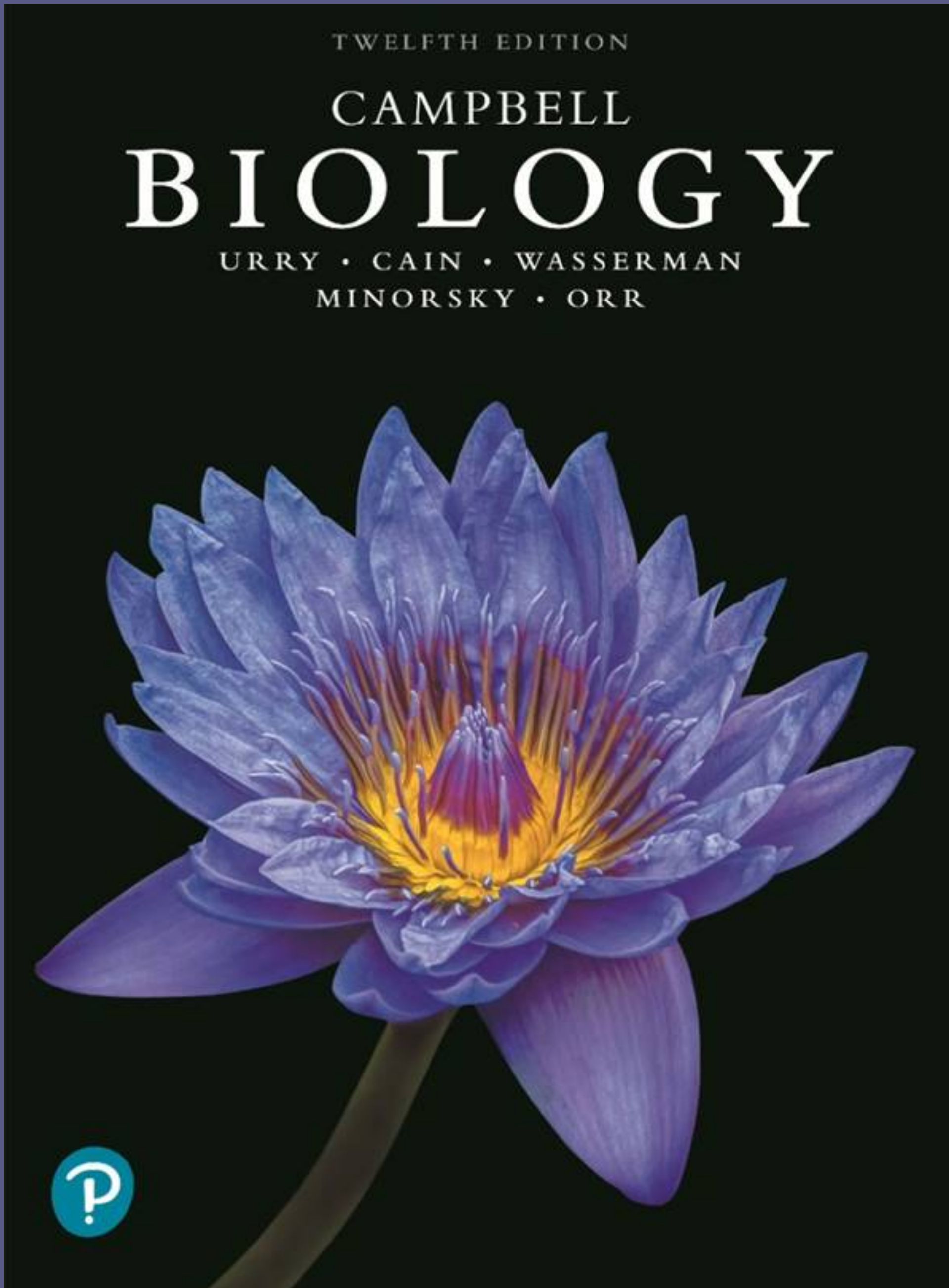


Chapter 47

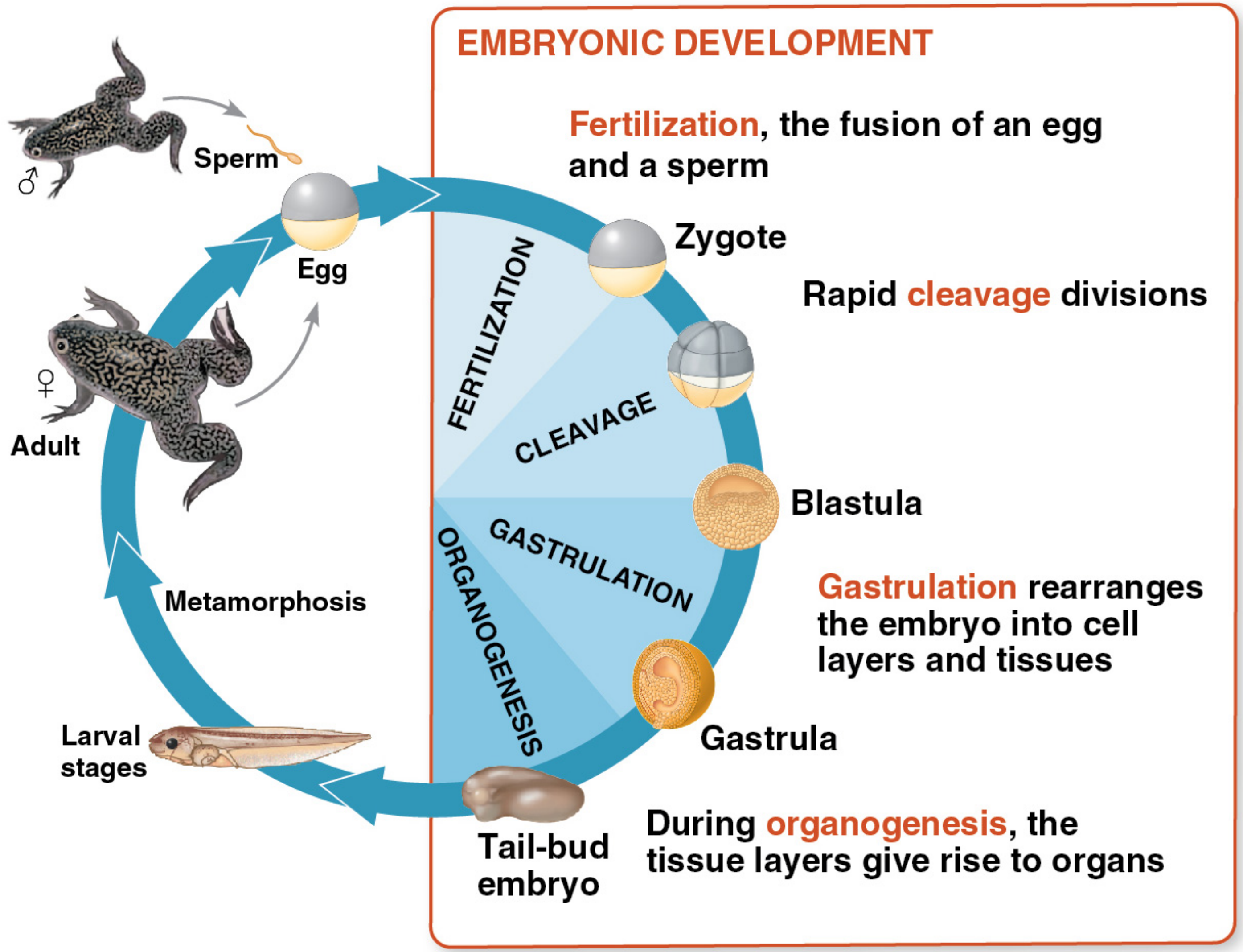
Animal Development

Lecture Presentations by
Nicole Tunbridge and
Kathleen Fitzpatrick

Figure 47.1a

Figure 47.1b

What processes transform an egg into an embryo with recognizable structures?



CONCEPT 47.1: Fertilization and cleavage initiate embryonic development

- Development occurs at many points in the life cycle of an animal
- In many animal species, embryonic development involves common stages that occur in a set order
- Lessons learned from studying one animal can often be broadly applied

- Biologists use **model organisms** to study development, chosen for the ease with which they can be studied in the laboratory
- **Fertilization** is the formation of a diploid zygote from a haploid egg and sperm

