Mechanisms of contractile ring tension production and constriction

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Abstract

The contractile ring is a remarkable tension-generating cellular machine that constricts and divides cells into two during cytokinesis, the final stage of the cell cycle. Since the ring's discovery, the parallels with muscle have been emphasized. Both are contractile actomyosin machineries, and long ago, a muscle-like sliding filament mechanism was proposed for the ring. This review focuses on the mechanisms that generate ring tension and constrict contractile rings. The emphasis is on fission yeast, whose contractile ring is sufficiently well characterized that realistic mathematical models are feasible, and possible lessons from fission yeast that may apply to animal cells are discussed. Recent discoveries relevant to the organization in fission yeast rings suggest a stochastic steady-state version of the classic sliding filament mechanism for tension. The importance of different modes of anchoring for tension production and for organizational stability of constricting rings is discussed. Possible mechanisms are discussed that set the constriction rate and enable the contractile ring to meet the technical challenge of maintaining structural integrity and tension-generating capacity while continuously disassembling throughout constriction.

Keywords Cytokinesis · Contractile ring tension · Anchoring · Actomyosin contractility · Constriction

Introduction

During cytokinesis, the final phase of the cell cycle, animals, fungi, and amoebas physically divide the cell into two using an equatorially positioned actomyosin contractile ring (Fujiwara and Pollard 1976; Maupin and Pollard 1986; Schroeder 1968). The contractile ring is a remarkable and much studied actomyosin contractile machine, but decades after its discovery, many aspects of the mechanisms that endow the ring with contractility and determine its rate of constriction remain poorly understood. The job performed by the ring is essential to life, and the ring must constrict at the right place and time and at the right rate to ensure equal chromosome segregation to the daughter cells.

This review addresses the mechanisms governing the fully assembled ring as a contractile machine. How does this machine generate tension? How does the tension drive or regulate constriction, and how does the ring

accomplish constriction while maintaining its integrity and tension-producing ability? What sets the constriction rate? Many excellent reviews have previously covered positioning and assembly of the ring and the final process of abscission (Mierzwa and Gerlich 2014; Nahse et al. 2017; Oliferenko et al. 2009), topics beyond the scope of the present review.

We will emphasize collective behavior of the ring components as a functional contractile machine, highlighting progress toward a quantitative understanding of the mechanisms that govern how the thousands of molecules in the ring cooperate. As for any machine, to understand its workings quantitatively and perfectly would require complete knowledge of the identity and characteristics of the parts and their architecture within the machine. Such complete knowledge is still remote, but for fission yeast, major steps have been accomplished, to the extent that rational, plausible quantitative models are now possible.

Many critical discoveries about fission yeast cytokinesis have been made in the Pollard lab and, in this issue of *Biophysical Reviews* in honor of Tom Pollard, our review focuses on fission yeast. Experimental advances will be emphasized, as well as mathematical modeling based on quantitative experimental findings. Ring constriction in animal cells is also briefly discussed, and we consider which lessons from fission yeast may apply to animal cells.

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The fully assembled contractile ring

During anaphase, fission yeast assembles the contractile ring from a broad band of membrane-anchored protein complexes called cytokinesis nodes, when actomyosin connections condense the nodes into a compact ring (Vavylonis et al. 2008; Wu et al. 2006). Cytokinesis nodes themselves result from an earlier merger of membrane-anchored type I interphase nodes, which localize near the nucleus (Daga and Chang 2005; Moseley et al. 2009), and type II interphase nodes which move along the membrane to merge with the type I nodes from ~ -240 to -150 min (Akamatsu et al. 2014) (we use the convention that spindle pole body (SPB) separation occurs at time zero (Nabeshima et al. 1998; Wu et al. 2003)). The type I nodes acquire the anillin Mid1 at ~ -230 min, which acts as a scaffold and helps in protein recruitment (Laporte et al. 2011). From ~ -8 min, some of the recruited proteins are the myosin-II Myo2, formin Cdc12 that nucleates and grows actin filaments, and the F-BAR protein Cdc15 (Wu et al. 2003; Wu and Pollard 2005). Actin filaments are nucleated and the nodes condense into a ring from $\sim +2$ to $+11$ min, and the cross-linker α -actinin accumulates from $+5$ min.

From $\sim +11$ to $+35$ min, the assembled ring then undergoes maturation during anaphase B, when the numbers of proteins already present are adjusted, such as the F-BAR protein Cdc15 and the IQGAP protein Rng2, and new proteins such as the unconventional myosin-II Myp2 (Wu et al. 2003) and the cell wall synthesizer Bgs1 (Goss et al. 2014) are added. At this point, the ring is fully assembled and ready to constrict, and Mid1 leaves the ring prior to constriction onset.

In animal cells, the ring assembles when Rho GTPase is activated in an equatorial zone at the plasma membrane. Active Rho activates formins to polymerize actin (Higashi et al. 2008; Otomo et al. 2005) and activates the Rho kinase ROCK, which induces myosin-II motor activity by myosin light chain phosphorylation (Amano et al. 1996; Kosako et al. 2000). An interesting study used light-mediated RhoA activation in interphase HeLa cells to specify rings at selected locations which assembled and constricted, suggesting that Rho-GTP is sufficient for ring assembly (Wagner and Glotzer 2016). Mechanical manipulation of the mitotic spindle in sea urchin embryos perturbs the zone of active Rho, suggesting the spindle plays a role in division site specification (Bement et al. 2005). The mechanism may involve the guanine nucleotide exchange factor (GEF) Ect2 which activates Rho at the membrane and is associated with the spindle midzone (Kimura et al. 2000; Su et al. 2011). Further, cortical flow delivers actin (Cao and Wang 1990) and myosin (Yumura 2001) to the ring.

The focus of this review is the fully assembled contractile ring that results from these processes. To establish a meaningful mathematical model of the ring as a contractile cellular

machine, a list of parts and the architecture of the machine are needed. This section reviews progress in establishing the identities, amounts, biochemical properties, and organization of the constituent proteins of the ring. Most progress has been made for fission yeast. Recent imaging studies in animal cells have revealed exciting new organizational features (Beach et al. 2014; Fenix et al. 2016; Henson et al. 2017).

Composition and organization of the fission yeast contractile ring

More than 150 cytokinesis proteins have been identified in fission yeast (Pollard and Wu 2010) and the time-dependent amounts of a number of key components were measured using quantitative fluorescence microscopy in the Pollard lab (Courtemanche et al. 2016; Wu and Pollard 2005). This powerful method uses quantitative immunoblotting to calibrate fluorescence intensity, so the latter provides a readout of molecule numbers. The mature ring at the onset of constriction contains ~ 2900 Myo2 polypeptides (~ 1450 dimers) and 2000 Myp2 polypeptides; over the course of constriction, their numbers decrease, but more slowly than the ring length such that their linear densities increase ~ 3 -fold (Wu and Pollard 2005). By titrating polymerized actin with mEGFP-LifeAct that binds actin filaments, $\sim 190,000$ molecules of actin were inferred at constriction onset ($\sim 500 \mu\text{m}$ of F-actin), decreasing proportionally to ring length as constriction progresses, so the linear density remains approximately constant (Courtemanche et al. 2016). At onset, ~ 200 dimers of formin Cdc12 and ~ 150 dimers of formin For3 are present, remaining almost constant throughout constriction until a late sharp decrease (Courtemanche et al. 2016).

These amounts tell us, at the most basic level, that the fission yeast ring is packed with actin and myosin, suggesting a machinery that might operate similarly to muscle. The fission yeast ring contains ~ 10 myosin heads per micrometer of actin, or an actin:myosin molecular ratio of 72 (given 1 actin subunit per 2.8 nm of actin filament). How do these numbers compare to muscle? In a vertebrate striated muscle myofibril, the sarcomere cross-section contains bipolar myosin filaments of ~ 600 heads each (Herzog et al. 1992; Squire et al. 2005) arranged in a hexagonal lattice of spacing ~ 47 nm. Actin filaments of length $\sim 1 \mu\text{m}$ (Herzog et al. 1992; Page and Huxley 1963) occupy the lattice with spacing ~ 27 nm formed from the centers of the triangles of the myosin lattice (Squire et al. 2005). Actin and myosin filaments are hence in the ratio 2:1, corresponding to ~ 300 myosin-II heads per micrometer of actin or ~ 2.4 actin subunits per myosin head pair (Squire et al. 2005). Thus, vertebrate striated muscle has ~ 30 -fold more myosin heads per actin subunit than the fission yeast ring.

Organization

In an important recent discovery, the Pollard lab found that punctate structures with composition and size indistinguishable from assembly nodes persist in constricting rings. Fluorescence photoactivation localization microscopy (FPALM) in live cells revealed Myo2, Cdc12, the IQGAP Rng2, and Cdc15 colocalizing in these membrane-anchored constriction nodes (Laplanche et al. 2016) (Fig. 1). Assuming 8 Myo2 dimers per node (Laplanche et al. 2016), this suggests ~ 180 nodes at constriction onset in the $\sim 11\text{-}\mu\text{m}$ -long ring. Thus, constriction nodes are quite tightly packed, with mean spacing $\sim 60\text{ nm}$ about half the $\sim 100\text{ nm}$ node diameter (Fig. 1).

Assuming each of the ~ 200 formin Cdc12 dimers caps an actin filament barbed end, about one formin-capped filament of mean length $\sim 2.5\text{ }\mu\text{m}$ emanates from each node (Fig. 2). This differs from the 4 Cdc12 dimers per assembly node reported by Laplanche et al. (Laplanche et al. 2016), an unexplained discrepancy. This line of reasoning assumes the For3 formins in the ring are not associated with F-actin. This has not been demonstrated; however, deletion of For3 does not appear to alter the total amount of LifeAct-mGFP-labeled actin in the ring (Coffman et al. 2013).

