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Understanding cytokinesis: lessons from fission yeast

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Abstract

For decades after the discovery that a contractile ring made of actin filaments and myosin II produces the force to constrict the cleavage furrow of animal cells, the complexity of cytokinesis has slowed progress in understanding the mechanism. Mechanistic insights, however, have been obtained by genetic, biochemical, microscopic and mathematical modelling approaches in the fission yeast *Schizosaccharomyces pombe*. Many features that have been identified in fission yeast are probably shared with animal cells, as both inherited many cytokinesis genes from their common ancestor about one billion years ago.

Cell division by cytokinesis completes the cell cycle for every cell. Cytokinesis in fungal, amoeboid and animal cells takes place in four steps (FIG. 1). The process begins when the cell marks the site of the future cleavage furrow relative to the sister chromatids, which are separated by the mitotic apparatus. Accurate placement of the cleavage plane is important because the aim of cytokinesis is to create two cells, each with its own nucleus. At the selected site the cell assembles a contractile ring, which comprises the motor protein myosin II, actin filaments and many other proteins and is attached to the plasma membrane. As in muscle contraction, interactions of myosin II with actin filaments produce force to constrict the contractile ring and to form a cleavage furrow in the plasma membrane. Remarkably, the contractile ring disassembles as it constricts, so it does not become thicker like contracting muscle does. Finally, proteins that bring together membranes for their fusion promote the reorganization of the plasma membrane at the base of the furrow and the separation of the two daughter cells.

The mechanism of cytokinesis through a contractile ring appeared about one billion years ago in the common ancestor of amoebas, fungi and animals. These organisms share most of the genes used for cytokinesis by the fission yeast *Schizosaccharomyces pombe*, so lessons learned about mechanisms in fission yeast should apply to animals. The membrane fusion machinery is older than the contractile ring, as plant cells fuse membrane vesicles to build new plasma membrane between the daughter nuclei rather than constricting a furrow[1]. Little is known about cytokinesis in eukaryotes that branched before algae and plants (for example, *Giardia* spp. and trypanosomes) except that their genomes also lack myosin II, so the mechanism of cytokinesis in these eukaryotes is different from that in amoebas, fungi and animals.

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Of all the commonly used model organisms, fission yeast offer many advantages for studying cytokinesis, so an active community of investigators is making rapid progress in deciphering the mechanisms of cytokinesis in fission yeast. Like in animal cells, the position of the mitotic apparatus (inside the nucleus in fungi) determines the position of the contractile ring in fission yeast. The fission yeast genome encodes ~ 4,940 proteins. Classical and reverse genetics have produced the best inventory of more than 130 cytokinesis genes (see Supplementary information S1 (table)) and conditional mutations for many of these genes[2,3]. TABLE 1 lists the proteins that are relevant to the contractile ring. Deletion strains for 98% of the ~ 4,900 of the total genes are available (Bioneer). The size and shape of the cells are ideal for quantitative microscopy and many cytokinesis proteins have been tagged with fluorescent proteins in the genome. These features made it possible to chart a high-resolution time line of cytokinetic events[4] and to quantitate the intracellular distributions of key cytokinesis proteins[5]. In a field dominated by genetics, biochemical analysis has been limited but is growing. Enough quantitative data are available to formulate and test mathematical models for some steps in cytokinesis[6,7]. This article discusses advances being made through research on fission yeast, with a focus on conserved features that are likely to be used by other cells.

Main pathway of cytokinesis

The advantages of fission yeast (discussed above) made it possible to show that events during cytokinesis occur like clockwork (see Supplementary information S2 (movie)). Events can be followed with a precision of one or two minutes on an absolute time-scale anchored to time zero, when the spindle pole bodies separate[4]. Spindle pole bodies are the structures that anchor micro-tubules of the mitotic spindle in fungi. Use of this timescale (FIG. 2) allows for comparisons of observations between laboratories and for detecting subtle problems, such as changes in timing that result from experimental manipulations. The following account summarizes our views regarding contractile ring assembly in fission yeast, but we want the reader to appreciate that questions remain regarding every step in the process.

Assembly of interphase nodes

Protein assemblies called nodes are precursors of the contractile ring[8–11]. The adaptor anillin-like protein, the product of the *mid1* (also known as *dmf1*) gene in fission yeast, appears in interphase nodes around the equator of interphase cells more than 1 hour before time zero[4,10], along with the kinases Cdr1, Cdr2 and Wee1 and other proteins (Blt1 (also known as SPBC1A4.05), kinesin-like protein 8 (Klp8) and Rho guanine nucleotide exchange factor Gef2)[12–14]. Assembly of these interphase nodes depends on the presence of kinase-active Cdr2, which interacts with Mid1[12,14] and might be anchored to the cell cortex through its carboxyl terminus[15]. Cdr1 and Cdr2 phosphorylate and inhibit Wee1, a kinase that holds the cell in G2 phase by phosphorylating the master cell cycle kinase cell division control protein 2 (Cdc2; also known as Cdk1), which controls cell cycle progression[13].