Fertilization

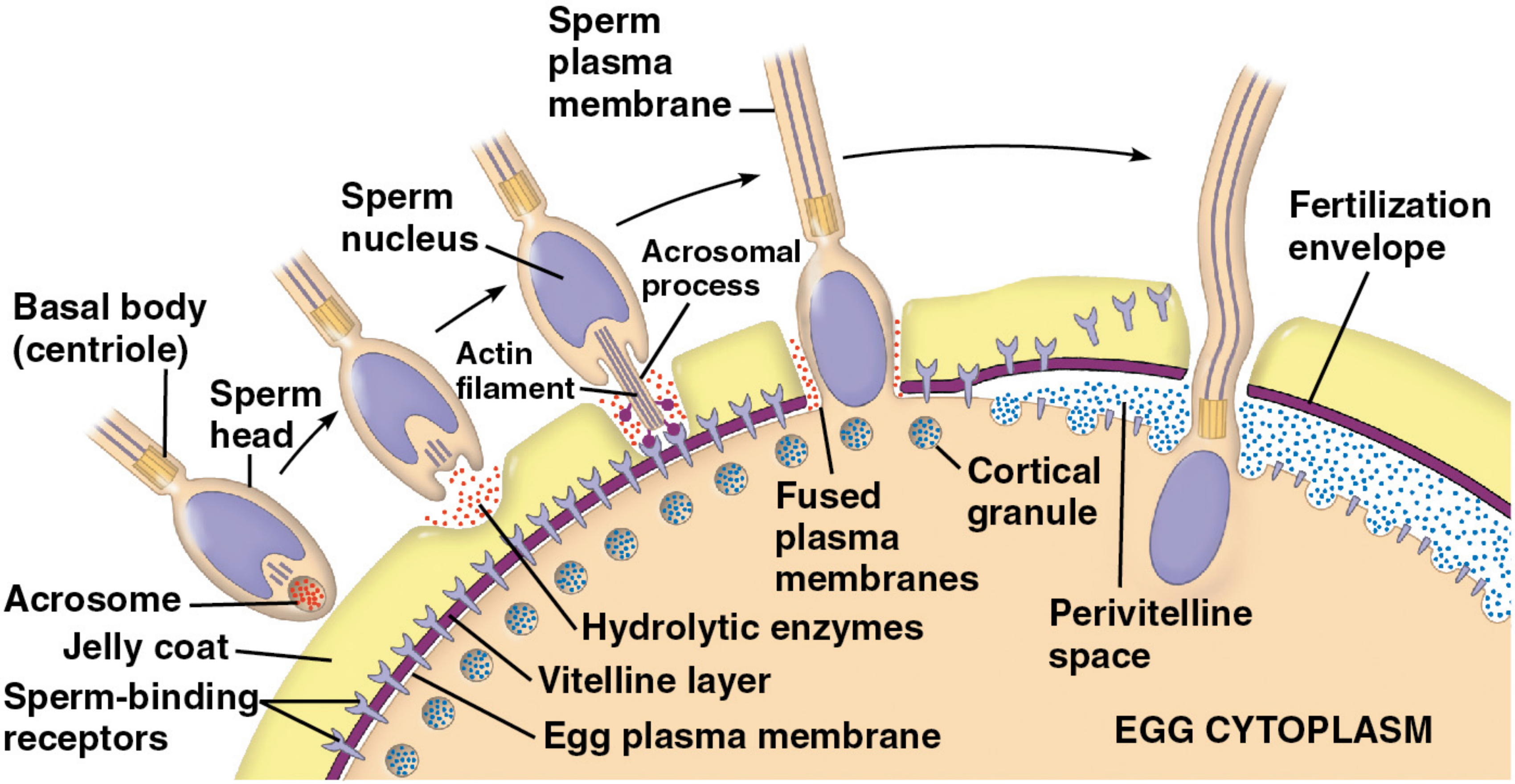
- When sea urchins release their gametes into the water, the jelly coat of the egg exudes soluble molecules that attract the sperm to the egg

The Acrosomal Reaction

- The **acrosomal reaction** is triggered when the sperm meets the egg
- The **acrosome** at the tip of the sperm releases hydrolytic enzymes that digest material surrounding the egg
- Recognition between the sperm and egg triggers fusion of their plasma membranes

- Gamete contact and/or fusion depolarizes the egg cell membrane and sets up a barrier to **polyspermy**
- Polyspermy is the entry of multiple sperm into the egg
- The depolarization occurs 1–3 seconds after a sperm binds the egg
- Thus, depolarization is a fast block to polyspermy

