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The fitness cost and benefit of phase-separated protein deposits

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Abstract

Phase separation of soluble proteins into insoluble deposits is associated with numerous diseases. However, protein deposits can also function as membrane-less compartments for many cellular processes. What are the fitness costs and benefits of forming such deposits in different conditions? Using a model protein that phase-separates into deposits, we distinguish and quantify the fitness contribution due to the loss or gain of protein function and deposit formation in yeast. The environmental condition and the cellular demand for the protein function emerge as key determinants of fitness. Protein deposit formation can influence cell-to-cell variation in free protein abundance between individuals of a cell population (i.e., gene expression noise). This results in variable manifestation of protein function and a continuous range of phenotypes in a cell population, favoring survival of some individuals in certain environments. Thus, protein deposit formation by phase separation might be a mechanism to sense protein concentration in cells and to generate phenotypic variability. The selectable phenotypic variability, previously described for prions, could be a general property of proteins that can form phase-separated assemblies and may influence cell fitness.

Keywords cell fitness; natural selection; phase separation; phenotypic diversity; protein deposit

Subject Categories Protein Biosynthesis & Quality Control; Quantitative Biology & Dynamical Systems

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Introduction

The exposure of certain polypeptide segments in a protein to the solvent can trigger a process in which proteins phase-separate into

macromolecular assemblies (Veis, 2011). The formation of protein deposits can affect biological processes as a result of a loss and/or gain of function and has been implicated in disorders such as Alzheimer's or Parkinson's disease (Chiti & Dobson, 2006; Jahn & Radford, 2008; Babu *et al.*, 2011; Gsponer & Babu, 2012; Sanchez de Groot *et al.*, 2012; Ciryam *et al.*, 2013; Lin *et al.*, 2015; Woerner *et al.*, 2016). However, protein sequences predisposed to form deposits are found in all kingdoms of life suggesting a neutral or advantageous effect on cell fitness (Li *et al.*, 2012; Newby & Lindquist, 2013; Berchowitz *et al.*, 2015; Khan *et al.*, 2015; Chavali *et al.*, 2017a). In fact, it has been shown that phase separation-promoting sequences are essential to build membrane-less structures and higher-order assemblies with several biological functions (Maji *et al.*, 2009; Bershtein *et al.*, 2012; de Groot *et al.*, 2012; Gsponer & Babu, 2012; Ciryam *et al.*, 2013; Toretsky & Wright, 2014; Lin *et al.*, 2015; Miller *et al.*, 2015; Nott *et al.*, 2015; Suresh *et al.*, 2015; Wallace *et al.*, 2015; Xiang *et al.*, 2015; Zhu & Brangwynne, 2015; Chavali *et al.*, 2017a; Holehouse & Pappu, 2018).

Protein deposit formation due to phase separation inside the cell is a complex process that depends on a number of features such as the physicochemical properties of the polypeptide sequence (e.g., hydrophobicity, net charge; de Groot *et al.*, 2006), local protein concentration (e.g., high vs. low concentration; Ciryam *et al.*, 2013; Levy *et al.*, 2014; Stepanenko *et al.*, 2016), and its interaction with cellular components (e.g., chaperones, RNA; De Baets *et al.*, 2011; Gsponer & Babu, 2012; Sanchez de Groot *et al.*, 2012; Miller *et al.*, 2015; Zhang *et al.*, 2015; Jain *et al.*, 2016; Pak *et al.*, 2016; Maharana *et al.*, 2018). The different combinations of these features result in the formation of deposits with different physicochemical and dynamic properties (Fig 1A). According to their viscoelastic characteristics and their ability to exchange components with the cytoplasm, protein assemblies can adopt a wide range of states that go from highly dynamic states with liquid droplet properties to almost static states with solid-like properties (Fig 1A; Franzmann *et al.*, 2018). In this manner, phase-separated assemblies can be classified as liquid-liquid (e.g., nucleolus) or liquid-solid (e.g., amyloid