The location of nodes during interphase depends on the kinase Pom1 and another unknown inhibitor[6,16–18]. Pom1 concentrates at both ends of the cell and restricts interphase nodes containing Cdr2 and Mid1 to the middle of the cell. As a cell grows longer, the inhibitory activities decline in the middle of the cell, allowing Cdr1 and Cdr2 to phosphorylate and inhibit Wee1. This releases the kinase Cdc2 to trigger the transition into mitosis, thus coupling growth to the cell cycle[12,13]. In addition to the ‘negative regulation’ that excludes interphase nodes from cell tips, the polo kinase Plo1 releases Mid1 from the nucleus before mitosis[19] and seems to prepare the ~ 65 interphase nodes around the equator of the cell for cytokinesis before the onset of mitosis. The position of the nucleus determines the location of these maturing nodes and, therefore, the position of the contractile ring by a mechanism that is still under investigation.

Maturation of Mid1 interphase nodes

Starting 10 minutes before spindle pole body separation, nodes containing ~ 25 copies of Mid1 mature by sequentially adding, from cytoplasmic pools, ~ 25 molecules of myosin II (each composed of 2 heavy chains and 4 light chains) and ~ 25 ring assembly protein 2 (Rng2; a member of the IQGAP family) molecules, followed by ~ 25 copies of the F-BAR domain-containing protein Cdc15 and ~ 2 dimers of the formin Cdc12, which makes the node competent for actin assembly5. We call these mature nodes cytokinesis nodes. Detecting the formin Cdc12 is difficult20,21 because it is the least abundant known cytokinesis node protein5 and because it arrives last, so most (younger) nodes have no detectable Cdc12 (REF. [4].) Some interphase node proteins (Cdr2, Blt1, Klp8 and Gef2) remain with Mid1 during the formation of the contractile ring, but Cdr2 leaves the ring during anaphase B12,13.

We know little about the assembly, architecture or attachment of nodes to the cortex in either interphase or mitosis, and they have not been seen by electron microscopy. Not much quantitative biochemical data are available on interactions among the large, poorly soluble, multi-domain node proteins. Mutation of Mid1 in a region called the amphipathic a-helix compromises its association with the cortex[22], but this element is part of a much larger insoluble domain of unknown architecture. Like other anillins, Mid1 has a C-terminal PH domain, but it is not required for association with the cortex[10]. Lateral diffusion of nodes in the plane of the membrane is very slow (20 nm^2 s^{-1}) up to time +2 minutes. Anchoring by actin filaments might constrain their movements, but they do not diffuse faster in the absence of actin filaments[7].

Actin filament assembly at time +2 minutes

The assembly of actin filaments for the contractile ring depends on the formin Cdc12[20,23,24] and a profilin — a small protein that can interact with actin monomers and sequences of multiple proline residues found in other proteins25. Formins nucleate actin filaments from free actin monomers26 and cooperate with profilin to elongate the filament26–[29]. Profilin–actin complexes bind to multiple polyproline sequences in the Cdc12 formin homology 1 (FH1) domain[20,23,26] and transfer rapidly onto the fast growing barbed end of the filament[26,28,29], whereas the FH2 domain moves processively on the growing end without dissociating[26,28]. Thus, Cdc12 might anchor actin filaments to the cytokinesis nodes.

Cdc12 cannot elongate actin filaments using actin fused to green fluorescent protein (GFP)[5], so contractile ring actin filaments can only be labelled indirectly with fluorescent phalloidin in fixed cells30 or with GFP fused to an actin filament-binding domain, such as a calponin homology domain, or Lifeact in live cells21,31. GFP–calponin homology domains decorate transient linear connections between cytokinesis nodes that might be single actin filaments[7], although this has not yet been verified by other methods. These putative actin filaments grow from cytokinesis nodes in random directions close to the plasma membrane at about 80 subunits per second and contact neighbouring cytokinesis nodes. The endoplasmic reticulum is closely opposed to the plasma membrane and might help to restrict these filaments to the plane close to the plasma membrane. Cdc8 (also known as tropomyosin) is an a-helical coiled-coil protein that binds along the actin filament helix and increases the rate of elongation of filaments by Cdc12 but can also dissociate Cdc12 from the barbed end or trap Cdc12 between two annealed filaments[32]. It is not known how cells control the association of Cdc12 with nodes or the nucleation activity of Cdc12.