The same FPALM study suggested the actin filaments in the ring form a $\sim 125\text{-nm}$ -thick bundle (Laplanche et al. 2016). At onset, given ~ 50 filaments in the cross section ($\sim 500\text{ }\mu\text{m}$ total actin length in a ring of length $\sim 11\text{ }\mu\text{m}$). This implies a filament spacing of $\sim 16\text{ nm}$, less than the $\sim 27\text{ nm}$ of vertebrate striated muscle and consistent with 3D electron cryotomography images of the ring cross-section (Swulius et al. 2018).

The second myosin-II isoform in the ring, Myp2, does not form dimers (Bezanilla and Pollard 2000) and Myp2 clusters

Fig. 1 Schematic of possible node-based organization in the fission yeast contractile ring, showing nodes only. A $\sim 800\text{ nm}$ section of the ring is represented, with all features drawn to scale. Anillin Mid1, the IQGAP Rng2, F-BAR protein Cdc15, formin Cdc12, and myosin-II Myo2 colocalize in each membrane-anchored node in stoichiometric ratios with the dimensions shown (Laplanche et al. 2016). We estimate 1 formin per node (see main text), whereas 4 formins were described in (Laplanche et al. 2016). At the onset of constriction, we estimate ~ 180 total nodes in the $\sim 11\text{-}\mu\text{m}$ -long ring, or a mean separation of $\sim 60\text{ nm}$. Several nodes are rendered translucent for clarity

Fig. 2 Schematics of possible node-based organization in the fission yeast contractile ring. A $\sim 500\text{ nm}$ section of the ring is represented, drawn to scale. Top: Each node hosts one actin filament, nucleated and elongated at the barbed end by the formin belonging to that node. Actin filaments may have clockwise or anticlockwise polarity. Typical filaments extend beyond this drawing (we estimate $\sim 2.5\text{ }\mu\text{m}$ mean filament length, see main text). The densely packed nodes provide an almost continuous band of Myo2 heads that bind and pull the actin filaments. Middle: Same as top schematic, but several nodes and their actin filaments are rendered translucent for clarity. Nodes move bidirectionally with velocities $\sim 22\text{ nm s}^{-1}$ (red arrows) (Laplanche et al. 2016). We propose that clockwise or anticlockwise motion is determined by the polarity of the actin filament hosted by that node, pulled by Myo2 in other nodes and Myp2 (see main text). Bottom: Same as middle schematic, but clusters of the unconventional myosin-II Myp2 and α -actinin dimers are shown. Myp2 may be unanchored and may contribute to tension by binding and pulling filaments of both polarities. Only $\sim 0.5\text{ }\alpha$ -actinin dimers per μm of actin filament are present. For symbols not shown in legend, see Fig. 1

of substantial size move around the constricting ring (Takaine et al. 2015). Whereas Myo2 appears to be membrane-anchored in nodes, Myp2 may be unanchored (Fig. 2). First, in confocal microscopy images during constriction, a Myp2 ring lies inside a Myo2 ring (Laplanche et al. 2015), consistent with super-resolution microscopy images (McDonald et al. 2017). Second, following disassembly of the actin ring by Latrunculin A (LatA), Myp2 disappears from the division site while Myo2 does not, suggesting Myp2 localizes to the ring by binding actin (Takaine et al. 2015). Third, in *myo2-E1* cells actin bundles that pull away from the membrane and form straight bridges contain Myp2, while Myo2 is left behind at the membrane (Laplanche et al. 2015).

Actin crosslinkers

The homodimeric α -actinin Ain1 and the monomeric fimbrin Fim1 are actin crosslinkers in the ring. α -Actinin is present in very small numbers, with only ~ 250 dimers at constriction onset (Wu and Pollard 2005) or about 1 dimer per $2\ \mu\text{m}$ of F-actin. The amount of Fim1 is unknown *ain1* or *fim1* deletion strains have no phenotype but the double mutants were not viable (Wu et al. 2001). Double mutants were used to show that during constriction, Fim1 has interactions with Rng2, Cdc15 (Nakano et al. 2001), and tropomyosin Cdc8 (Skau and Kovar 2010).

Other ring components

As the ring constricts, transmembrane β -glucan synthases Bgs1 localize adjacent to the ring to synthesize new cell wall. At constriction onset, several thousand Bgs1 are present at the division plane, together with other β -glucan synthases Bgs2, Bgs3, and Bgs4, and the α -glucan synthase Ags1p (Arasada and Pollard 2014; Cortes et al. 2005; Cortes et al. 2002; Cortes et al. 2007; Cortes et al. 2012; Goss et al. 2014; Martin et al. 2003). During the maturation episode, in cells depleted of Cdc15 that showed delayed Bgs1 accumulation, rings slid along the membrane, suggesting a ring-anchoring role for Bgs1 (Arasada and Pollard 2014).

Many of the Cdc15 molecules at the division site appear to lie outside nodes, since ~ 1600 Cdc15 dimers belong to nodes at constriction onset (see above) whereas a total of ~ 8000 was measured (Wu and Pollard 2005). It has been proposed that membrane-bound, oligomerized Cdc15 molecules provide a scaffold for the ring (McDonald et al. 2015). A FPALM study on fixed cells yielded similar ring component locations to those documented above and a three-layered ring architecture was proposed (McDonald et al. 2017). The center of Myo2 was radially displaced $\sim 166\ \text{nm}$ from the membrane, while the center of Myp2 lay $\sim 193\ \text{nm}$ from the membrane, and the actin bundle had a thickness of $\sim 160\ \text{nm}$, greater than the $\sim 125\ \text{nm}$ reported by Laplante et al. (Laplante et al. 2016).

Turnover of ring components

Actin turns over through formin-mediated nucleation and polymerization of actin filaments (Kovar et al. 2003), cofilin-mediated severing (Andrianantoandro and Pollard 2006; Nakano and Mabuchi 2006) and possibly formin dissociation. Consistent with actin turnover, the actin ring disassembles in a few minutes following high doses of the actin monomer-sequestering drug Latrunculin A or in temperature-sensitive *cdc12* mutants (Yonetani et al. 2008; Zhou et al. 2015). Fluorescence recovery after photobleaching shows that Myo2 and Cdc15 turn over rapidly, with half times of 13 s (Sladewski et al. 2009) and 15 s (Clifford et al. 2008),

respectively. Myp2 (Takaine et al. 2015), Rlc1 (Clifford et al. 2008), and Cdc12 (Yonetani et al. 2008) all show turn-over half times of $\sim 30\text{s}$.

Organization of animal cell contractile rings

Maupin and Pollard reported that actin filament ends were anchored to the plasma membrane in Hela cells (Maupin and Pollard 1986). In early furrows of isolated sea urchin cortices, 3D structured illumination microscopy (SIM) showed myosin-II clusters spaced by a few hundred nanometers, reminiscent of fission yeast assembly nodes (Henson et al. 2017). The same study revealed linear bundles of myosin filaments oriented parallel to the ring in late-stage cleavage cortices, and myosin S1-decorated actin filaments of both polarities were visualized by transmission electron microscopy (TEM) oriented parallel to the ring as previously reported (Otto and Schroeder 1990; Sanger and Sanger 1980). Bipolar myosin filaments were also seen in rings of LLC-Pk1 cells by total internal reflection fluorescence SIM (TIRF-SIM) (Beach et al. 2014). These filaments comprised both non-muscle myosin IIA and IIB, in contrast to fission yeast where the two myosin-II isoforms reside in separate structures (see above). In HeLa cell furrows, SIM images show bipolar filaments stacked laterally that form a striated pattern reminiscent of sarcomeric organization (Fenix et al. 2016).

Mechanism of tension generation

Presumably, the principal task of the ring is to generate tension, thought to drive furrow ingression. Once actin filaments and myosin molecules were discovered in the contracting ring (Fujiwara and Pollard 1976; Schroeder 1970; Schroeder 1973), the parallel with muscle was striking, and Schroeder proposed a muscle-like sliding filament mechanism (Schroeder 1968). Finding that the volume of contractile rings in sea urchin eggs was constant during the first third of constriction but thereafter decreased, he then proposed a modified sliding filament mechanism with disassembly (Schroeder 1972).