Figure 47.2

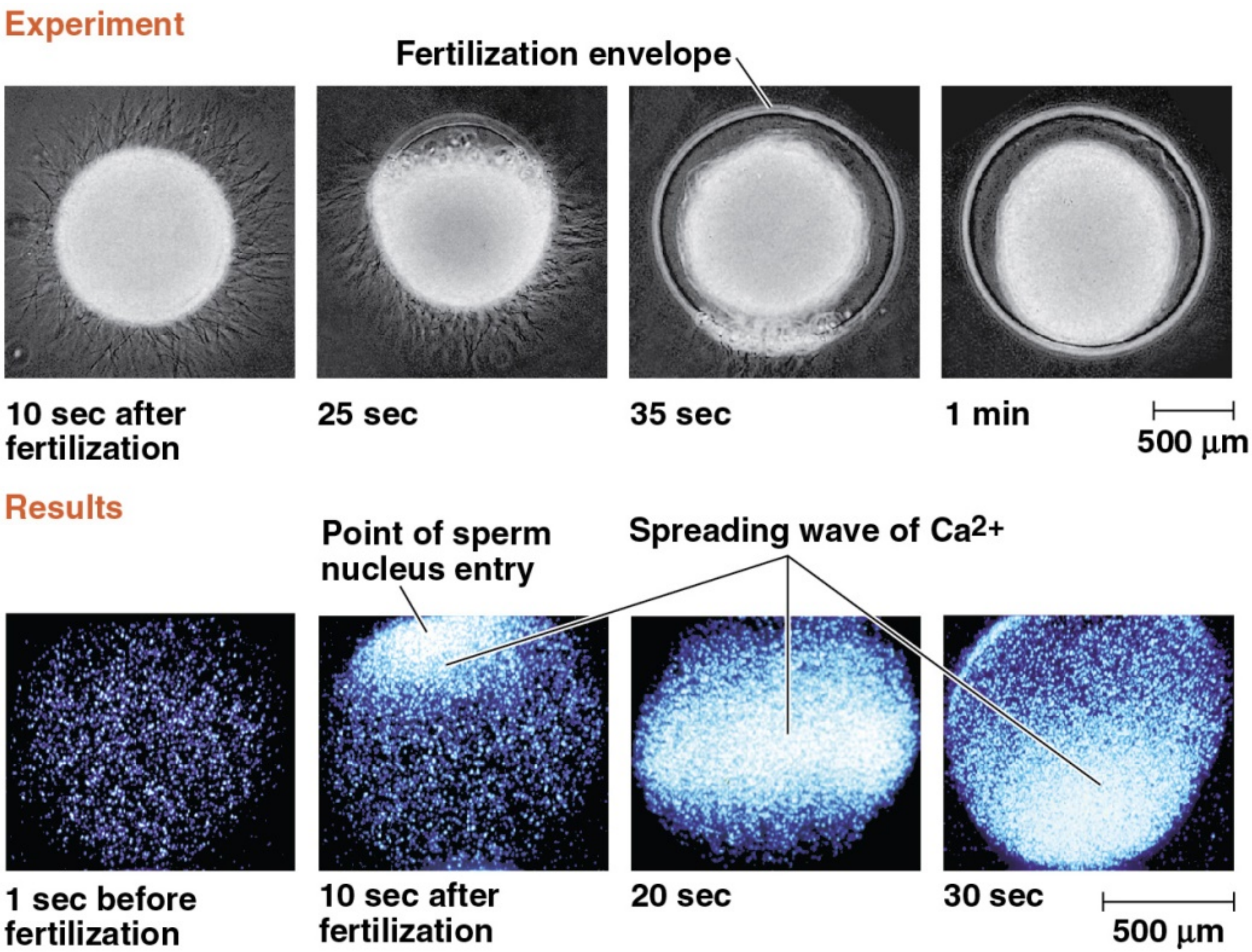

Sperm plasma membrane
Sperm nucleus
Acrosomal process
Basal body (centriole)
Sperm head
Actin filament
Fertilization envelope
Cortical granule
Fused plasma membranes
Perivitelline space
Acrosome
Jelly coat
Sperm-binding receptors
Hydrolytic enzymes
Vitelline layer
Egg plasma membrane
EGG CYTOPLASM

The Cortical Reaction

- Fusion of egg and sperm also initiates the cortical reaction
- Seconds after the sperm binds to the egg, vesicles just beneath the egg plasma membrane release their contents and form a fertilization envelope
- The fertilization envelope acts as a slow block to polyspermy