Cytokinesis nodes condense into a contractile ring

As soon as actin filaments appear in the cortex around the equator at time +2 minutes, cytokinesis nodes start moving at about 30 nm s^{-1} in short bursts of ~ 20 seconds. Over 10 minutes these stochastic movements condense the nodes into a nearly continuous ring around

the equator[7]. Our hypothesis to explain these intermittent movements is that myosin II (Myo2) in cytokinesis nodes captures the actin filaments growing from neighbouring nodes. The nodes are then pulled together transiently until the actin filament connection is broken by the dissociation of myosin II from the filament, thereby severing the filament (probably by the actin filament severing the protein cofilin), or by Cdc12 turnover (FIG. 3). Monte Carlo simulations (a stochastic simulation method based on the probability of each reaction) of a simple search, capture, pull and release model, with parameters similar to those measured in live cells, reproduce the assembly of the contractile ring in the correct time of 10 minutes, providing that the mechanism includes frequent breaks in the connections between the cytokinesis nodes[7].

Bundles of actin filaments form naturally during the condensation of cytokinesis nodes into a contractile ring and several groups have proposed that contractile rings form by cross-linking filaments in a 'leading cable' that is nucleated from a single 'spot' containing Cdc12[20,23,33–35]. This was a reasonable idea, as Cdc12 is more obvious after actin filaments and nodes form bundles than during the short interval between time zero and the onset of cytokinesis node condensation, when each node contains just a few Cdc12 molecules. Similarly, bundles of actin filaments are much easier to image than the thin connections between dispersed cytokinesis nodes early in the process. The existence of spots that promote the formation of leading cables depends on the actin filament cross-linking protein α-actinin-like 1 (Ain1), but normal contractile rings can form without Ain1 or the spot[20,21]. Electron micrographs of permeabilized anaphase cells treated with the myosin head domain were interpreted to show that contractile rings consist of two bundles of actin filaments with opposite polarities that originate from a single source[35]. However, some of the filaments in these bundles appear to us to be anti-parallel, consistent with mechanisms other than the leading cable model, such as the search and capture mechanism. Electron micrographs of filaments early in the assembly process might help to explain the relationship between dispersed networks of cytokinesis nodes connected by short filaments and the bundled filaments in more mature contractile rings.

Many mechanistic questions remain about contractile ring assembly. We do not know whether formin-dependent polymerization of actin filaments suffices to explain the onset of cytokinesis node condensation, or whether cells must also regulate the activity of Myo2 with the UCS domain-containing protein Rng3 (REF. 36), phosphorylation of myosin II heavy chains11,37 or light chains37,38, or other mechanisms.

Maturation of the contractile ring

Contractile rings do not change in size or shape between time +11 and +35 minutes, but many proteins are exchanged with others from the cytoplasmic pool[20,39,40]. During this time the ring acquires other proteins, such as capping protein, the unconventional myosin II (Myp2; also known as Myo3) and the F-BAR domain-containing protein Imp2, and loses Mid1. Contractile rings can form without input from the septation initiation network (SIN) signalling pathway, which consists of a GTPase and three protein kinases41, but the polo kinase Plo1 and the SIN pathway are required for maturation of a compact contractile ring42. A network of proteins including the F-BAR domain-containing proteins Cdc15 and Imp2, the C2 domain-containing protein Fic1 and paxillin-related protein 1 (Pxl1) also stabilize the ring40,43,44. The number of proteins in the mature ring is known, but how they are organized and how the ring is attached to the plasma membrane are unknown. Adjacent to the contractile ring, the anillin-like protein Mid2 and four GTP-binding proteins called septins polymerize to form two rings that remain after the contractile ring has constricted[4,45–47].

Contractile ring constriction and disassembly

Starting at time +35 minutes, the ring constricts circumferentially down to a small spot at about 5nm s^{-1} (REFS 4,39,48) — a linear rate that is almost 50 times slower than the large contractile rings of sea urchin eggs49 and nematode embryos[50], following the trend that constriction rate is proportional to the circumference of the ring[50]. Constriction is presumed to occur by a sliding filament mechanism, similar to that in striated muscles, but the details are unknown. As in sea urchin eggs[51] and nematode embryos[50], the ring loses actin filaments and actin-binding proteins, by an uncharacterized mechanism, in proportion to the decline in circumference[4,5]. The actin filament concentration is therefore constant. In contrast to nematode embryos[50], fission yeast contractile rings concentrate myosin II as they constrict[4].

