How one becomes many: blastoderm cellularization in *Drosophila melanogaster*

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**Summary**

Embryonic development in *Drosophila melanogaster* begins with a rapid series of mitotic nuclear divisions, unaccompanied by cytokinesis, to produce a multinucleated single cell embryo, the syncytial blastoderm. The syncytium then undergoes a process of cell formation, in which the individual nuclei become enclosed in individual cells. This process of cellularization involves integrating mechanisms of cell polarity, cell–cell adhesion and a specialized form of cytokinesis. The detailed molecular mechanism, however, is highly complex and, despite extensive analysis, remains poorly understood. Nevertheless, new insights are emerging from recent studies on aspects of membrane polarization and insertion, which show that membrane components from intracellular organelles are involved. In addition, actin and actin-associated proteins have been heavily implicated while new evidence shows that microtubule cytoskeletal elements are mechanistically involved in all aspects of cellularization. The detailed molecular mechanisms and the new data to provide a current perspective on the nature of cellular blastoderm formation in *Drosophila melanogaster*. BioEssays 24:1012–1022, 2002. © 2002 Wiley Periodicals, Inc.

**Introduction**

In the fruit fly *Drosophila melanogaster*, fertilization of the egg is followed by a rapid sequence of mitotic nuclear cleavage divisions, unaccompanied by cytokinesis. As the nuclear divisions proceed, the daughter nuclei move outward toward the periphery, to form the so-called syncytial blastoderm. This stage is quickly succeeded by formation of a multicellular embryo, the blastoderm, as each of the nuclei at the surface becomes enclosed in its own jacket of cytoplasm by a process of membrane growth and extension. In effect, the process of cellularization in the early fruit fly embryo is a specialized form of cytokinesis that allows syncytial blastoderm to cleave into individual cells, with defined plasma membrane boundary and single nucleus. There are, however, several other manifestations of cytokinetic processes in *Drosophila* namely asymmetric cytokinesis and incomplete cytokinesis of the oocytes. Nevertheless, all these different variations of cytokinesis share certain aspects of mechanism and molecular composition despite some genetic specialization: in each form of cytokinesis, the actomyosin ring complex constricts and leads to furrow ingression.

Nearly all insect species exhibit the embryonic cellularization; for example, in *Tribolium*, the early cleavage and blastoderm formation proceeds in similar fashion to that in *Drosophila*. Cellularization of a syncytium is also found in some other organisms, such as the acellular slime mold *Physarum polycephalum*. Cellularization is thus not just an insect-specific mechanism and the large number of insect species in which it occurs makes it one of the most common and frequent developmental events in the biological world. The *Drosophila* embryo, however, remains the system for its investigation.

The nuclear cleavage stage of *Drosophila* embryogenesis consists of 13 rapid nuclear divisions with cellularization of the embryo occurring during cycle 14. Cellularization is a monopolar and modified form of cytokinesis that depends on the co-ordination of microtubules and microfilaments, membrane export and fusion processes and a continuous dynamic sequence of changes in cytoskeletal organization. In this review, we will discuss some major recent findings, the possible mechanisms that they suggest and some future directions in the exploration of *Drosophila* blastoderm cellularization.

**Mechanism of blastoderm cellularization**

*Drosophila* embryogenesis starts with 13 nuclear division cycles taking place in a common syncytium without accompanying cytokinosis. Cycles 0 to 9 occur in the interior of the embryo (Fig. 1A, B). By the end of cycle 9, all the nuclei move towards the cortex of the embryo, leaving behind some yolk nuclei in the interior (3–6) (Fig. 1B). At the cortex, nuclei divide...
four times (10 to 13) (6–8) (Fig. 1C) and finally cellularize to form ~6000 blastoderm epithelial cells in the cycle 14 (3) (Fig. 1D, E). During the entire period, centrosomes are present at the apical end of the nuclei. (9) The cellularization process starts in the interphase of cycle 14 and lasts for ~65 to 70 min. (5) In cycle 14, plasma membrane invaginates to form cleavage furrows between the cortical nuclei. Fulfillove and Jacobson (10) named the leading edge of the cleavage furrow the “furrow canal” (FC) and it is now known to be associated with actin and myosin II-based contractile apparatus. (11, 12) Furthermore, the ingrowth of plasma membrane during cellularization requires a number of proteins and membrane materials, which are recruited by microtubule-dependent pathway.