Several decades later, the parallels remain inescapable, but key differences are apparent. First, the *S. pombe* ring shows no sign of sarcomeric periodicity and in animal cells, although some images suggest some spatially periodic organization (Sanger and Sanger 1980; Fenix et al. 2016), definitive evidence of sarcomeric order is lacking (Laplante et al. 2015; Thiagarajan et al. 2015; Wollrab et al. 2016). Second, the actomyosin machinery is renewed every few minutes in fission yeast, including Myo2, Myp2, and actin, all replaced in about a minute or less (Sladewski et al. 2009; Takaine et al. 2015; Yonetani et al. 2008). Similarly, components turn over in animal cells (Table 1). Third, when striated muscle

Table 1 Comparison among different organisms of cytokinetic ring dimensions, constriction times, and component turnover times

Organism	Width* (μm)	Thickness** (μm)	Initial diameter (μm)	Mean rate of diameter decrease ($\mu\text{m min}^{-1}$)	Constriction time (min)	Myosin-II turnover half-time (s)
<i>S. pombe</i>	$\sim 0.13^a$	$\sim 0.13^a$	$\sim 3.7^b$	0.1^b	$\sim 34^b$	13^c
HeLa cells	$\sim 4^d$	$\sim 0.1\text{--}0.2^e$	20^f	2.8^g	$\sim 7^g$	$\sim 100^h$
<i>C. elegans</i> embryo, one-cell stage	$\sim 2.4^i$	$\sim 0.3^i$	30^i	6^i	5^i	$\dagger$
<i>Drosophila</i> S2	$\sim 3^j$	$\sim 0.5^j$	$\sim 12^k$	$\sim 1^k$	$\sim 10^k$	$\sim 7^l$
Sea urchin egg	8^m	0.2^m	$\sim 70\text{--}110^{m,n}$	$\sim 14\text{--}18^n$	$\sim 5\text{--}10^n$	$\dagger\dagger$

* Ring dimension in direction of the long axis of the dividing cell

** Ring dimension in radial direction within the division plane

^a Measured using FPALM (Laplanche et al. 2016)

^b From measurements of ring dimension versus time using fluorescence microscopy (Chen et al. 2015)

^c From fluorescence recovery after photobleaching (FRAP) experiments using YFP-Myo2 (Sladewski et al. 2009)

^d We estimated this value from structural illumination microscopy (SIM) images (Fenix et al. 2016)

^e Measured from electron micrographs (Schroeder 1970)

^f From fluorescence microscopy images (Wollrab et al. 2016)

^g Measured using phase contrast microscopy (Fenix et al. 2016)

^h Measured using FRAP (Kondo et al. 2011)

ⁱ Measured from confocal microscopy images (Carvalho et al. 2009)

^j We estimated this value from fluorescence microscopy images (D'Avino et al. 2004)

^k Measured using time lapse spinning disk confocal microscopy (Kechad et al. 2012)

^l Measured using FRAP (Uehara et al. 2010)

^m Measured in eggs of *Arbacia punctulata* using electron microscopy (Schroeder 1972)

ⁿ Measured in eggs of several sea urchin species using fluorescence microscopy (Mabuchi 1994)

[†] Component delivery from the cortex and dissociation to the cytoplasm were reported, but not exchange with the cytoplasm (Khaliullin et al. 2018)

^{††} We are unaware of measurements

contracts beyond a certain limit, of order 50% its natural length, the tension drops precipitously, while the contractile ring appears to suffer no tension crisis as it continues shortening (Gordon et al. 1966).

These differences suggest contractile rings employ a qualitatively different tension-generating mechanism than muscle, albeit actomyosin-based. How can tension emerge from the relative disorder of the contractile ring? And how can the ring sustain this tension throughout the entire constriction episode while drastically shortening? In this section, we review the underlying mechanisms suggested by experimental and modeling studies.

Measuring ring tension

The critical test of a mathematical model of the contractile ring is whether it can generate realistic tensions. Since the ring's discovery, few experimental measurements related to ring tension have been available, making it difficult to test mathematical models. Net inward furrowing forces of $\sim 10\text{--}50$ nN were measured by Rappaport from bending of a calibrated needle (Rappaport 1967; Rappaport 1977), and Hiramoto inferred a

furrow force of tens of nanonewtons from the deformation of a ferrofluid droplet (Hiramoto 1975). Yoneda and Dan measured cortical tension from the longitudinal stiffness of a dividing cell and used a force balance at the furrow to derive a lower bound of ~ 60 nN on the ring tension (Yoneda and Dan 1972). However, the method assumes spatially uniform cortical tension and that spherical lobes flank the furrow.

A mean contractile ring tension of ~ 400 pN was measured in fission yeast protoplasts, cells that osmotically swell into spherical shapes following enzymatic digestion of the cell wall (Fig. 3a) (Stachowiak et al. 2014a). The method measures the ring tension itself, rather than the net furrow force, which for animal cells includes an opposing cortical tension contribution. In protoplasts, a tense ring furrows the membrane and slides along the membrane as it constricts; thus, the ring tension could be obtained from a force balance at the furrow between ring tension and membrane tension (Fig. 3b). For the force balance, the furrow angles and cell dimensions were optically measured and the membrane tension measured by micropipette aspiration during interphase, assuming the interphase membrane tension is the same as the membrane tension when a contractile ring is present. The method exploits the fact that fission yeast lacks an

Fig. 3 Experimental method to measure ring tension in fission yeast protoplasts. **a** Enzymatic digestion of the cell wall of an intact fission yeast cell yields a protoplast. Protoplasts osmotically swell into spherical shapes; some assemble a contractile ring. **b** Ring tension T is obtained from a force balance between the inward radial force from ring tension and the net outward radial force from the membrane tensions in

the two lobes $\gamma_{mb}^1, \gamma_{mb}^2$ (left). Angles, lobe radii, and ring radius are measured optically. The membrane tension, measured by micropipette aspiration on an interphase cell (right), is assumed equal to the mean of the lobe tensions

extended actomyosin cortex, so that in the absence of cell wall, osmotic pressure is presumably balanced by a measurable membrane tension that is uniform within each lobe. Consistent with this assumption, the lobes are almost perfectly spherical caps. No such approach is possible when the actin cortex is present, since cortical tension is generally non-uniform due to spatial variations in myosin-II density, actin network morphology, and other local properties.

Taking 400 pN for the fission yeast ring tension and 125 nm for the diameter of the actin bundle at the heart of the ring (Laplante et al. 2016), the ring generates a tensile stress of $\sim 33 \text{ nN } \mu\text{m}^{-2}$, similar to Rappaport's estimate of $\sim 8 \text{ nN } \mu\text{m}^{-2}$ in echinoderm eggs (Rappaport 1977), but 6 times smaller than the $\sim 200 \text{ nN } \mu\text{m}^{-2}$ measured in rabbit skeletal muscle myofibrils (Joumaa et al. 2008). That the contractile ring stress should be less than that of muscle is expected, given the actin:myosin ratio is 30-fold higher.

Lateral anchoring of actin barbed ends generates ring tension

If one accepts the organization of the *S. pombe* ring depicted in Fig. 2, it clearly exerts tension by a simple mechanism: Myo2 binds actin filaments and pulls them laterally, parallel to the ring, so the filaments become tense. A given actin filament belongs to a particular node via the formin dimer belonging to that node that caps this filament's barbed end; the filament will develop tension provided the membrane anchor of its host node provides sufficient lateral resistance to oppose the myosin-II pulling force (Figs. 4 and 5). Note that each of the Myo2 heads that bind the actin filament in question is itself laterally restrained because it belongs to a laterally anchored node. The ring tension at any location is the sum of the tensions of all filaments passing through the ring cross-section at that location (Fig. 4). (A more complete argument should include Myp2, see below.)

Fig. 4 Mechanism of ring tension production by lateral anchoring of actin filament barbed ends. Two nodes of opposite polarity are shown. The barbed end of each actin filament is anchored to its host node via the formin belonging to that node. Myosin molecules of one node bind and pull the actin filament emanating from the other node (blue arrows). The pulling is resisted by lateral membrane drag force acting on the node

anchor, such that the filaments develop tension (blue arrowheads). The total ring tension is the sum of the tensions of all filaments passing through the cross-section at a given location. Pulling forces move nodes laterally with velocities (red arrows) well below the load-free myosin-II velocity, a necessary condition for the filaments to develop tension (see main text)

Fig. 5 Two types of anchoring in the contractile ring: lateral and radial anchoring. Top: Lateral anchoring of an actin filament barbed end enables the filament to develop tension when pulled by myosin Myo2. The same filament is also radially anchored by Myo2, the Myo2 is anchored to its host node, and the node is radially anchored to the plasma membrane. Bottom: Schematic of the ring (Myp2 not shown). Lateral anchoring forces enable the ring to generate tension (pink arrows) while radial anchoring forces support the actin filaments in a bundle and support the ring at the membrane (blue arrows). Some nodes and their actin filaments are rendered translucent for clarity

Thus, sufficiently strong lateral anchoring of actin barbed ends to the plasma membrane generates ring tension. Quantitatively, “sufficiently strong” means sufficient that the lateral node velocities in the membrane lie well below the load-free velocity of myosin-II, v_{myo}^0 (Fig. 4). This ensures the relative actin-myosin velocity does not lie far enough along the myosin-II force-velocity relation to substantially reduce the force (for example, the force would vanish for a relative velocity v_{myo}^0).

This mechanism is supported by several lines of evidence. (i) FPALM measured bidirectional lateral node velocities of order $\sim 22 \text{ nm s}^{-1}$ (Fig. 2) (Laplanche et al. 2016), significantly below $v_{\text{myo}}^0 \approx 300 \text{ nm s}^{-1}$ from in vitro motility assays (Stark et al. 2010). (ii) A molecularly explicit model with formins and node-like clusters of Myo2 independently anchored to the membrane reproduced the experimentally measured tensions of $\sim 400 \text{ pN}$ with a realistic stall force per Myo2 head of 1 pN (Stachowiak et al. 2014a), similar to the value measured for muscle myosin-II (Molloy et al. 1995; Tyska et al. 1999). The lateral anchoring mechanism emerging from that simulation is very similar to that described above. (iii) The same mechanism is used to produce tension in actin filaments connecting membrane-anchored nodes during assembly of the fission yeast ring: a formin belonging to one node grows an actin filament that is grabbed and pulled by Myo2 in another node, and the tension in the actin filament draws the nodes together (Vavylonis et al. 2008).

Barbed-end anchoring may be a natural and practical anchoring choice because formin machinery that processively caps and polymerizes the barbed end provides a potential attachment point. Further, such anchoring orients filaments

optimally for tension, because any myosin binding the filament is then guaranteed to pull the filament away from its barbed end and make it tense. (Compare to the worst case of pointed-end anchoring, when filaments would be compressed by any interaction with myosin.)