The SIN pathway is required for constriction and disassembly of the contractile ring, but the mechanisms of these processes are not known owing to limited information about the substrates of the SIN pathway proteins[52], except for the Sid2 kinase. Sid2 phosphorylates Cdc14-like phosphatase 1 (Clp1), creating a binding site for the 14-3-3 serine phosphate-binding protein Rad24, which retains Clp1 in the cytoplasm[53]. Mid1 anchors Clp1 in the contractile ring[54], where it dephosphorylates Cdc15 and contributes to the stability of the ring.

Backup pathway for ring assembly

The ability of fission yeast cells to form contractile rings and divide without Mid1 or cytokinesis nodes[4,8,11,42,55–57] revealed a mechanism that corrects defects in the normal assembly pathway[31,43] (see BOX 1 for the different views of geneticists and biophysicists on what it means to be essential). During mitosis, cells without Mid1 form strands of contractile ring proteins (including Myo2, actin, Cdc12 and Cdc15) scattered over the cortex. These proteins can therefore assemble without Mid1 as a scaffold. In some cells, these strands become connected into rings oriented at random angles and positions relative to the long axis of the cell. These oblique rings can slowly constrict the plasma membrane and direct the formation of a septum, but are usually off-centre, so they do not reliably separate the two daughter nuclei.

This backup pathway depends on the SIN pathway42 and activation of this pathway in interphase may produce contractile rings by this mechanism[58]. This alternative pathway works better in cells with a temperature sensitive mutation of 1,3β glucan synthase component 1 (Bgs1; also known as Cps1), by allowing oblique contractile rings to slide into a normal orientation that is perpendicular to the long axis of the cell[57,59]. Nothing is known about how the mechanisms of this pathway relate to the normal search, capture, pull and release pathway, or to the normal disappearance of Mid1 before constriction.

Septation and membrane scission

Cells use the SIN pathway to coordinate the formation of a specialized cell wall, called the septum, with ring constriction and fusion and scission of the plasma membrane[41]. Supplementary information S1 (table) lists more than 70 genes, including septins, an anillin (Mid2), enzymes, GTPases and membrane trafficking machinery, that contribute to septum formation and membrane fusion and scission. The role of Bgs1 in restricting the motion of contractile rings[57,59] suggests that the contractile ring might be physically connected to the enzymes that make the septum.

Major open questions

We understand the assembly, constriction and disassembly of contractile rings in fission yeast better than in any other organism, but our understanding is incomplete and much work is yet to be done. The identification of the long list of cytokinesis genes in Supplementary information

S1 (table) is a remarkable achievement for this small field. One might hope that the list is close to completion, but it has doubled in 10 years, so some cytokinesis genes are probably yet to be discovered. The less complete inventories of cytokinesis proteins in animals overlap with the proteins used by fission yeast. The participation of anillin, myosin II, actin and formins, as well as the general order of events, indicate that mechanisms of cytokinesis are likely to be similar in fission yeast and animals. More detailed studies on animals will be required to document the extent of these similarities and any fundamental differences. Punctate contractile ring precursors containing myosin II and anillin have been seen in animal cells, and condensation of these precursors into a contractile ring depends on the formin cytokinesis defect protein 1 (CYK-1) in *Caenorhabditis elegans* embryos[60]. More work is required to learn how similar the mechanism is to that in fission yeast.

Learning how well the molecular mechanisms of cytokinesis are conserved will depend on better inventories of cytokinesis genes from the main branches of the phylogenetic tree and a better understanding of the reactions at the system level. The current state of knowledge suggests that most new cytokinesis genes that appeared during evolution were conserved in subsequent branches of the tree. Actin is the most ancient component, having arisen in the common ancestor of all forms of life. Prokaryotes use actin for many interesting processes, but apparently not for cytokinesis. After algae and plants diverged, primitive amoeboid eukaryotes evolved myosin II and the contractile ring mechanism based on actin filaments. Amoebas, fungi and animals retained this mechanism for reliable cell division. The genes for membrane traffic and scission are more ancient than the genes that encode myosin II and are still used by all higher eukaryotes.

Certain aspects of cytokinesis are better understood in systems other than fission yeast. For example, we understand how mitotic spindle microtubules, Rho family GTPases and chromosomal passenger proteins control contractile ring positioning, assembly and constriction better in animals than in fission yeast[61]. Numerous examples show that organisms adapted ancient proteins for novel cytokinesis strategies, illustrating how evolution can stumble upon any number of strategies based on available materials. However, we are more impressed by the conservation of basic mechanisms, so deciphering elements of the system in a favourable organism should provide insights into cytokinesis in other cells.