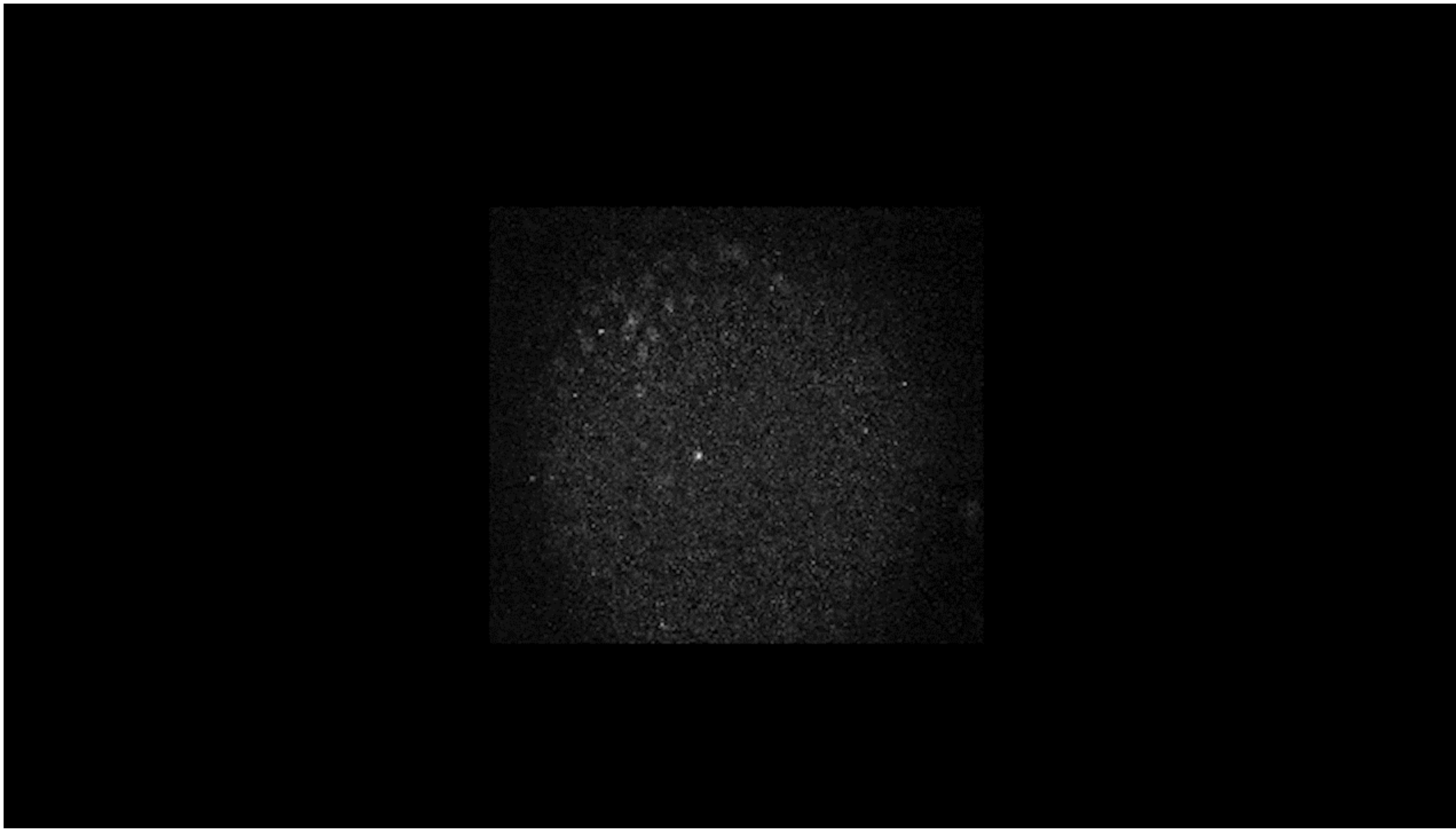
- The cortical reaction requires a high concentration of calcium ion (Ca^{2+}) ions in the egg
- The reaction is triggered by a change in Ca^{2+} concentration
- Ca^{2+} spread across the egg correlates with the appearance of the fertilization envelope