Further, no ordered sarcomeric or other architecture is required since the mechanism is robust with respect to disorder. Each filament is almost independently made tense regardless of its location; random positioning of the nodes along the membrane does not compromise the tension. For significant tension, the only requirement is that many myosins bind each filament, but the particular binding location along the filament is unimportant. A typical $\sim 2.5\text{-}\mu\text{m}$ -long actin filament of ~ 920 actin subunits binds ~ 13 molecules of myosin, using the actin:myosin molecular ratio of 72. Estimating that each 2-headed molecule exerts $\sim 1 \text{ pN}$ of force per head, the bound myosin generates a net tension at the filament barbed end of $\sim 26 \text{ pN}$, implying a mean tension along the filament of $\sim 13 \text{ pN}$, since with distance from the barbed end, the tension decreases down to zero at the free pointed end. Thus, the ~ 50 filaments in the cross-section exert a total tension of 650 pN , somewhat larger than but similar to the $\sim 400 \text{ pN}$ reported in (Stachowiak et al. 2014a).

How does this picture compare to Schroeder’s original sliding filament hypothesis? The mechanism described here is a highly dynamic stochastic sliding filament mechanism, where Myo2 in nodes of one polarity pulls on and slides past actin filaments emanating from nodes of the opposite polarity, and vice versa (Fig. 4) (Thiyagarajan et al. 2017). (A node’s polarity is defined by the orientation of the actin filament it hosts.) Thus, nodes of opposite polarity are continuously drawn toward one

another, a process occurring everywhere around the ring between all oppositely oriented node pairs. A second “fixed filament” contribution to tension is generated by chains of interconnected, like-oriented nodes encircling the ring.

An important point is that the qualitative conclusions above, while phrased in the “one formin per node” language, are essentially unchanged even if nodes in fact contain several formins (Laplane et al. 2016) and nucleate several actin filaments. In that case, due to variations in filament polarity, different nodes would possess different net polarities (clockwise or anticlockwise) leading to a qualitatively similar node velocity distribution and essentially the same tension mechanism.

A different picture was presented in a molecularly explicit 3D simulation of the fission yeast ring that generated tensions ~ 250 pN using an organization that did not involve nodes and had unanchored actin filaments (Nguyen et al. 2018).

It is noteworthy that while muscle uses distinct sarcomere-based mechanisms, some kind of barbed-end anchoring of actin filaments nevertheless features. In myofibrils of vertebrate striated muscle, barbed ends of thin filaments of opposite polarities from adjacent sarcomeres are connected in Z-lines (Squire et al. 2005). In smooth muscle, actin filament barbed ends appear anchored to dense bodies (Ashton et al. 1975; Bond and Somlyo 1982; Gunst and Tang 2000), whose role for tension may be similar to that of the nodes in the fission yeast ring. Smooth muscle, though not as dynamic as the contractile ring, has a more dynamic length-tension relationship than does skeletal muscle (Wang et al. 2001).

Whether a barbed-end-anchoring-based mechanism generates tension in animal cells is unknown. However, actin filaments may be anchored to the plasma membrane in HeLa cells (Maupin and Pollard 1986), and actin ring thicknesses are remarkably similar across cells of very different sizes in different species (Table 1), suggesting that actin filament anchoring to the plasma membrane may play a similar role in generating ring tension.

Myo2 radially anchors and bundles actin filaments in the fission yeast contractile ring

Unlike actin, there is no reason to suppose that ring tension requires myosin-II to be laterally anchored: unanchored myosin-II is expected to spontaneously migrate to regions of net zero polarity in the ring, where the number of clockwise- and anticlockwise-oriented actin filaments are equal. At such locations, the myosin-II cluster is stationary and productive despite being unanchored, making a tensile contribution by exerting equal forces in both directions. This theoretical expectation is supported by an experimental study of in vitro actomyosin bundles in which, following ATP addition, muscle myosin-II self-organized into puncta along the bundle whose spatial distribution was consistent with the expected spatial distribution of actin polarity zeroes (Stachowiak et al. 2012).

A mathematical model predicted a power law distribution of distances x between myosin puncta, $P(x) \sim x^{-\frac{3}{2}}$, in quantitative agreement with experiment.

This suggests that in the fission yeast ring, Myp2 could still exert tension even if unanchored, as is suggested by several experimental observations (see earlier discussion and Fig. 2). Myp2 would then contribute to tension similarly to Myo2, pulling on barbed-end-anchored actin filaments and helping make them tense. Consistent with this hypothesis, in protoplasts with the *myo2-E1* temperature-sensitive mutation, contractile rings appear to generate tension because they constrict (Stachowiak et al. 2014a), despite Myo2-E1 having minimal ATPase activity (Lord and Pollard 2004). Thus, unanchored Myp2 may generate the residual tension.

If myosin anchoring is not required for tension, why is Myo2 membrane-anchored in nodes? Examining again the organization depicted in Fig. 2, it is apparent that unanchoring Myo2 from the membrane would partially untether the actomyosin core bundle from the membrane (imagine separating every Myo2 cluster from its host node by severing its C-terminal connections to the node). The effect would be drastic, as actin filaments would now be attached to the membrane by their barbed ends only, and would presumably straighten due to Laplace forces acting centripetally on tense filaments with curvature. Unanchored Myo2 and Myp2 would presumably bundle the straightened filaments into bridges making straight shortcuts between points on the circular ring. Indeed, almost precisely, this phenotype is observed in live *myo2-E1* cells. The Myo2-E1 mutant binds actin weakly (Lord and Pollard 2004; Stark et al. 2013), and straight bridges containing actin filaments and Myp2 detach from the plasma membrane leaving Myo2 behind (Laplane et al. 2015). This situation is slightly different to the Myo2 unanchoring thought experiment, but similar: in this case, actin filaments are apparently cut loose from Myo2, but with similar effects.

Thus, anchoring of Myo2 to the membrane appears to be essential. Unlike actin, however, the anchoring is radial, not transverse. A major job of Myo2, in addition to exerting tensile force, appears to be radial anchoring and bundling of the actin filaments constituting the core of the contractile ring (Fig. 5). To exert these radial anchoring forces, the Myo2 must of course itself be radially anchored to the plasma membrane.

Role of passive cross-linkers

The cross-linkers α -actinin Ain1 and fimbrin Fim1 are present in the *S. pombe* ring (Wu et al. 2001). α -Actinin is often thought of as a spacer allowing myosin-II heads to interpolate between actin filaments, consistent with the 36 nm length of a human- α -actinin-2 dimer (Ribeiro Ede et al. 2014), although the *S. pombe* α -actinin dimer may be shorter as it has two fewer spectrin repeats (Li et al. 2016). However, at

constriction onset, only ~250 dimers of α -actinin or 0.5 α -actinin cross-linkers per micron of F-actin are present. A spatial separation of ~9 nm between actin-binding sites was reported for Fimbrin Fim1 (Klein et al. 2004), but the number of molecules in the ring is unknown. In vitro TIRF studies measured Ain1 and Fim1 residence times in actin bundles of ~0.3 s and ~30 s, respectively, and showed that both crosslink parallel and antiparallel filaments (Li et al. 2016; Skau et al. 2011). Overall, the dynamical role of α -actinin may be relatively minor and Myo2 may be the principal cross-linker and bundler in the fission yeast ring.

Bundling proteins in animal cell contractile rings include anillin (Field and Alberts 1995), plastin or fimbrin (Ding et al. 2017), and α -actinin (Fujiwara et al. 1978). Variations in the amounts of these proteins affect the rate of furrow ingression (Ding et al. 2017; Mukhina et al. 2007). In *C. elegans* zygotes depleted of anillin, the maximum furrowing speed peaked when anillin levels were 50% of wild-type (Descovich et al. 2018).

Ring constriction

Given that the ring generates tension, how does this lead to constriction, and at what rate? The relation between ring tension and constriction rate is complex. One might imagine the constriction rate is determined by the ring tension and a friction coefficient associated with dissipative processes that resist constriction. But which dissipative processes are dominant is far from obvious, and ring tension is not the only force involved in furrow ingression. In animal cells, the ring is contiguous with an actomyosin cortex whose contractility supplies a force directed toward the poles thought to oppose furrow ingression (Sedzinski et al. 2011). For *S. pombe*, ring constriction is accompanied by septum growth and the ring cannot constrict unless the septum obliges by inward growth (Johnson et al. 1973).

What is the outcome of these competing forces, and what sets the constriction rate? How does the constricting contractile machine remain tensile and functional as it continuously shortens? This section reviews studies that have illuminated these and related questions.

Onset of constriction

Constriction onset must be tightly regulated to ensure that ring constriction does not interfere with equal chromosome segregation to the daughter cells. In fission yeast, the protein kinase Sid2 and its binding partner Mob1 (Salimova et al. 2000) localize to the ring from the SPBs where they are thought to initiate constriction (Hou et al. 2004). Sid2 arrives at the ring at ~+30 min, just before constriction onset at +36 min (Pu et al. 2015). These events are part of a signaling cascade called the septation initiation network (SIN) (Balasubramanian et al.

1998; Simanis 2015). SIN activity is also responsible for dispersing type I node components into the cytoplasm ~15 min before constriction onset (Pu et al. 2015).

Fission yeast rings can be made to assemble and constrict even during interphase. On activation of the GTPase Spg1 which belongs to the SIN cascade during interphase, either through its overexpression or by inactivation of the Spg1 GAP, rings assemble and septa ingress (Hachet and Simanis 2008; Schmidt et al. 1997). A few other members of the SIN are required for this effect (Balasubramanian et al. 1998; Schmidt et al. 1997). These experiments suggest that the SIN cascade is sufficient for constriction onset. However, the rings appear to assemble using filamentous actomyosin structures, unlike the normal assembly process via nodes.