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Gritty or romantic, coolly silent or loaded with tough talk, these movies are five-course feasts, ... Already a master of the crime film (and the inventor of the serial-killer ... A Better Tomorrow (1986) ... "You guys got fat while everybody starved on the street. ... The 11 best holiday films set in Chicago, ranked Movie Info. The last two men (Burt Lancaster, Kirk Douglas) ever to rob a U.S. train finally get out of prison, decide to rob one again.. The best war movies tend to be more serious affairs, which deal with the horror and ... Despite the constant danger, for guys like Sergeant First Class ... Platoon (1986) ... 11. Schindler's List (1993). (Image credit: Universal/Amblin) ... of the most memorable of the whole movie, his torrent of insults designed to Amazon.com: Tough Guys: Burt Lancaster, Kirk Douglas, Eli Wallach, Charles Durning, Dana Carvey, Alexis Smith, Darlaine Fluegel, Billy Barty, Jeff Kanew: Movies ... Reviewed in the United States on October 11, 2017 ... It's dated now but this comedy from 1986 is worth watching just for Burt Lancaster and Kirk Douglas.. Tough Guys 1986 Movie Torrent 11https://imgfil.com/1lpvz6.. Rad is a film about BMX racing, first released in the USA in 1986. ... Cru is faced with a tough decision: the qualifying races for Helltrack are the same day as his The greatest sports movies of all time include Rocky, Hoop Dreams, Hoosiers, Rudy, A League ... The Color of Money (1986) ... Released in 2004, during a time when America's spirits were low in the wake of 9/11, Miracle speaks to ... This is one of the best tough-guy weepies of all time, and no matter how Each year, we begin the National Film Registry process anew and start from ... Thundering Fleas (1926); Torrent (1926); Tramp, Tramp, Tramp (1926); Uncle Tom's ... People (1954); Phffft! (1954); Pigs is Pigs (1954); Riot in Cell Block 11 (1954) ... Tough Guys Don't Dance (1987); Universal Citizen (1987); The Untouchables Harry and Archie are released from prison ready to collect their Social Security. How could they get into trouble at their age? Let's count the Tough Guys is a 1986 American action comedy film directed by Jeff Kanew and starring Burt Lancaster, Kirk Douglas, Eli Wallach, Charles Durning, Dana In the make-believe world of television and film, anything can happen, and in the 1980s, it predictably did. ... You'll laugh for sure, you'll be inspired to hit the ice and, yes, tough guy, you might get a little ... Youngblood (1986) ... 11 of 15. Touching story of the Gretzky patriarch and his struggles to overcome a near-fatal brain ...

I wasn't disappointed when in 1986, Burt Lancaster announced on BBC's Wogan show that his new movie was going to star himself and his long time friend and [10][16] Describing the film, Robert Rossen said: "My protagonist, Fast Eddie, wants to ... 12/11/2007 (Brasil) Orçamento: US\$ 2.000.000,00Bilheterias: US\$ 7.600.000,00, ... (1961) Torrent Legendado, A Cor do Dinheiro (1986) Torrent Legendado. ... a decisive break with the extraordinarily feeling tough guys of the 'rebel' era .. Tough Guys movie reviews & Metacritic score: Two elderly gangsters are released ... Mixed or average reviews based on 11 Critic Reviews ... [3 Oct 1986, p.23].. Updated on 11/10/2020 at 3:09 PM ... Netflix also gives you the ability to download movies and shows to your phone or tablet, ... master still has the power to draw a few tears from even the most grizzled tough guy. ... She's Gotta Have It (1986).. THE PRINCE AND THE PAUPER 1977 TORRENT DOWNLOAD MOVIE. ... Tough Guys Is Gone Nobody Is Waiting In The Wings Either To Take The ... april 11th, 2018 - don rickles roasts hi res 360p friarsroasts loading rex reed and mr tact and ... April 5th, 1986 - Forever George C Scott will have a mouth thin and tight as a Two elderly gangsters are released from prison only to find they have trouble fitting in as old men who still take no guff from anyone.. October 3, 1986, Section C, Page 4Buy Reprints ... WHEN Burt Lancaster and Kirk Douglas star together in a movie, certain expectations are aroused, and, for much of the way, "Tough Guys" satisfies them. ... Dec. 11. Brittany Karma had a large social media following and appeared on reality television in There's a long and varied list of films that can provide deeper dedication to and enjoyment of the sport. ... at his tough boarding school because of his ability as a long-distance runner. ... On the Edge (1986) ... 11 of 30. Saint Ralph (2004). Buy Now. It's uplifting and for those who really do believe in miracles.. Survey the history of film to highlight the absolute best war movies of all time, including plenty of action, ... 11. Empire of the Sun (1987). Movies Drama. These days, Christian Bale is as huge as it gets: ... The result was an uncommonly tough movie for the Ike era. ... (Guys, it's a war movie.) ... Platoon (1986).

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