The process of cellularization occurs in four distinct phases (13, 14) although previously it was divided into slow and fast phases. (10, 15) Immediately after cycle 13, spherical nuclei of 5 μm diameter appear beneath the plasma membrane and localize under a dome-shaped structure, known as somatic bud. In phase 1 (Fig. 2A), which lasts for 10 min, cellularization begins with the formation of furrow canal. Additionally, during this phase, nuclei start elongating. (13, 14) The next three phases last 20 min each; in phase 2 (Fig. 2B), all the nuclei complete their elongation and the rates of inward movement of the furrow canals are very slow, until they reach the basal end of the elongated nuclei in phase 3 (Fig. 2C). At this point, phase 4 begins; the rate of inward movement of furrow canals increases by two-fold. Four membrane domains are formed at the end of phase 4: apical membrane, apico-lateral membrane, lateral membrane and basal membrane. (16) The end result is a monolayer of ~6000 blastoderm cells (Fig. 2D). Basal adherens junctions start forming as cellularization proceeds, and attach next to the furrow canals, resolving at the end of the process (17) (Fig. 2A, D). In addition, apical adherens junctions (Fig. 2C) start to appear from mid-cellularization and form zonula adherens during gastrulation. (18, 19) A number of proteins, which are distributed asymmetrically during cellularization, help to form polarized blastoderm epithelium cells.

Role of cytoskeletal elements involved during cellularization

Microtubules, actin filaments, and myosin II play crucial roles in accomplishing the dynamic process of cellularization (Fig. 3). At the onset of cycle 14, long microtubules arise from pairs of centrosomes at the apical end and extend the plus-ends towards the interior of the embryo, covering the nuclei as inverted baskets (20, 21) (Fig. 3B). This process is essential: when the embryos are microinjected with colcemid at the onset of cycle 14 or during the slow phase, the inward movement of furrow canals stops. However, colchicine injection during the rapid phase did not affect the membrane invagination. (6) Furthermore, actin filaments play a central role in co-ordinating several events involved in reorganizing the cytoskeletal framework as the embryos cellularize. The actin filaments are densely populated in the cortex above the nuclei at the beginning of cycle 14 (Fig. 3B) but, as cellularization starts, the filamentous actins become more concentrated at the furrow

Figure 1. Drosophila melanogaster nuclear cycles during early embryogenesis. In preblastoderm (cycle 1–9), nuclei divide in the interior of the embryo. A: Axial movement of the nuclei during cycles 4–6. B: Nuclear migration towards cortex occurs during cycle 8 to 9. C: The majority of the nuclei reach the cortex by cycle 10, leaving behind some yolk nuclei at the interior and become polyploid. Pole cells form at the posterior end of the embryo during cycle 10. At the cortex, the nuclei divide three times (cycle 10–13) to form the syncytial blastoderm. D–E: Cellularization begins during cycle 14 where plasma membrane invaginates between the blastoderm nuclei to form ~6000 blastoderm cells. Sectional views taken from confocal images of cellular blastoderm of D. melanogaster stained with propidium iodide (PI) to mark the DNA.
Strategies and analysis of genes involved in cellularization