It is interesting to compare these findings with the optogenetic experiments of Wagner et al., where a localized light signal activated Rho and caused furrowing in non-adherent interphase HeLa and NIH3T3 cells within ~2 min of the illumination being switched on (Wagner and Glotzer 2016). The rings of *S. pombe* constricted ~50% slower than wild-type but appear to complete constriction, whereas the rings of HeLa and NIH3T3 cells did not constrict beyond ~70%.

What determines the constriction rate?

In fission yeast, as the plasma membrane-anchored ring constricts the septum grows inwards on the other side of the membrane. Given the large cell wall modulus (Atilgan et al. 2015), the ring tension is far too weak to mechanically deform the septum (Thiyagarajan et al. 2015). Thus, assuming the membrane does not detach from the cell wall, the process of septation presumably sets the constriction rate, not the ring tension itself. Assuming cell volume decreases as the septum grows inwards, the growth processes must perform work against osmotic pressure, which is much higher than in animal cells (Atilgan et al. 2015; Tinevez et al. 2009).

However, ring tension may influence the septation rate if septum synthesis is mechanosensitive. It was hypothesized that this effect explains how proper septum closure is achieved (Thiyagarajan et al. 2015). The septum hole of initial perimeter ~11 μ m closes by the action of several thousand cell wall-growing glucan synthases at the membrane (Arasada and Pollard 2014; Goss et al. 2014). Were each synthase to grow septum material independently, given the inevitable stochasticity of molecular growth rates, the circular septum hole would become rough and irregular and would fail to close down as a nearly perfectly circular hole, possibly preventing the daughter cells from being properly encased in new cell wall. It was hypothesized that this fate could be avoided were the synthesis rate increased by inward radial force from ring tension. Growth would then be faster in regions of higher curvature due to

Fig. 6 Contractile ring tension may regulate septum closure in fission yeast. **a** If the several thousand glucan synthases around the septum edge grew septum independently of one another, due to intrinsic stochasticity of molecular growth processes, the constricting septum edge would become increasingly rough and close improperly (top). If septum growth rates are mechanosensitive and the growth machinery mechanically coupled to the ring, higher curvature regions grow faster because the inward Laplace force from ring tension is higher. This mechanism smooths irregularities and closes the septum properly

Laplace's law (Fig. 6a). Valleys in the septum edge would grow faster than peaks, tending to restore circularity.

A mathematical model implementing mechanosensitive septum growth demonstrated that septum edges become smoothed, and the degree of smoothing is set by an effective diffusivity parameter depending on the ring tension and the mechanosensitivity of the synthesis machinery. When the effect was attributed to β -glucan synthase Bgs1, a mechanosensitivity 0.15 pN^{-1} was inferred (the fractional increase in synthesis rate per piconewton of force applied to the Bgs1) by comparing model-predicted septum edges with edges measured in live cells from fluorescence images (Fig. 6b). This value is similar to measured mechanosensitivities of other cellular machineries including formins ($\sim 0.4\text{--}1 \text{ pN}^{-1}$ (Courtemanche et al. 2013; Jegou et al. 2013)) and stress fibers (0.7 pN^{-1} (Stachowiak et al. 2014b)). The model predicted that the amplitude of roughness of a septum edge over a length scale x increases with a

(bottom). **b** Confocal fluorescence micrograph of the division plane of a fission yeast cell expressing GFP-Bgs1 and Rlc1-tdTomato. GFP-Bgs1 labels the septum and Rlc1-tdTomato labels the ring. The septum edge is almost circular. Scale bar: $1 \mu\text{m}$. **c** Mean roughness of septum edges versus length scale. Comparison of roughness data from simulated septum edges and from fluorescence micrographs of septa in live cells. Both sets of data exhibit a power law growth of roughness with exponent 0.47. Image reproduced from (Thiyagarajan et al. 2015)

characteristic power law $\sim x^{1/2}$ (Fig. 6c), in agreement with roughness measurements of septum edges in live cells using edge detection. This is the same power law as predicted by the classic Edwards-Wilkinson and Kardar-Parisi-Zhang models of stochastic interface growth with diffusive smoothing (Edwards and Wilkinson 1982; Kardar et al. 1986).

In animal cells, furrow ingression is presumably promoted by ring tension but resisted by forces from the actomyosin cortex. An early mathematical model invoked a gradient of surface tension to produce constriction, highest at the equator and lowest at the poles (White and Borisy 1983). A recent model used active gel theory to describe the shape evolution of dividing sand-dollar zygotes (Turlier et al. 2014). Myosin activity was assumed highest at the furrow due to an active RhoA signal, and viscous cortical forces and osmotic pressure were accounted for. Predicted furrowing rates and shapes were consistent with experiment. Several studies show ring

constriction rates are affected when myosin-II activity or concentrations of actin bundling proteins are altered (Descovich et al. 2018; Ding et al. 2017; Fenix et al. 2016). In *C. elegans* embryos, a model hypothesized a positive feedback mechanism where regions of high negative Gaussian curvature enhance actin filament alignment and thus contractility, leading to faster furrowing in such regions and even more negative curvature (Dorn et al. 2016). Solutions showed asymmetric furrows sustained for most of constriction as seen experimentally, seeded close to onset by small asymmetries in filament alignment due to thermal fluctuations.

How does the contractile ring remain functional while constricting?

As an actomyosin contractile machine, the contractile ring is called upon to meet a significant technical challenge during constriction: it must exert tension while undergoing dramatic shortening. Muscle accomplishes this by contractile sliding of F-actin filaments relative to myosin-II thick filaments, a reversible process in which the densities of molecules increase and sarcomeres thicken without shedding molecules (Squire et al. 2005).

Contractile rings use fundamentally different shortening mechanisms. Not long after the discovery of the contractile ring, Schroeder measured a decreasing contractile ring volume in sea urchin eggs, and proposed that molecules dissociate from the shortening ring (Schroeder 1972). It is now known that the contractile ring in *S. pombe* disassembles as it shortens while maintaining an approximately constant density of actin per unit length of ring (Courtemanche et al. 2016; Goss et al. 2014; Wu and Pollard 2005). In

C. elegans embryos, the densities of myosin II (NMY-2), septin (UNC-59), and anillin (ANI-1) remain approximately constant throughout constriction (Carvalho et al. 2009), and during cellularization of *Drosophila* embryos, the total levels of F-actin and Myosin-2 decrease in proportion to ring size (Xue and Sokac 2016).

How does the ring remain a functional contractile machine while shedding material as it shortens? One theoretical possibility is that its organization is fixed, possibly consisting of many repeat sarcomere-like units, each of which shortens without changing the global organization. In this model, memory of the ring organization is retained throughout constriction. In a second model, the molecules turn over so rapidly that the contractile ring machinery is replaced on a timescale much less than the constriction time (Fig. 7). For fission yeast, the evidence supports the latter model, since Myo2 and Cdc15 turn over in 13 s (Sladewski et al. 2009) and 15 s (Clifford et al. 2008), respectively; Myp2 (Takaine et al. 2015), Rlc1 (Clifford et al. 2008), and Cdc12 (Yonetani et al. 2008) turn over in ~ 30 s; and the actin turnover time is about 1 min (Yonetani et al. 2008). In molecularly explicit simulations incorporating these turnover processes, incoming components self-assembled into the ring structure (Stachowiak et al. 2014a). Thus, every 1–2 min, the ring is rebuilt, allowing it to quasi-statically shorten on the much longer constriction timescale (~ 30 min) without damaging its working mechanisms. The self-assembly processes include zippering of newly nucleated actin filaments into the ring by myosin Myo2, and lateral pulling of recently bound Myo2 clusters into the body of the ring (Stachowiak et al. 2014a). These are similar to the node-condensing

Fig. 7 Continuous rebuilding mechanism to maintain organization and functionality of the contractile ring as it constricts. Incoming components self-assemble and replace dissociated components. The mechanism requires fast turnover/self-assembly relative to the constriction rate, so that organizational homeostasis and tension is maintained or regulated. Were the rebuilding rate less than the constriction rate, the component densities would be expected to increase, disrupting organization and tension production

processes during ring assembly (Vavylonis et al. 2008). Thus, the constricting ring continuously recapitulates the assembly process as it constricts.

It is unclear how incoming components are targeted to the vicinity of the fission yeast ring as it constricts. However, the ring is presumably stabilized at the deepest point of the ingression furrow by its own tension, and if an incoming node were to bind nearby and make an F-actin connection, it may be pulled into the ring according to the self-assembly mechanism described in (Stachowiak et al. 2014a).

In animal cells, myosin and actin turnover times are much less than constriction times (Table 1). Thus, the same broad mechanism as in fission yeast may prevail.

However, in some cases, some components may not turn over and other processes may organize components in the ring. In *C. elegans* embryos, rings continued to constrict if LatA was added after constriction onset, suggesting that under normal conditions, actin may not be polymerized (Carvalho et al. 2009), and cortical flow was measured to align actin filaments into the furrow (Reymann et al. 2016).

In another study of *C. elegans* embryos, myosin density in the ring was measured to increase throughout constriction, which was attributed to compression of the cortex as it flowed into the furrow (Khaliullin et al. 2018).