Beyond an account of the participating molecules, understanding the mechanisms will depend on better ideas, more information about the participating molecules, high quality quantitative measurements in live cells and mathematical models. Better ideas are needed because some fundamental concepts are missing, such as strategies to assemble contractile ring precursors. Our understanding of the mechanisms of most cytokinesis proteins (IQGAPs, for example) is still primitive. Even where characterization is advanced, such as for actin, myosin II and formins, gaps remain, such as in understanding the mechanisms regulating the activity of Cdc12. GFP fusion proteins and spectacular new microscopes enable the precise measurement of cellular events, but this work is in its infancy. Mathematical models have been useful for formulating and testing some ideas about cytokinesis, and we expect them to be the indispensable gold standard for designing and interpreting experiments in the future.

Box 1

On being ‘essential’

What does it mean to say that a gene or protein is ‘essential’ for a complicated process such as cytokinesis? Geneticists and biophysics use the word essential in different ways. From the genetics perspective, a gene or protein is essential if the viability of the organism depends on it and ‘non-essential’ if the organism can survive without it, even if survival is a struggle. From the biophysics perspective, a gene or protein is essential if the system does not work

normally in its absence, showing that the component is required for normal timing and/or fidelity. Some genes such as the anillin-like *mid1* (also known as *dmf1*) are not essential in the sense that strains lacking *mid1* are viable. However, cells lacking the Mid1 protein do not grow well and cytokinesis is far from normal, so the protein is absolutely required for the 'normal' process of cytokinesis. The fact that some cells lacking Mid1 manage to cleave in two illustrates the important point that cells have mechanisms to correct serious defects that occur along the normal pathway.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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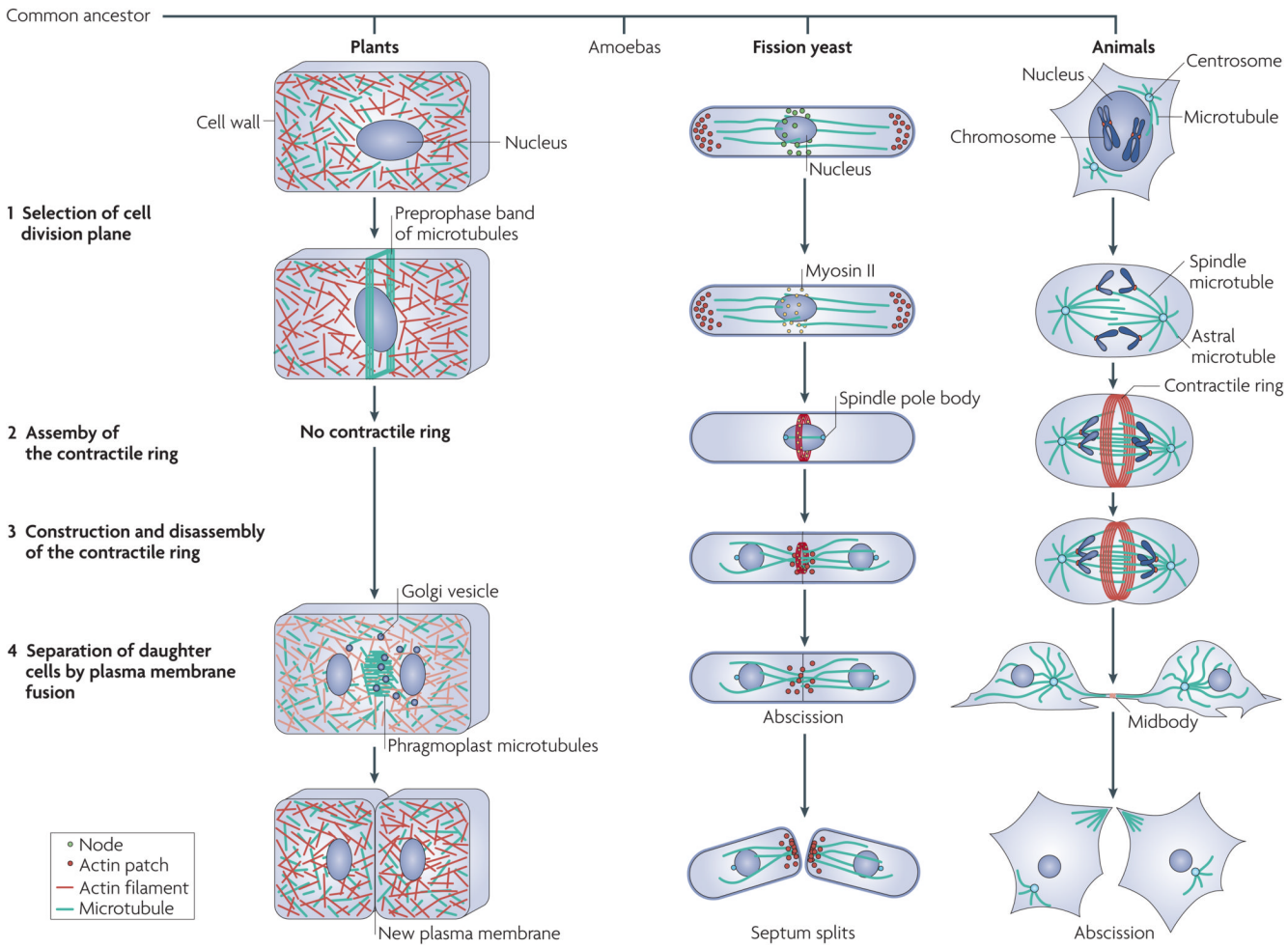