What precisely triggers the initiation of cellularization is not well understood, but it has been proposed that zygotically transcribed gene products may be involved. The transcription of zygotic genes starts by cycle 11, increases in rate through cycles 11 to 14 and decreases at the end of cellularization. When α-amanitin, an inhibitor of transcription, is injected during cycle 13 or earlier, it completely blocks cellularization, indicating the importance of transcription for this process. Experimentally induced actin depolymerization blocks the inward movement of the furrow canals in the slow phase but does not affect cellularization at the rapid phase of membrane invagination. However, the actomyosin contractile apparatus is insufficient to provide the driving force to pull the furrow canal inward. Furthermore, it is not clear how these contractile apparatus crawl on the microtubules. As will be discussed, it is likely that plus-end directed motors contribute to the mechanical force in the inward movement of the furrow canal by cross-linking the components of the membrane through microtubules.

Canals,(22) where myosin II combines with actin to form actomyosin contractile apparatus.(23–25) These furrow canals finally pinch inward to form polarized blastoderm epithelium (Fig. 3B–E). During the slow phase of membrane invagination, the actomyosin contractile apparatus forms a hexagon around each nucleus. These hexagons interconnect to form a network over the entire embryo surface (Fig. 4A, C). During the fast phase of membrane invagination, the shape of the actin hexagons changes into rings (Fig. 4A, C) and the diameter of the rings diminishes gradually, as they pull the furrow canals deeper into the cytoplasm to finally pinch off and form blastoderm cells (Fig. 3E). Experimentally induced actin depolymerization blocks the inward movement of the furrow canals in the slow phase but does not affect cellularization at the rapid phase of membrane invagination. However, the actomyosin contractile apparatus is insufficient to provide the driving force to pull the furrow canal inward. Furthermore, it is not clear how these contractile apparatus crawl on the microtubules. As will be discussed, it is likely that plus-end directed motors contribute to the mechanical force in the inward movement of the furrow canal by cross-linking the components of the membrane through microtubules.

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Figure 2. Four distinct phases in the process of cellularization. First three phases are slow compared to the fourth phase, where the rate of movement of furrow canal increases by two fold. A: Phase 1 starts with the formation of furrow canal where the basal adherens junctions attach next to furrow canal. Nuclear elongation starts during this phase. B: Nuclei complete their elongation in phase 2. C: The rate of movement of furrow canals is slow until they reach the basal ends of the nuclei in phase 3. D: At the end of phase 4, four membrane domains are formed as indicated. Basic concept of this drawing has been adapted from Tepass U, Tanentzapf G, Ward R and Fehon R. Ann Rev Genet. 2001; 35:747–784 with permission from Annual Reviews, www.annualreviews.org.
Table 2 lists the two categories of genes implicated in cellularization. While the functional dissection of zygotic genes have been reported in some detail, some of the precise roles of maternal contributions are in question as they also appear to be required in the earlier stage of meiotic cytokinesis.

The structural integrity of actin hexagons during slow phase of cellularization depends on these three zygotically expressed genes mentioned above. Co-localization studies show that these gene products overlap with the actin filaments in wild-type embryos. The proper localization of serendipity-α to the hexagonal array of actomyosin complex is dependent on nullo. Absence of serendipity-α and nullo, results in gaps in the hexagonal array producing multinucleated cells (Fig. 4E). However, the nullo mutants differ from serendipity-α in producing many multinucleated cells. In the mutants of bottleneck, the hexagons change into rings much earlier, resulting in constrictions at the apical end to produce bottle-shaped nuclei (Fig. 4F). These observations suggest that bottleneck acts as a temporal regulator of the structural change from hexagons to rings.