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Compliance with ethical standards

Conflict of interest Ben O'Shaughnessy declares that he has no conflict of interest. Sathish Thiyagarajan declares that he has no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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References

- Akamatsu M, Berro J, Pu KM, Tebbs IR, Pollard TD (2014) Cytokinetic nodes in fission yeast arise from two distinct types of nodes that merge during interphase. *J Cell Biol* 204:977–988. <https://doi.org/10.1083/jcb.201307174>
- Amano M et al (1996) Phosphorylation and activation of myosin by rho-associated kinase (rho-kinase). *J Biol Chem* 271:20246–20249
- Andrianantoandro E, Pollard TD (2006) Mechanism of actin filament turnover by severing and nucleation at different concentrations of ADF/cofilin. *Mol Cell* 24:13–23. <https://doi.org/10.1016/j.molcel.2006.08.006>
- Arasada R, Pollard TD (2014) Contractile ring stability in *S.pombe* depends on F-BAR protein Cdc15p and Bgs1p transport from the Golgi complex. *Cell Rep* 8:1533–1544. <https://doi.org/10.1016/j.celrep.2014.07.048>
- Ashton FT, Somlyo AV, Somlyo AP (1975) The contractile apparatus of vascular smooth muscle: intermediate high voltage stereo electron microscopy. *J Mol Biol* 98:17–29
- Atilgan E, Magidson V, Khodjakov A, Chang F (2015) Morphogenesis of the fission yeast cell through cell wall expansion. *Curr Biol* 25:2150–2157. <https://doi.org/10.1016/j.cub.2015.06.059>
- Balasubramanian MK et al (1998) Isolation and characterization of new fission yeast cytokinesis mutants. *Genetics* 149:1265–1275
- Beach JR, Shao L, Remmert K, Li D, Betzig E, Hammer JA 3rd (2014) Nonmuscle myosin II isoforms coassemble in living cells. *Curr Biol* 24:1160–1166. <https://doi.org/10.1016/j.cub.2014.03.071>
- Bement WM, Benink HA, von Dassow G (2005) A microtubule-dependent zone of active RhoA during cleavage plane specification. *J Cell Biol* 170:91–101. <https://doi.org/10.1083/jcb.200501131>
- Bezanilla M, Pollard TD (2000) Myosin-II tails confer unique functions in *Schizosaccharomyces pombe*: characterization of a novel myosin-II tail. *Mol Biol Cell* 11:79–91
- Bond M, Somlyo AV (1982) Dense bodies and actin polarity in vertebrate smooth muscle. *J Cell Biol* 95:403–413
- Cao LG, Wang YL (1990) Mechanism of the formation of contractile ring in dividing cultured animal cells. II. Cortical movement of microinjected actin filaments. *J Cell Biol* 111:1905–1911
- Carvalho A, Desai A, Oegema K (2009) Structural memory in the contractile ring makes the duration of cytokinesis independent of cell size. *Cell* 137:926–937. <https://doi.org/10.1016/j.cell.2009.03.021>
- Chen Q, Courtemanche N, Pollard TD (2015) Aip1 promotes actin filament severing by cofilin and regulates constriction of the cytokinetic contractile ring. *J Biol Chem* 290:2289–2300. <https://doi.org/10.1074/jbc.M114.612978>
- Clifford DM, Wolfe BA, Roberts-Galbraith RH, McDonald WH, Yates JR 3rd, Gould KL (2008) The Clp1/Cdc14 phosphatase contributes to the robustness of cytokinesis by association with anillin-related Mid1. *J Cell Biol* 181:79–88. <https://doi.org/10.1083/jcb.200709060>
- Coffman VC, Sees JA, Kovar DR, Wu JQ (2013) The formins Cdc12 and For3 cooperate during contractile ring assembly in cytokinesis. *J Cell Biol* 203:101–114. <https://doi.org/10.1083/jcb.201305022>
- Cortes JC, Carnero E, Ishiguro J, Sanchez Y, Duran A, Ribas JC (2005) The novel fission yeast (1,3)beta-D-glucan synthase catalytic subunit Bgs4p is essential during both cytokinesis and polarized growth. *J Cell Sci* 118:157–174. <https://doi.org/10.1242/jcs.01585>
- Cortes JC, Ishiguro J, Duran A, Ribas JC (2002) Localization of the (1,3)beta-D-glucan synthase catalytic subunit homologue Bgs1p/Cps1p from fission yeast suggests that it is involved in septation, polarized growth, mating, spore wall formation and spore germination. *J Cell Sci* 115:4081–4096
- Cortes JC et al (2007) The (1,3)beta-D-glucan synthase subunit Bgs1p is responsible for the fission yeast primary septum formation. *Mol Microbiol* 65:201–217. <https://doi.org/10.1111/j.1365-2958.2007.05784.x>
- Cortes JC et al (2012) Fission yeast Ags1 confers the essential septum strength needed for safe gradual cell abscission. *J Cell Biol* 198:637–656. <https://doi.org/10.1083/jcb.201202015>
- Courtemanche N, Lee JY, Pollard TD, Greene EC (2013) Tension modulates actin filament polymerization mediated by formin and profilin. *Proc Natl Acad Sci U S A* 110:9752–9757. <https://doi.org/10.1073/pnas.1308257110>
- Courtemanche N, Pollard TD, Chen Q (2016) Avoiding artefacts when counting polymerized actin in live cells with LifeAct fused to fluorescent proteins. *Nat Cell Biol* 18:676–683. <https://doi.org/10.1038/ncb3351>