Figure 1. Strategies for cytokinesis used by plant, fission yeast and animal cells

Plants, amoebas, fungi and animals all arose from a common ancestor, branching off as shown. In plants, the cell division plane is selected by the nucleus specifying the position of a preprophase band of microtubules around the equator. Plants lack key proteins to make a contractile ring, so they depend on membrane fusion to separate the two daughter cells. Phragmoplast microtubules transport Golgi vesicles to the midplane to form the new plasma membrane. Amoebas divide much like animal cells and are not illustrated. In fission yeast, the cell division plane is selected by the nucleus specifying the position of nodes around the equator, whereas in animals, spindle and astral microtubules specify the position of the contractile ring. Fission yeast and animal cells assemble a contractile ring of actin filaments and myosin II around the equator of the cell between the chromosomes, which are separated by microtubules of the mitotic apparatus. The ring constricts and the daughter cells separate by membrane fusion. See also Fig. 2 for more details on the process in fission yeast.

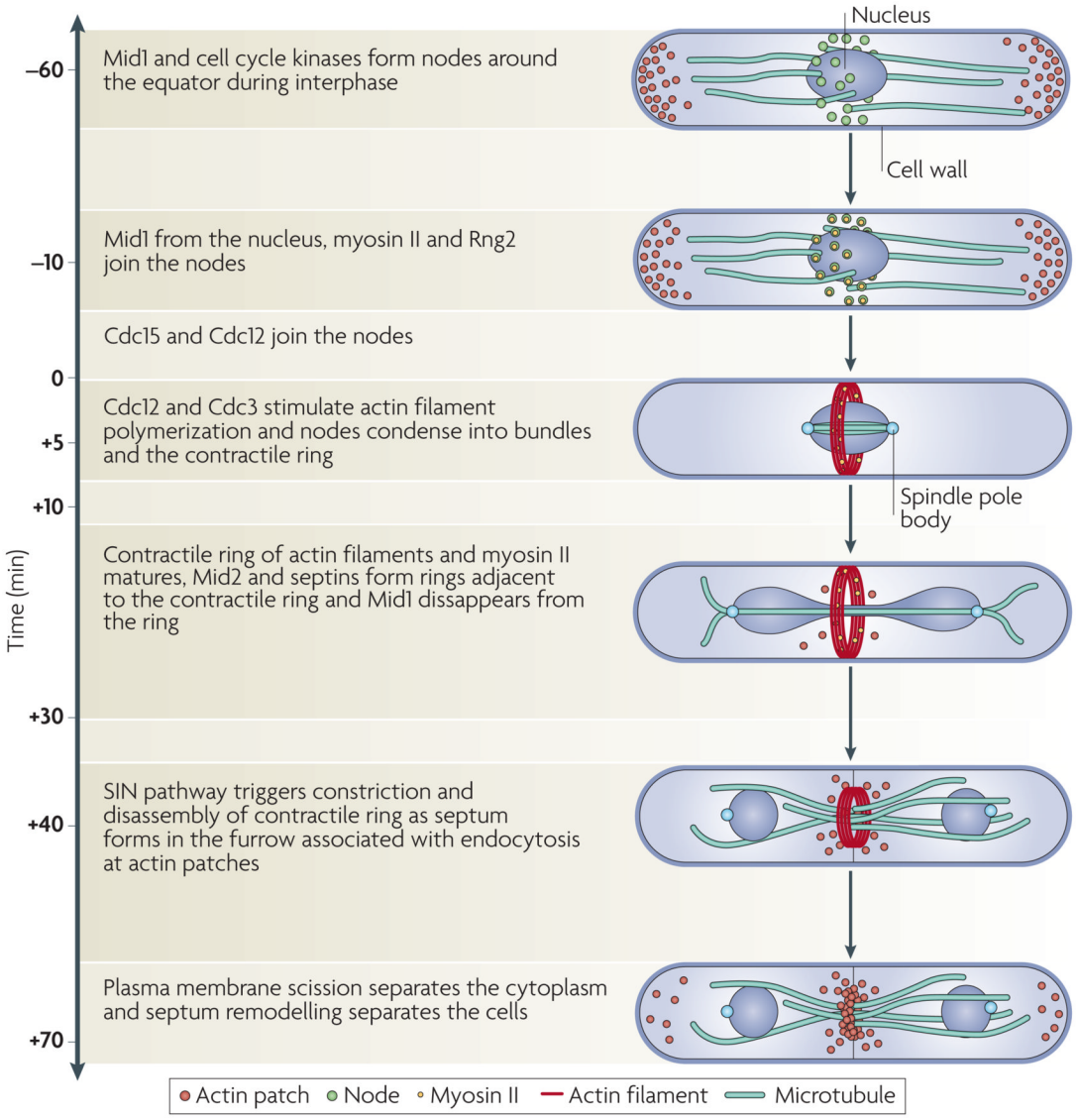

Figure 2. Time course of cytokinesis in fission yeast

Time zero is defined as the time when the spindle pole bodies separate. Starting at time −60 minutes, interphase nodes containing the anillin-like protein Mid1 (also known as Dmf1) and cell cycle kinases form near the plasma membrane. Negative signals from the ends of the cell position these nodes around the equator. Dynamic microtubules push the nucleus to the centre of the cell. At time −10 minutes, interphase nodes begin to mature into cytokinesis nodes by the addition of myosin II (Myo2), ring assembly protein 2 (Rng2; a member of the IQGAP family), the F-BAR domain-containing protein cell division control protein 15 (Cdc15) and the formin Cdc12. Following spindle pole body separation, Cdc12 and Cdc3 (also known as profilin) stimulate the polymerization of actin filaments that bind tropomyosin and cross-linking proteins. During anaphase A (at time +5 minutes), interactions of myosin II with actin filaments condense nodes into a contractile ring, which matures by adding more Cdc15, capping protein, unconventional myosin II (Myp2; also known as Myo3) and other proteins. In anaphase B (at time +10 to +30 minutes) the mitotic spindle elongates and the anillin-like protein Mid2 and septins form double rings adjacent to the contractile ring. Mid1 disappears from the ring at the onset of its constriction. At the end of anaphase, a signalling pathway

consisting of a GTPase and three protein kinases (the septation initiation network (SIN)) triggers constriction of the contractile ring (at time +40 minutes), membrane invagination and synthesis of a new cell wall to form a septum. Constriction ends at time +70 minutes. After another 30 minutes, scission of the plasma membrane separates the cytoplasm and septum remodelling separates the cells.