**Nullo**, a zygotic gene, is specifically required for organization of the cellularization front in the *Drosophila* embryo. This protein acts to stabilize the accumulation of cadherins and catenins at the nascent basal membrane. In *slam* mutants, the level of myosin in the furrow canals is much less. Discs Lost (Dlt), a novel protein, in *slam* mutants, the level of myosin in the furrow canals is much less. Discs Lost (Dlt),
also plays a crucial role in the polarization of embryonic epithelia during cellular blastoderm formation.\(^{(76)}\)

Mutant embryos of nuclear fallout (\(nuf\)),\(^{(51)}\) a maternally transcribed gene and a centrosomal protein, has a similar cellularization phenotype as shown in the mutants of \(nullo\) and \(serendipity\)-\(\alpha\). \(Nuf\) mutants show incomplete metaphase furrow formation, allowing neighboring nuclei to collide, resulting in severe mitotic defects. \(Nuf\) also delivers actin and Discontinuous Actin Hexagon (DAH) to the invaginating cortical furrows via membrane transport along microtubules.\(^{(51)}\) Discontinuous Actin Hexagon (DAH) is found to be a membrane-associated, dystrophin-like molecule, and it has been proposed that DAH may stabilize and link actin cytoskeleton to the invaginating membrane during cellularization.

The interactions of DAH with membrane and actin-binding proteins have been shown to be critically regulated by phosphorylation.\(^{(52)}\) Drosophila formin homology (FH) protein, Diaphanous (\(dia\)), plays a critical role in various actin-mediated cellular processes including cytokinesis.\(^{(53)}\) Immuno-colocalization studies show that it is concentrated at the tip of the cellularization front and at the site of membrane invagination. At the end of cellularization, it localizes to the basal end of each newly formed cell where the contractile ring pinches off. In \(dia\) mutants, there are defects in the hexagonal actin, microtubule array and nuclear positioning. The localization of Anilin and Peanut, the latter a septin protein, are abnormal in \(dia\) mutants implying that it is necessary for recruitment of these components to the cellularization front.\(^{(63)}\)
The main purpose of cellularization is to encapsulate all the nuclei present in the common syncytium by membrane, to form ~6000 blastoderm cells. However, the membranes needed are more extensive than the membrane that covers the surface of syncytial blastoderm. Earlier models proposed that the plasma membrane above all the nuclei are not needed that the plasma membrane above all the nuclei are not