Figure 47.3

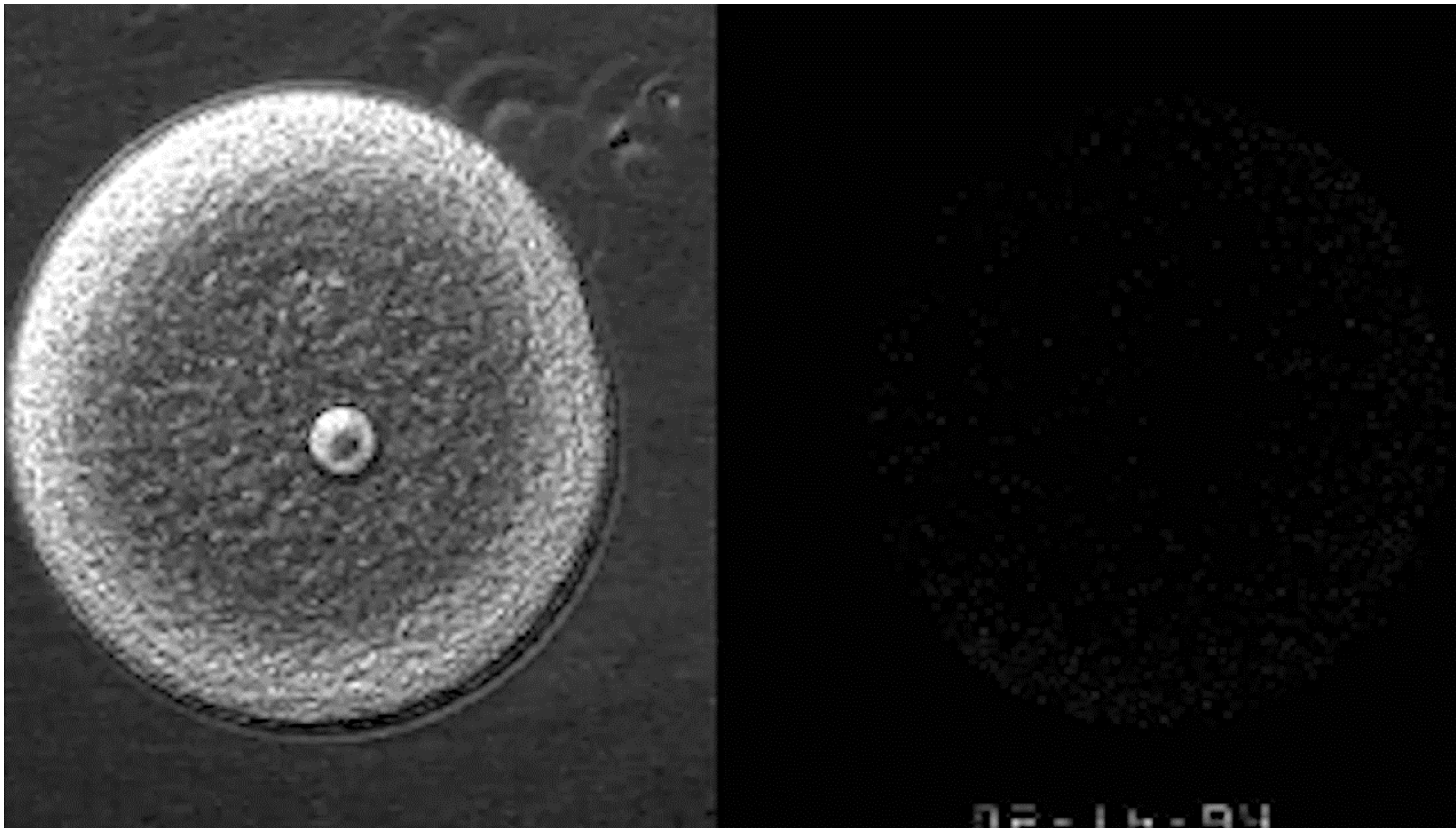


Data from R. Steinhardt et al., Intracellular calcium release at fertilization in the sea urchin egg, *Developmental Biology* 58:185–197 (1977); M. Hafner et al., Wave of free calcium at fertilization in the sea urchin egg visualized with Fura-2, *Cell Motility and the Cytoskeleton* 9:271–277 (1988).

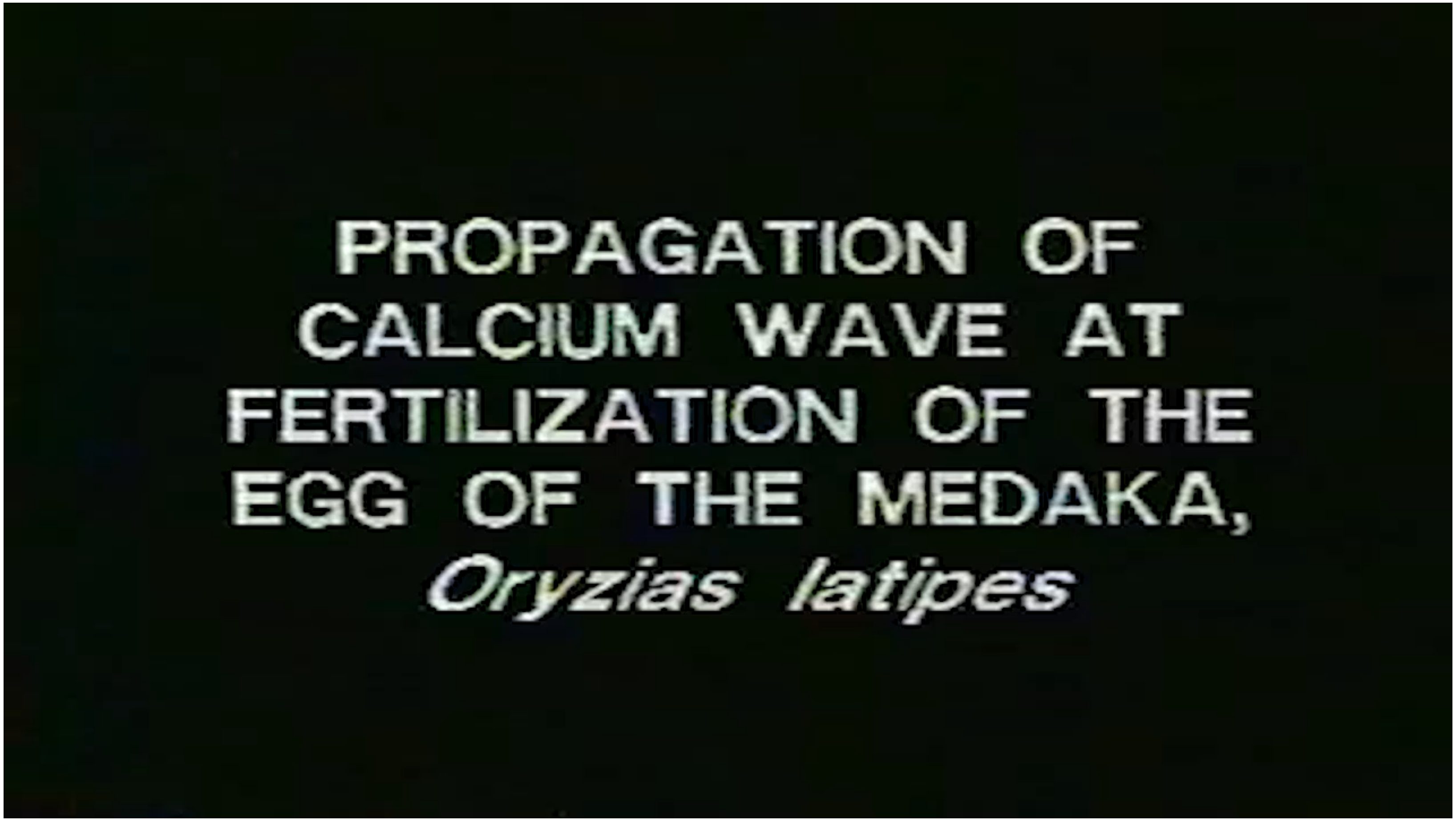
Video: Cortical Granule Fusion Following Egg Fertilization