- D'Avino PP, Savoian MS, Glover DM (2004) Mutations in sticky lead to defective organization of the contractile ring during cytokinesis and are enhanced by Rho and suppressed by Rac. *J Cell Biol* 166:61–71. <https://doi.org/10.1083/jcb.200402157>
- Daga RR, Chang F (2005) Dynamic positioning of the fission yeast cell division plane. *Proc Natl Acad Sci U S A* 102:8228–8232. <https://doi.org/10.1073/pnas.0409021102>
- Descovich CP et al (2018) Cross-linkers both drive and brake cytoskeletal remodeling and furrowing in cytokinesis. *Mol Biol Cell* 29:622–631. <https://doi.org/10.1091/mbc.E17-06-0392>
- Ding WY et al (2017) Plastin increases cortical connectivity to facilitate robust polarization and timely cytokinesis. *J Cell Biol* 216:1371–1386. <https://doi.org/10.1083/jcb.201603070>
- Dorn JF, Zhang L, Phi TT, Lacroix B, Maddox PS, Liu J, Maddox AS (2016) A theoretical model of cytokinesis implicates feedback between membrane curvature and cytoskeletal organization in asymmetric cytokinetic furrowing. *Mol Biol Cell* 27:1286–1299. <https://doi.org/10.1091/mbc.E15-06-0374>
- Edwards SF, Wilkinson DR (1982) The surface statistics of a granular aggregate. *Proceedings of the Royal Society of London A Mathematical and Physical Sciences* 381:17–31. <https://doi.org/10.1098/rspa.1982.0056>
- Fenix AM, Taneja N, Buttler CA, Lewis J, Van Engelenburg SB, Ohl R, Burnette DT (2016) Expansion and concatenation of non-muscle myosin IIA filaments drive cellular contractile system formation during interphase and mitosis. *Mol Biol Cell* <https://doi.org/10.1091/mbc.E15-10-0725>
- Field CM, Alberts BM (1995) Anillin, a contractile ring protein that cycles from the nucleus to the cell cortex. *J Cell Biol* 131:165–178
- Fujiwara K, Pollard TD (1976) Fluorescent antibody localization of myosin in the cytoplasm, cleavage furrow, and mitotic spindle of human cells. *J Cell Biol* 71:848–875
- Fujiwara K, Porter ME, Pollard TD (1978) Alpha-actinin localization in the cleavage furrow during cytokinesis. *J Cell Biol* 79:268–275
- Gordon AM, Huxley AF, Julian FJ (1966) Tension development in highly stretched vertebrate muscle fibres. *J Physiol* 184:143–169
- Goss JW, Kim S, Bledsoe H, Pollard TD (2014) Characterization of the roles of Btlp in fission yeast cytokinesis. *Mol Biol Cell* 25:1946–1957. <https://doi.org/10.1091/mbc.E13-06-0300>
- Gunst SJ, Tang DD (2000) The contractile apparatus and mechanical properties of airway smooth muscle. *Eur Respir J* 15:600–616
- Hachet O, Simanis V (2008) Mid1p/anillin and the septation initiation network orchestrate contractile ring assembly for cytokinesis. *Genes Dev* 22:3205–3216. <https://doi.org/10.1101/gad.1697208>
- Henson JH et al (2017) The ultrastructural organization of actin and myosin II filaments in the contractile ring: new support for an old model of cytokinesis. *Mol Biol Cell* 28:613–623. <https://doi.org/10.1091/mbc.E16-06-0466>
- Herzog W, Kamal S, Clarke HD (1992) Myofilament lengths of cat skeletal muscle: theoretical considerations and functional implications. *J Biomech* 25:945–948
- Higashi T et al (2008) Biochemical characterization of the rho GTPase-regulated actin assembly by diaphanous-related formins, mDia1 and Daam1, in platelets. *J Biol Chem* 283:8746–8755. <https://doi.org/10.1074/jbc.M707839200>
- Hiramoto Y (1975) Force exerted by cleavage furrow of sea-urchin eggs. *Develop Growth Differ* 17:27–38
- Hou MC, Guertin DA, McCollum D (2004) Initiation of cytokinesis is controlled through multiple modes of regulation of the Sid2p-Mob1p kinase complex. *Mol Cell Biol* 24:3262–3276
- Jegou A, Carlier MF, Romet-Lemonne G (2013) Formin mDia1 senses and generates mechanical forces on actin filaments. *Nat Commun* 4:1883. <https://doi.org/10.1038/ncomms2888>
- Johnson BF, Yoo BY, Calleja GB (1973) Cell division in yeasts: movement of organelles associated with cell plate growth of *Schizosaccharomyces pombe*. *J Bacteriol* 115:358–366
- Joumaa V, Leonard TR, Herzog W (2008) Residual force enhancement in myofibrils and sarcomeres. *Proc Biol Sci* 275:1411–1419. <https://doi.org/10.1098/rspb.2008.0142>
- Kardar M, Parisi G, Zhang YC (1986) Dynamic scaling of growing interfaces. *Phys Rev Lett* 56:889–892. <https://doi.org/10.1103/PhysRevLett.56.889>
- Kechad A, Jananji S, Ruella Y, Hickson GR (2012) Anillin acts as a bifunctional linker coordinating midbody ring biogenesis during cytokinesis. *Curr Biol* 22:197–203. <https://doi.org/10.1016/j.cub.2011.11.062>
- Khaliullin RN, Green RA, Shi LZ, Gomez-Cavazos JS, Berns MW, Desai A, Oegema K (2018) A positive-feedback-based mechanism for constriction rate acceleration during cytokinesis in *Caenorhabditis elegans*. *Elife* 7. <https://doi.org/10.7554/eLife.36073>
- Kimura K, Tsuji T, Takada Y, Miki T, Narumiya S (2000) Accumulation of GTP-bound RhoA during cytokinesis and a critical role of ECT2 in this accumulation. *J Biol Chem* 275:17233–17236. <https://doi.org/10.1074/jbc.C000212200>
- Klein MG et al (2004) Structure of the actin crosslinking core of fimbrin. *Structure* 12:999–1013. <https://doi.org/10.1016/j.str.2004.04.010>
- Kondo T, Hamao K, Kamijo K, Kimura H, Morita M, Takahashi M, Hosoya H (2011) Enhancement of myosin II/actin turnover at the contractile ring induces slower furrowing in dividing HeLa cells. *Biochem J* 435:569–576. <https://doi.org/10.1042/BJ20100837>
- Kosako H, Yoshida T, Matsumura F, Ishizaki T, Narumiya S, Inagaki M (2000) Rho-kinase/ROCK is involved in cytokinesis through the phosphorylation of myosin light chain and not ezrin/radixin/moesin proteins at the cleavage furrow. *Oncogene* 19:6059–6064. <https://doi.org/10.1038/sj.onc.1203987>
- Kovar DR, Kuhn JR, Tichy AL, Pollard TD (2003) The fission yeast cytokinesis formin Cdc12p is a barbed end actin filament capping protein gated by profilin. *J Cell Biol* 161:875–887. <https://doi.org/10.1083/jcb.200211078>
- Laplace C, Berro J, Karatekin E, Hernandez-Leyva A, Lee R, Pollard TD (2015) Three myosins contribute uniquely to the assembly and constriction of the fission yeast cytokinetic contractile ring. *Curr Biol* 25:1955–1965. <https://doi.org/10.1016/j.cub.2015.06.018>
- Laplace C, Huang F, Tebbis IR, Bewersdorf J, Pollard TD (2016) Molecular organization of cytokinesis nodes and contractile rings by super-resolution fluorescence microscopy of live fission yeast. *Proc Natl Acad Sci U S A* 113:E5876–E5885. <https://doi.org/10.1073/pnas.1608252113>
- Laporte D, Coffman VC, Lee JJ, Wu JQ (2011) Assembly and architecture of precursor nodes during fission yeast cytokinesis. *J Cell Biol* 192:1005–1021. <https://doi.org/10.1083/jcb.201008171>
- Li Y et al (2016) The F-actin bundler alpha-actinin Ain1 is tailored for ring assembly and constriction during cytokinesis in fission yeast. *Mol Biol Cell* 27:1821–1833. <https://doi.org/10.1091/mbc.E16-01-0010>
- Lord M, Pollard TD (2004) UCS protein Rng3p activates actin filament gliding by fission yeast myosin-II. *J Cell Biol* 167:315–325. <https://doi.org/10.1083/jcb.200404045>
- Mabuchi I (1994) Cleavage furrow: timing of emergence of contractile ring actin filaments and establishment of the contractile ring by filament bundling in sea urchin eggs. *J Cell Sci* 107(Pt 7):1853–1862
- Martin V, Garcia B, Camero E, Duran A, Sanchez Y (2003) Bgs3p, a putative 1,3-beta-glucan synthase subunit, is required for cell wall assembly in *Schizosaccharomyces pombe*. *Eukaryot Cell* 2:159–169
- Maupin P, Pollard TD (1986) Arrangement of actin filaments and myosin-like filaments in the contractile ring and of actin-like filaments in the mitotic spindle of dividing HeLa cells. *J Ultrastruct Mol Struct Res* 94:92–103

- McDonald NA, Lind AL, Smith SE, Li R, Gould KL (2017) Nanoscale architecture of the *Schizosaccharomyces pombe* contractile ring. *Elife* 6 doi:ARTN e28865 <https://doi.org/10.7554/eLife.28865.001>
- McDonald NA, Vander Kooi CW, Ohi MD, Gould KL (2015) Oligomerization but not membrane bending underlies the function of certain F-BAR proteins in cell motility and cytokinesis. *Dev Cell* 35:725–736. <https://doi.org/10.1016/j.devcel.2015.11.023>
- Mierzwa B, Gerlich DW (2014) Cytokinetic abscission: molecular mechanisms and temporal control. *Dev Cell* 31:525–538. <https://doi.org/10.1016/j.devcel.2014.11.006>
- Molloy JE, Burns JE, Kendrick-Jones J, Tregear RT, White DC (1995) Movement and force produced by a single myosin head. *Nature* 378:209–212. <https://doi.org/10.1038/378209a0>
- Moseley JB, Mayeux A, Paoletti A, Nurse P (2009) A spatial gradient coordinates cell size and mitotic entry in fission yeast. *Nature* 459:857–860. <https://doi.org/10.1038/nature08074>
- Mukhina S, Wang YL, Murata-Hori M (2007) Alpha-actinin is required for tightly regulated remodeling of the actin cortical network during cytokinesis. *Dev Cell* 13:554–565. <https://doi.org/10.1016/j.devcel.2007.08.003>
- Nabeshima K et al (1998) Dynamics of centromeres during metaphase-anaphase transition in fission yeast: Dis1 is implicated in force balance in metaphase bipolar spindle. *Mol Biol Cell* 9:3211–3225
- Nahse V, Christ L, Stenmark H, Campsteijn C (2017) The abscission checkpoint: making it to the final cut. *Trends Cell Biol* 27:1–11. <https://doi.org/10.1016/j.tcb.2016.10.001>
- Nakano K, Mabuchi I (2006) Actin-depolymerizing protein Adf1 is required for formation and maintenance of the contractile ring during cytokinesis in fission yeast. *Mol Biol Cell* 17:1933–1945. <https://doi.org/10.1091/mbc.e05-09-0900>
- Nakano K, Satoh K, Morimatsu A, Ohnuma M, Mabuchi I (2001) Interactions among a fimbrin, a capping protein, and an actin-depolymerizing factor in organization of the fission yeast actin cytoskeleton. *Mol Biol Cell* 12:3515–3526. <https://doi.org/10.1091/mbc.12.11.3515>
- Nguyen LT, Swilius MT, Aich S, Mishra M, Jensen GJ (2018) Coarse-grained simulations of actomyosin rings point to a nodeless model involving both unipolar and bipolar myosins. *Mol Biol Cell* 29:1318–1331. <https://doi.org/10.1091/mbc.E17-12-0736>
- Oliferenko S, Chew TG, Balasubramanian MK (2009) Positioning cytokinesis. *Genes Dev* 23:660–674. <https://doi.org/10.1101/gad.1772009>
- Otomo T, Otomo C, Tomchick DR, Machius M, Rosen MK (2005) Structural basis of rho GTPase-mediated activation of the formin mDia1. *Mol Cell* 18:273–281. <https://doi.org/10.1016/j.molcel.2005.04.002>
- Otto JJ, Schroeder TE (1990) Association of actin and myosin in the contractile ring. *Ann N Y Acad Sci* 582:179–184
- Page SG, Huxley HE (1963) Filament lengths in striated muscle. *J Cell Biol* 19:369–390
- Pollard TD, Wu JQ (2010) Understanding cytokinesis: lessons from fission yeast. *Nat Rev Mol Cell Biol* 11:149–155. <https://doi.org/10.1038/nrm2834>
- Pu KM, Akamatsu M, Pollard TD (2015) The septation initiation network controls the assembly of nodes containing Cdr2p for cytokinesis in fission yeast. *J Cell Sci* 128:441–446. <https://doi.org/10.1242/jcs.160077>
- Rappaport R (1967) Cell division - direct measurement of maximum tension exerted by furrow of echinoderm eggs. *Science* 156:1241–& <https://doi.org/10.1126/science.156.3779.1241>
- Rappaport R (1977) Tensiometric studies of cytokinesis in cleaving sand dollar eggs. *J Exp Zool* 201:375–378. <https://doi.org/10.1002/jez.1402010304>
- Reymann AC, Stanisla F, Erzberger A, Salbreux G, Grill SW (2016) Cortical flow aligns actin filaments to form a furrow. *Elife* 5. <https://doi.org/10.7554/eLife.17807>
- Ribeiro Ede A Jr et al (2014) The structure and regulation of human muscle alpha-actinin. *Cell* 159:1447–1460. <https://doi.org/10.1016/j.cell.2014.10.056>
- Salimova E, Sohrmann M, Fournier N, Simanis V (2000) The *S. pombe* orthologue of the *S. cerevisiae* *mob1* gene is essential and functions in signalling the onset of septum formation. *J Cell Sci* 113(Pt 10):1695–1704
- Sanger JM, Sanger JW (1980) Banding and polarity of actin filaments in interphase and cleaving cells. *J Cell Biol* 86:568–575
- Schmidt S, Sohrmann M, Hofmann K, Woollard A, Simanis V (1997) The Spg1p GTPase is an essential, dosage-dependent inducer of septum formation in *Schizosaccharomyces pombe*. *Genes Dev* 11:1519–1534
- Schroeder TE (1968) Cytokinesis: filaments in the cleavage furrow. *Exp Cell Res* 53:272–276
- Schroeder TE (1970) The contractile ring. I. Fine structure of dividing mammalian (HeLa) cells and the effects of cytochalasin B. *Zellforsch Mikrosk Anat* 109:431–449
- Schroeder TE (1972) The contractile ring. II. Determining its brief existence, volumetric changes, and vital role in cleaving *Arbacia* eggs. *J Cell Biol* 53:419–434
- Schroeder TE (1973) Actin in dividing cells: contractile ring filaments bind heavy meromyosin. *Proc Natl Acad Sci U S A* 70:1688–1692
- Sedzinski J, Biro M, Oswald A, Tinevez JY, Salbreux G, Paluch E (2011) Polar actomyosin contractility destabilizes the position of the cytokinetic furrow. *Nature* 476:462–466. <https://doi.org/10.1038/nature10286>
- Simanis V (2015) *Pombe's* thirteen - control of fission yeast cell division by the septation initiation network. *J Cell Sci* 128:1465–1474. <https://doi.org/10.1242/jcs.094821>
- Skau CT, Courson DS, Bestul AJ, Winkelman JD, Rock RS, Sirotkin V, Kovar DR (2011) Actin filament bundling by fimbrin is important for endocytosis, cytokinesis, and polarization in fission yeast. *J Biol Chem* 286:26964–26977. <https://doi.org/10.1074/jbc.M111.239004>
- Skau CT, Kovar DR (2010) Fimbrin and tropomyosin competition regulates endocytosis and cytokinesis kinetics in fission yeast. *Curr Biol* 20:1415–1422. <https://doi.org/10.1016/j.cub.2010.06.020>
- Sladewski TE, Previs MJ, Lord M (2009) Regulation of fission yeast myosin-II function and contractile ring dynamics by regulatory light-chain and heavy-chain phosphorylation. *Mol Biol Cell* 20:3941–3952. <https://doi.org/10.1091/mbc.E09-04-0346>
- Squire JM, Al-Khayat HA, Knupp C, Luther PK (2005) Molecular architecture in muscle contractile assemblies. *Adv Protein Chem* 71:17–87. [https://doi.org/10.1016/S0065-3233\(04\)71002-5](https://doi.org/10.1016/S0065-3233(04)71002-5)
- Stachowiak MR, Laplante C, Chin HF, Guirao B, Karatekin E, Pollard TD, O'Shaughnessy B (2014a) Mechanism of cytokinetic contractile ring constriction in fission yeast. *Dev Cell* 29:547–561. <https://doi.org/10.1016/j.devcel.2014.04.021>
- Stachowiak MR, McCall PM, Thoresen T, Balcioglu HE, Kasiewicz L, Gardel ML, O'Shaughnessy B (2012) Self-organization of myosin II in reconstituted actomyosin bundles. *Biophys J* 103:1265–1274. <https://doi.org/10.1016/j.bpj.2012.08.028>
- Stachowiak MR et al (2014b) A mechanical-biochemical feedback loop regulates remodeling in the actin cytoskeleton. *Proc Natl Acad Sci U S A* 111:17528–17533. <https://doi.org/10.1073/pnas.1417686111>
- Stark BC, James ML, Pollard LW, Sirotkin V, Lord M (2013) UCS protein Rng3p is essential for myosin-II motor activity during cytokinesis in fission yeast. *PLoS One* 8:e79593. <https://doi.org/10.1371/journal.pone.0079593>
- Stark BC, Sladewski TE, Pollard LW, Lord M (2010) Tropomyosin and myosin-II cellular levels promote actomyosin ring assembly in fission yeast. *Mol Biol Cell* 21:989–1000. <https://doi.org/10.1091/mbc.E09-10-0852>
- Su KC, Takaki T, Petronczki M (2011) Targeting of the RhoGEF Ect2 to the equatorial membrane controls cleavage furrow formation during