### Table 1. Maternally transcribed genes

<table>
<thead>
<tr>
<th>Components</th>
<th>Proposed function</th>
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<tbody>
<tr>
<td>Chickadee (Chic)</td>
<td>Encodes profilin, a low molecular weight actin-binding protein that modulates F-actin polymerization. chic mutant fails to form acto-myosin contractile ring during meiosis.</td>
</tr>
<tr>
<td>Twinstar (tsr)</td>
<td>Drosophila collin and actin-binding protein. It is required for the normal formation and function of contractile ring.</td>
</tr>
<tr>
<td>Anillin (anillin)</td>
<td>An actin-binding protein implicated in cytokinesis. Present at the metaphase furrow and at the cellularization front.</td>
</tr>
<tr>
<td>Peanut (pnu) Septin 1 (sep1), Septin 2 (sep2)</td>
<td>Implicated in having secondary effect on the assembly and progression of cellularization front.</td>
</tr>
<tr>
<td>Nuclear-fallout (nuf)</td>
<td>A centrosomal protein required for proper localization of actin and discontinuous actin hexagon (dah) to cleavage furrow.</td>
</tr>
<tr>
<td>Diaphanous (dia)</td>
<td>An actin-binding protein required for actin filaments to organize in metaphase furrows and cellularization furrows.</td>
</tr>
<tr>
<td>Discontinuous actin hexagon (dah)</td>
<td>A membrane-associated protein required for the proper formation of metaphase furrow during syncytial blastoderm and cleavage furrow during cellularization.</td>
</tr>
<tr>
<td>Zipper (zip)</td>
<td>MyosinII/Myosin heavy chain: it is diffusely distributed until syncytial blastoderm and then localizes to the cortex and pole cells. At the time of cellularization, it is observed at the cleavage furrow and canals.</td>
</tr>
<tr>
<td>Spaghetti-squash (sqh)</td>
<td>Encodes myosin light chain of non-muscle myosin II and is implicated in cytokinesis, metaphase furrow and cleavage furrow formation.</td>
</tr>
<tr>
<td>Jaguar (jar)</td>
<td>It is also known as Mhc95F, Myosin VI or Class VI unconventional myosin. It is a minus-end directed actin-based motor needed for proper formation of pseudocleavage furrow formation during syncytial blastoderm.</td>
</tr>
<tr>
<td>Alpha-spectrin (alpha-Spec)</td>
<td>Located on both plasma membrane and Golgi bodies during cellularization.</td>
</tr>
<tr>
<td>Karst (kst)</td>
<td>It encodes for heavy-Spectrin, which is associated with the invaginating furrow canals and in a region of the lateral membrane.</td>
</tr>
<tr>
<td>Rho1 (Rho1), Cdc42 (Cdc42)</td>
<td>Play antagonistic roles in bringing about the cytoskeletal reorganization during cellularization.</td>
</tr>
<tr>
<td>Pebble (pbl)</td>
<td>A RhoGEF required for the formation of the contractile ring, and initiation of cytokinesis.</td>
</tr>
<tr>
<td>KLP3A (Klp3a)</td>
<td>Has been localized at the mid-zone of central spindle during cytokinesis of male meiosis of D. melanogaster. In mutants, the protein is absent from both central spindle and contractile ring.</td>
</tr>
<tr>
<td>LAVA Lamp (lava)</td>
<td>It is a Golgi-associated protein required for progression of furrow canal.</td>
</tr>
<tr>
<td>CLIP-190</td>
<td>Required for linking vesicles and organelles to microtubule plus-ends. During cellularization, it is present in the furrow front.</td>
</tr>
<tr>
<td>Shibire (shi)</td>
<td>Blocks cellularization in temperature-sensitive mutants.</td>
</tr>
<tr>
<td>Syntaxin1A (Syx1A)</td>
<td>Drosophila syntaxin 1 mutants form large acellular patches during cellularization and proposed to be required for fusion of intracellular membrane vesicles with the surface.</td>
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### Insertion of new membrane and proteins during blastoderm cellularization

The main purpose of cellularization is to encapsulate all the nuclei present in the common syncytium by membrane, to form ~6000 blastoderm cells. However, the membranes needed are more extensive than the membrane that covers the surface of syncytial blastoderm. Earlier models proposed that the plasma membrane above all the nuclei are not needed that the plasma membrane above all the nuclei are not

### Table 2. Zygotically transcribed genes required for cellularization

<table>
<thead>
<tr>
<th>Components</th>
<th>Time of expression</th>
<th>Proposed function</th>
</tr>
</thead>
<tbody>
<tr>
<td>nullo</td>
<td>It is detected in the interphase of cycle 13 and the expression increases during this cycle. It reaches the peak in slow phase of cycle 14 and the level decreases during the fast phase.</td>
<td>Required for the stability of microfilament basal junction at the onset of cellularization. In mutants, many multinucleated cells are formed.</td>
</tr>
<tr>
<td>Serendipity-z</td>
<td>First detectable in cycle 12 and the level increases in the cycle 13. In early cycle 14, it reaches the peak and disappears at the end of this cycle.</td>
<td>Required for maintaining the integrity of microfilaments during cellularization. In the absence of sry-z a few multinucleated cells are formed.</td>
</tr>
<tr>
<td>bottleneck</td>
<td>Appears during cycle11 and reaches the peak during cycle 14, when there is no sign of membrane invagination, then decreases.</td>
<td>Required for proper organization of actin filaments. In the absence of bottleneck hexagons change into rings much earlier than membrane invagination.</td>
</tr>
<tr>
<td>Slow-as molasses</td>
<td>Slam expression rapidly increases during cycle 13 and reaches the peak during slow phase of cellularization. During fast phase it rapidly decreases and reach the low level at the onset of gastrulation.</td>
<td>Slam expression rapidly increases during cycle 13 and reaches the peak during slow phase of cellularization. During fast phase it rapidly decreases and reach the low level at the onset of gastrulation.</td>
</tr>
</tbody>
</table>
smooth but have microvilli, which are the source of membranes, during cellularization.10,77,78 Another hypothesis was that new membranes derived from Golgi apparatus, in the form of vesicles of various diameters are present in the cortical cytoplasm between the nuclei, these vesicles fusing with one another and with the furrows could provide the source of membranes.79