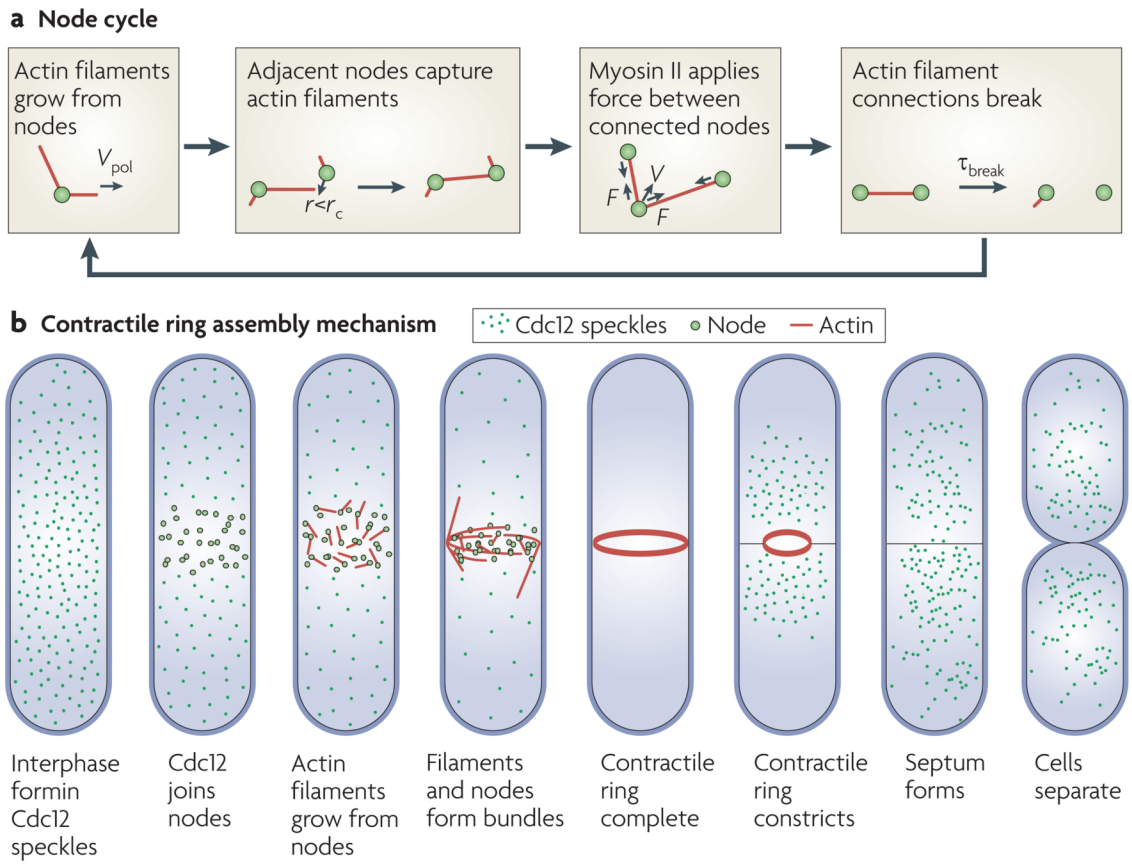

Figure 3. Mechanism of contractile ring assembly in fission yeast

a. | the cycle of reactions hypothesized in the search, capture, pull and release mechanism of contractile ring assembly. Cytokinesis nodes contain the anillin-like protein Mid1 (also known as Dmf1), myosin II (Myo2) and the formin cell division control protein 12 (Cdc12). Actin filaments grow in random directions from nodes by adding subunits at rate V_{pol} (the rate of actin polymerization). If a filament approaches a node within distance r, less than a defined distance r_c (capture radius), myosin II can capture the filament. Myosin II applies force on attached filaments and moves nodes at velocity V. Actin filament connections between nodes break owing to severing or other reactions, with a time constant of τ_{break}, after which the cycle is repeated. **b** | An overview of contractile ring assembly and constriction in fission yeast. During interphase, Cdc12 is distributed throughout the cell in small clusters called speckles. At time zero minutes, Cdc12 joins nodes around the equator and nucleates actin filaments. The actin filaments form bundles as myosin II pulls the cytokinesis nodes into a ring. As the contractile ring constricts, the septum forms between the daughter cells, which separate by membrane fusion.

Table 1

Identified cytokinesis proteins in fission yeast

Generic name	***Schizosaccharomyces pombe* name**[*]