Video: Calcium Release Following Egg Fertilization



Video: Calcium Wave Propagation in Fish Eggs



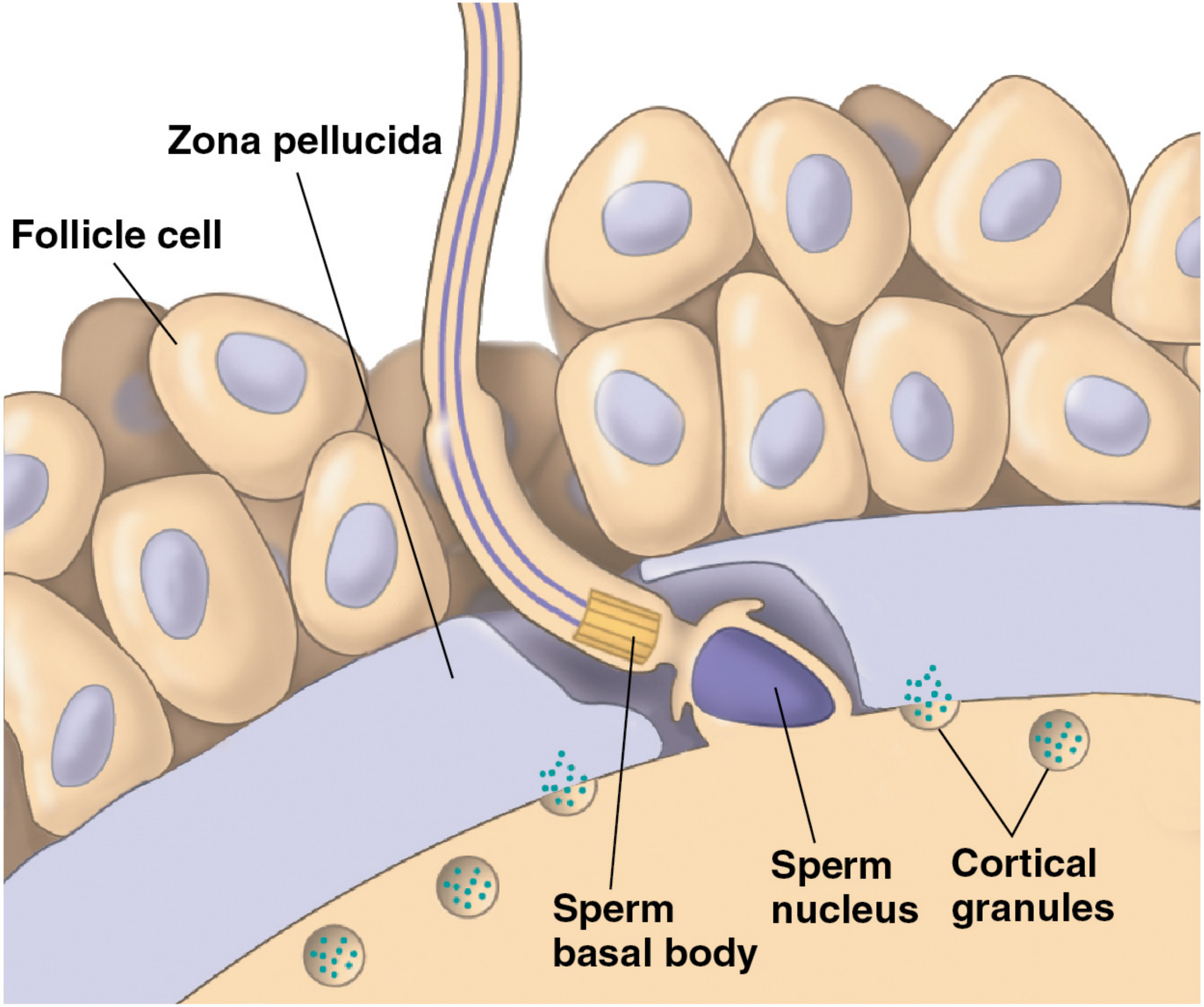
Egg Activation

- A rise in calcium concentration increases rates of cellular respiration and protein synthesis by the egg cell
- With these rapid changes in metabolism, the egg is said to be activated
- The sperm nucleus fuses with the egg nucleus, and cell division begins 90 minutes after fertilization
- The proteins and mRNAs needed for activation are already present in the egg