Recently, Lecuit and Wieschaus,13 followed the membrane flow during cellularization and found that most of the membrane is actually recruited from the interior of the embryo and inserted during different phases of cellularization (Fig. 3). To understand this mechanism, they labeled the plasma membrane by injecting fluorescent lectin, wheat germ agglutinin (WGA) in the perivitelline space of the living embryo. WGA binds to N-ethylglucosamine and N-acetyl-neuramic acid (sialic acid) residues found on membrane glycoproteins. When WGA was injected during phase 1, it labels the entire apical surface of the somatic bud. However, by the end of this phase, WGA was no longer on the apical surface but displaced and inserted during different phases of cellularization (Fig. 3). The precise mechanism for membrane delivery to specific sites of plasma membrane and membrane targeting for cellularizing embryo in Drosophila remains elusive. An attractive candidate for the molecular machinery for polarized membrane insertion is the components of a conserved protein complex termed exocyst.13,77,80–81 In particular, Sec6/Sec8, which localize to the specific sites of membrane delivery, in contrast to t-SNAREs, in budding yeast and mammalian MDCK cells, may be more relevant for membrane targeting and fusion events than syntaxins in Drosophila cellularization.13 Identification of two orthologues of sec6 and sec8 in Drosophila82 raise the possibility of genetically dissecting the functional role of these and other components that might participate in polarized membrane delivery.

**Why blastoderm cellularization is a modified form of cytokinesis in Drosophila?**

Cytokinesis is a highly complex process, which accomplishes the mechanical separation of two daughter cells after each cell division. One challenging aspect to understanding this process lies in determining whether a unified yet diverse molecular mechanism exists in many different cell types. Two major features of cytokinesis, namely, the acto-myosin ring assembly/contraction and the furrow ingression of the cellular cortex have been examined in several systems using different strategies and, in spite of differences in the details of these processes, the molecular components are often the same.

Recent models of cytokinesis and polarized insertion of new membrane during cellularization of the syncytial blastoderm, suggest that membrane exocytosis accompanied by fusion is part of the same mechanism of both the processes. It is not known, however, why normal cytokinesis is prevented in early syncytial divisions in Drosophila, but, interestingly, the four zygotic genes, which are expressed during cellularization (nullo, serendipity-2, bottleneck and slam), are not required for normal cytokinesis.41,83

Although signaling events take center stage in understanding cytokinesis in animal cells, the role of the different signaling pathways and their components are less obvious in Drosophila blastoderm cellularization. Thus, Rho A GEF, Pebble, is required for cytokinesis but not for cellularization.1 A GEF, Pebble, is required for cytokinesis but not for cellularization.1 Nevertheless, the small GTPase Rho family proteins Rho1 and Cdc42, seem to play antagonistic roles in bring about cytoskeletal reorganization during cellularization.61,62 These may, however, involve direct effects on the regulation of components required for cell shape changes, rather than mediation through signaling pathways.
Structural proteins, mainly the cytoskeletal elements and associated proteins, actin, myosin, microtubules and formin homology (FH) domain proteins, such as Dia, are commonly shared in both normal cytokinesis and cellularization. An intriguing question that arises about the roles of several actin and microtubule-associated proteins is whether the same proteins that associate with the contractile ring and central spindle during cytokinesis are also mechanistically involved in cellularization. Recent observations show that several proteins can cross-link with both microtubule and actin filaments during cellularization. The finding that a plus-end kinesin, KLP3A, which has already been implicated in Drosophila male meiotic cytokinesis, can at least weakly bind to actin columns during early embryogenesis, is tantalizing and may hint at the possibility that such proteins orchestrate a dynamic interplay between actin and microtubule, possibly providing the force required for final cell cleavage in both the processes.

