetime is derived that is accurate for a broad range of cluster parameters. A scaling equation for the variation of the cluster lifetime with the total number of available bonds is presented that holds already for relatively small clusters. While we focus on consideration of catch bond clusters, the derived equations are applicable also for description of lifetime of clusters including standard slip bonds.

© 2018 Elsevier B.V. All rights reserved.

1. Introduction

Single-molecule force experiments have been proved powerful in obtaining information on intrinsic properties of adhesion bonds, such as binding strengths, energy landscape along the dissociation pathway and kinetics of conformational changes [1–4]. Biological and man-made adhesive contacts often involve not just one but several molecular pairs of the same or different species [5–8]. The number of molecular pairs in an adhesion cluster may range from several (e.g., for nanoscale tribological contacts) to 10^{-5} (e.g., in mature cell–matrix contacts). Adhesion cluster may consist of standard slip bonds, for which the lifetime decreases with increasing applied forces, as well as of catch bonds possessing the unusual physical property that at intermediate forces their lifetimes increase rather than decrease with increasing force [9,10]. In contrast to single molecule pulling experiments, where the rebinding of a broken bond is often negligible due to the elastic relaxation of the transducer, in adhesion clusters operating under force the broken bonds may rebind as long as the remaining intact bonds hold ligands and receptors in close proximity.

Response of bond cluster to the external force is not simply the sum of single-bond responses but is influenced by temporal dynamics across the entire ensemble of bonds. The way how the response of individual bonds can be averaged to yield the cluster's response has been the focus of intense research in the past decade [11–19], however many key aspects of cluster dynamics are still not well understood. A non-equilibrium dissociation of adhesion clusters under force has been first considered in a seminal paper by Bell [11], where a deterministic mean-field equation for the average number of

---

* Corresponding author.
E-mail address: urbakh@post.tau.ac.il (M. Urbakh).

https://doi.org/10.1016/j.physa.2018.05.053
0378-4371/© 2018 Elsevier B.V. All rights reserved.

closed (connected) bonds has been introduced. Later this approach has been extended to describe time-dependent linear loading of adhesion clusters [12–15], which is studied in dynamic force spectroscopy experiments. While the mean-field approach provides a reasonable description of time evolution of the bond population for large clusters, it generally does not allow calculating one of the most important characteristics of the cluster, its lifetime. The latter requires a consideration of fluctuation effects, which are neglected within the mean-field approximation. Contribution of fluctuations is also important for consideration of an average number of closed bonds in small adhesion clusters. The stochastic rupture and formation of bonds in a cluster of parallel bonds can be described by master equations for the probability of having n closed bonds at a given time t, which have been solved numerically for scenarios involving a constant force [16–18] or linear loading [19].

The main objective of this work is to clarify a contribution of fluctuation effects to observable quantities and to obtain analytical results for the lifetime of adhesion clusters, τ. We discuss in details different approximate solutions of this problem focusing on catch bond clusters. We found that the saddle-point approximation of the exact equation for τ is accurate for a broad range of cluster parameters. A scaling equation for the variation of the cluster lifetime with the total number of available bonds has been derived that holds already for relatively small clusters. While we focus on consideration of catch bond clusters, the derived equations are applicable also for description of lifetime of clusters including standard slip bonds.

2. The model

Following previous theoretical studies of forced unbinding of adhesion clusters [16–18], we consider a cluster with a given total number N_t of parallel bonds. At any given time, each of the different bonds can be either open or closed, and we denote by n $(0 \leq n \leq N_t)$ the instantaneous number of closed bonds, i.e. the cluster size. The constant force F applied to the cluster is assumed to be shared equally between the n closed bonds. The stochastic dynamics of the bond cluster can be described by the following master equation [16,17]:

$$\frac{dP(n,t)}{dt} = P(n+1,t)\,r(n+1) + P(n-1,t)\,g(n-1) - P(n,t)\,(r(n)+g(n)) \tag{1}$$

where $P(n,t)$ is the probability that n bonds are closed at time t, and $r(n)$ and $g(n)$ are the rates at which one bond unbinds from or binds to a cluster of size n, respectively. The equations for $r(n)$ and $g(n)$ follow from dissociation and association rates of single bonds. Here, in agreement with majority of single molecule force experiments showing that unbinding and rebinding processes can be described in terms of rate constants [1], we assume a Markovian kinetics of bond formation and rupture. However, some recent experiments and simulations found significant deviations from the Markovian dynamics, which result from complex multidimensional energy landscape of biological molecules [20–22].

Here we focus on the consideration of clusters consisting of catch-bonds [9,10], for which the lifetime increases with increasing force at intermediate forces, f, and decreases with f for higher forces. Thus, a single-bond lifetime of a catch bond is maximal at some finite force. Such behavior can be described by the two-pathway model [9], for which the force-dependence of the dissociation rate of a single bond is given by the following equation

$$r(f) = k_s \exp\left[\frac{x_s}{k_BT}\cdot f\right] + k_c \exp\left[-\frac{x_c}{k_BT}\cdot f\right] \tag{2}$$

where k_c, k_s and x_c, x_s are the force-free dissociation rate constants and barrier widths for each pathway, respectively. The lifetime in Eq. (2) exhibits a maximum as a function of f under the condition $a = \frac{k_c x_c}{k_s x_s} > 1$, and τ is maximized at critical force $f_{cr} = \frac{k_BT}{x_s + x_c}\ln(a)$.

The rate of association is assumed to be independent of the applied force, as the bond is unstressed in its unbound state. It should be noted that the association rate can be force dependent, since the bond stretching required for rebinding may increase with f leading to a corresponding increase of binding potential barrier. This effect is proportional to a square of the applied force, and is small under typical experimental conditions [23]. Correspondingly, the dissociation and association rates $r(n)$ and $g(n)$ entering Eq. (1) can be written as

$$r(n,f) = nr\left(\frac{f}{n}\right),\ g(n,N_t) = k_{on}(N_t - n) \tag{3}$$

where the association rate is assumed to be proportional to the number of available, unbound bonds with an association rate k_{on}. In the calculations presented below the values of k_c/k_s, x_c/x_s have been chosen to fit lifetimes of bonds between FNIII$_{7-10}$ and $\alpha_5\beta_1$ [18,24] and bonds between sPSGL-1 and L-selectin bonds [9,25]. Eq. (1) should be supplemented by boundary conditions at $n = 0$ and $n = N_t$. In most biological and artificial systems the completely dissociated state is prevented from re-association, and therefore in the following we set $g(0) = 0$ in order to model an absorbing boundary at $n = 0$. At $n = N_t$ the association rate given by Eq. (3) equals zero that guarantees $n \leq N_t$ and represents a reflecting boundary condition. The temporal evolution of the number of closed bonds (mean cluster size), $\langle n \rangle$, is given by:

$$\frac{d\langle n\rangle}{dt} = \sum_{n=1}^{N_t}\left[n\frac{dP(n,t)}{dt}\right] = \langle g(n,t)\rangle - \langle r(n,t)\rangle \tag{4}$$

Download English Version:

https://daneshyari.com/en/article/7374805

Download Persian Version:

https://daneshyari.com/article/7374805

Daneshyari.com