- cytokinesis. *Dev Cell* 21:1104–1115. <https://doi.org/10.1016/j.devcel.2011.11.003>
- Swulius MT, Nguyen LT, Ladinsky MS, Ortega DR, Aich S, Mishra M, Jensen GJ (2018) Structure of the fission yeast actomyosin ring during constriction. *Proc Natl Acad Sci U S A* 115:E1455–E1464. <https://doi.org/10.1073/pnas.1711218115>
- Takaine M, Numata O, Nakano K (2015) An actin-myosin-II interaction is involved in maintaining the contractile ring in fission yeast. *J Cell Sci* 128:2903–2918. <https://doi.org/10.1242/jcs.171264>
- Thiyagarajan S, Munteanu EL, Arasada R, Pollard TD, O'Shaughnessy B (2015) The fission yeast cytokinetic contractile ring regulates septum shape and closure. *J Cell Sci* 128:3672–3681. <https://doi.org/10.1242/jcs.166926>
- Thiyagarajan S, Wang S, O'Shaughnessy B (2017) A node organization in the actomyosin contractile ring generates tension and aids stability. *Mol Biol Cell* 28:3286–3297. <https://doi.org/10.1091/mbc.E17-06-0386>
- Tinevez JY, Schulze U, Salbreux G, Roensch J, Joanny JF, Paluch E (2009) Role of cortical tension in bleb growth. *Proc Natl Acad Sci U S A* 106:18581–18586. <https://doi.org/10.1073/pnas.0903353106>
- Turlier H, Audoly B, Prost J, Joanny JF (2014) Furrow constriction in animal cell cytokinesis. *BpJ* 106:114–123
- Tyska MJ et al (1999) Two heads of myosin are better than one for generating force and motion. *Proc Natl Acad Sci U S A* 96:4402–4407
- Uehara R, Goshima G, Mabuchi I, Vale RD, Spudich JA, Griffiths ER (2010) Determinants of myosin II cortical localization during cytokinesis. *Curr Biol* 20:1080–1085. <https://doi.org/10.1016/j.cub.2010.04.058>
- Vavylonis D, Wu JQ, Hao S, O'Shaughnessy B, Pollard TD (2008) Assembly mechanism of the contractile ring for cytokinesis by fission yeast. *Sci* 319:97–100. <https://doi.org/10.1126/science.1151086>
- Wagner E, Glotzer M (2016) Local RhoA activation induces cytokinetic furrows independent of spindle position and cell cycle stage. *J Cell Biol* 213:641–649. <https://doi.org/10.1083/jcb.201603025>
- Wang L, Pare PD, Seow CY (2001) Selected contribution: effect of chronic passive length change on airway smooth muscle length-tension relationship. *J Appl Physiol* (1985) 90:734–740. <https://doi.org/10.1152/jappl.2001.90.2.734>
- White JG, Borisy GG (1983) On the mechanisms of cytokinesis in animal-cells *JTBio* 101:289–316 [https://doi.org/10.1016/0022-5193\(83\)90342-9](https://doi.org/10.1016/0022-5193(83)90342-9)
- Wollrab V, Thiagarajan R, Wald A, Kruse K, Riveline D (2016) Still and rotating myosin clusters determine cytokinetic ring constriction. *Nat Commun* 7:11860. <https://doi.org/10.1038/ncomms11860>
- Wu JQ, Bahler J, Pringle JR (2001) Roles of a fimbrin and an alpha-actinin-like protein in fission yeast cell polarization and cytokinesis. *Mol Biol Cell* 12:1061–1077. <https://doi.org/10.1091/mbc.12.4.1061>
- Wu JQ, Kuhn JR, Kovar DR, Pollard TD (2003) Spatial and temporal pathway for assembly and constriction of the contractile ring in fission yeast cytokinesis. *Dev Cell* 5:723–734
- Wu JQ, Pollard TD (2005) Counting cytokinesis proteins globally and locally in fission yeast. *Science* 310:310–314. <https://doi.org/10.1126/science.1113230>
- Wu JQ, Sirotkin V, Kovar DR, Lord M, Beltzner CC, Kuhn JR, Pollard TD (2006) Assembly of the cytokinetic contractile ring from a broad band of nodes in fission yeast. *J Cell Biol* 174:391–402. <https://doi.org/10.1083/jcb.200602032>
- Xue Z, Sokac AM (2016) Back-to-back mechanisms drive actomyosin ring closure during *Drosophila* embryo cleavage. *J Cell Biol* 215:335–344. <https://doi.org/10.1083/jcb.201608025>
- Yoneda M, Dan K (1972) Tension at the surface of the dividing sea-urchin egg. *J Exp Biol* 57:575–587
- Yonetani A, Lustig RJ, Moseley JB, Takeda T, Goode BL, Chang F (2008) Regulation and targeting of the fission yeast formin cdc12p in cytokinesis. *Mol Biol Cell* 19:2208–2219
- Yumura S (2001) Myosin II dynamics and cortical flow during contractile ring formation in *Dictyostelium* cells. *J Cell Biol* 154:137–146
- Zhou Z, Munteanu EL, He J, Ursell T, Bathe M, Huang KC, Chang F (2015) The contractile ring coordinates curvature-dependent septum assembly during fission yeast cytokinesis. *Mol Biol Cell* 26:78–90. <https://doi.org/10.1091/mbc.E14-10-1441>