**Model and perspective**

Whether different pools of vesicles exist in the syncytial Drosophila embryos, which, upon receiving the appropriate signals, are recruited into the pre-existing plasma membrane and then fuse with each other to generate the new membrane in the cellularizing Drosophila embryo is now an important issue. The signals that may initiate cellularization, and the mechanism by which membranes are recruited for the growth of new membrane and insertion into the pre-existing plasma membrane remain to be fully elucidated. Two recent studies by Lecuit and Wieschaus and Sisson et al. have strongly established a link between export of Golgi-derived membranes and the plasma membrane. Additionally, they have shown that the membrane needed for cellularization originates from the intracellular organelles.

What has not been addressed specifically is the question of whether molecular motors participate in the active transport in the delivery of membrane proteins and lipid components to the growing plasma membrane during cellularization. We surmise that a number of minus-end directed motors, such as dynein, minus-end kinesin-like proteins, and even myosins may play major roles in this process (Fig. 5). Indeed, it has been demonstrated recently that, in polarized epithelial cells, KIFC3, a minus-end kinesin, is localized on membrane organelles immediately beneath the apical plasma membrane of renal tubular epithelial cells in vivo and polarized MDCK II cells in vitro. This observation is in keeping with the previous reports about the role of dynein and class I myosins in endocytotic traffic in polarized cells. Taken together, these observations lead us to propose a model for Drosophila blastoderm cellularization, involving molecular motors for energy-driven membrane/protein transport and delivery at specific sites of the polarized epithelia. We speculate that microtubule minus-end motors play a crucial role in the apical membrane delivery whereas, plus-end kinesins, such as KLP3A, could be important in recruiting catenin/cadherin-associated junctional proteins to the basal end during the initial phases of adherens junction formation. The validity of such a model for plus-end motor function in cellularization would require detailed

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**Figure 5.** Schematic model representing molecules that are known or speculated to have crucial roles in membrane transport, insertion and polarization during cellularization. Unlike conventional cytokinesis, no role of any regulatory kinases is known.
experimental dissection of the molecules involved. We expect
that plus-end molecular motors, including the bi-directional
heterotetrameric kinesins (kinesin II), may also exert forces for
farrow ingestion during cellularization (Fig. 5). Additionally,
we do not discount a component of the propulsive force being
provided directly by membrane insertion, where the force is
guided and stabilized by actomyosin network, as proposed by
Lecuit and Wieschaus.  

Conclusion
Cellularization is one of the most central and critical events
for embryonic development in most species of insect and a
number of other organisms. Genetic analysis and genome
sequencing continue to reveal new zygotic genes that may
regulate the onset of cellularization. It remains to be seen,
however, how these gene activities are co-ordinated to bring
about dramatic changes in cytoskeletal order and reshape the
embryos. A further challenging issue to be explored concerns
how the synchrony of this morphogenetic change is activated.
A full understanding of this mechanism will require a thorough
multidisciplinary approach including live imaging of cellulariz-
ing embryos with marked molecular components, as many of
the interactions may be too transient and subtle for detection in
genetic and biochemical analysis. New inhibitory agents that
specifically block major events of membrane delivery or any
motor activity could prove quite useful in understanding the
generation of polarized membrane insertion—a fundamental
aspect of cellularization. In addition, the use of RNAi techni-
ques and antibody microinjection into developing embryos at
the onset of cellularization could be highly informative for
analyzing the role of individual molecular components.

Acknowledgments
We like to thank Veronica Rodrigues and K. Vijay Raghavan
for continuous help, support and encouragement.

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