Cleavage furrow placement proteins	
GIN4 family kinase	Cdr2
Ser/Thr kinase	Kin1
Anillin-like protein	Mid1 (Dmf1)
γ-Tubulin complex subunits	Mto1 (Mbo1) and Mto2
Polo kinase	Plo1
DYRK kinase	Pom1
Contractile ring assembly and maturation proteins	
Capping protein	Acp1 and Acp2
Actin	Act1 (cps8)
Cofilin	Cof1 (Adf1)
α-Actinin	Ain1
Aurora B kinase	Ark1 (Aim1)
Microtubule cross-linking factor	Ase1
Survivin	Bir1 (Cut17)
Novel protein	Blt1 (SPBC1A4.05)[‡]
Formin	Cdc12
F-BAR domain containing protein	Cdc15
Profilin	Cdc3
Myosin II light chain	Cdc4
Tropomyosin	Cdc8
Cdc14 phosphatase	Clp1 (Flp1)
Fimbrin	Fim1
Rho GEF	Gef2[‡]
Hsp90 chaperone	Hsp90 (Swo1)
Kinesin	Klp8[‡]
Myosin II heavy chains	Myo2 (Rng5) and Myp2 (Myo3)
Borealin	Nbl1
Phosphoinositide-dependent kinase	Pdk1 (Ppk21)
Inner centromere protein (INCENP)	Pic1
GEF for Rho1	Rgf3 (Lad1)
Myosin II regulatory light chain	Rlc1
IQGAP family protein	Rng2
UCS domain-containing protein	Rng3

Acp, F-actin-capping protein; Act, actin; Ain1, α-actinin-like protein 1; Ase1, anaphase spindle elongation protein 1; Cdc, cell division control; Clp1, Cdc14-like phosphatase 1; GEF, guanine nucleotide exchange factor; Hsp, heat shock protein; Klp8, kinesin-like protein 8; Myo2, myosin II; Myp2, unconventional myosin II; Rlc1, regulatory light chain 1; Rng, ring assembly.

[*] Alternative protein names are provided in brackets.

[‡] The role needs to be further tested.