Fertilization in Mammals

- Fertilization in mammals and other terrestrial animals is internal
- A sperm must travel through a layer of follicle cells surrounding the egg before it reaches the **zona pellucida**, or extracellular matrix of the egg
- Sperm binding triggers a cortical reaction
- In mammals, the first cell division occurs 12–36 hours after sperm binding

Figure 47.4

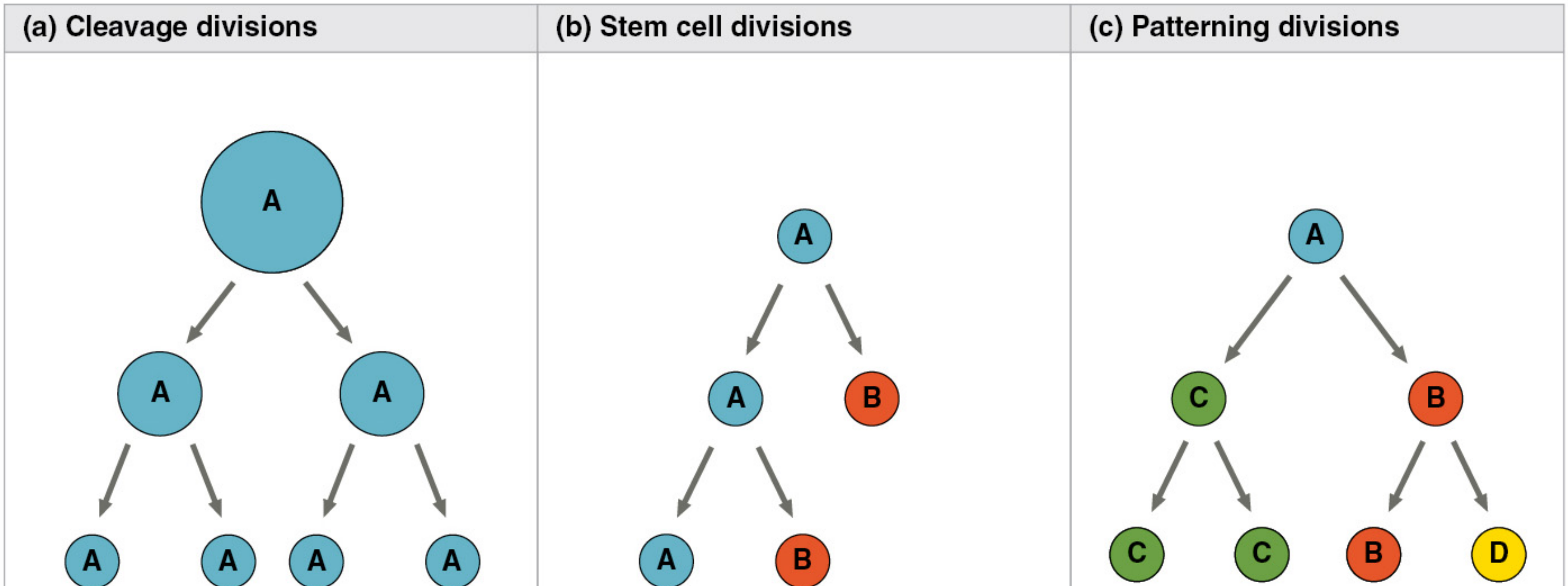


Zona pellucida
Follicle cell
Sperm basal body
Sperm nucleus
Cortical granules

Cleavage

- Fertilization is followed by **cleavage**, a period of rapid cell division without growth
- Cleavage partitions the cytoplasm of one large cell into many smaller cells called **blastomeres**
- The **blastula** is a ball of cells with a fluid-filled cavity called a **blastocoel**

Figure 47.5

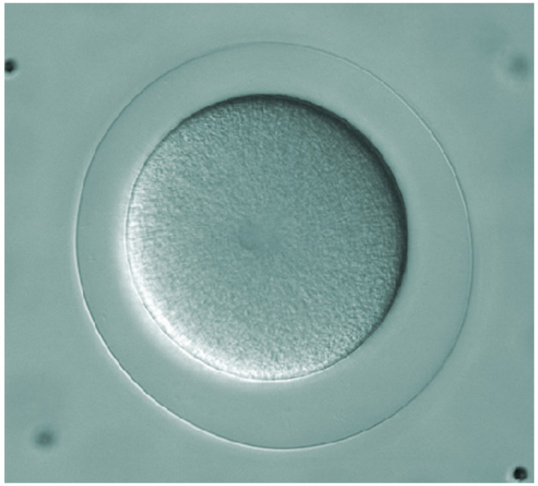


Rapid mitotic divisions in early development: Cell number increases but cell size decreases, leaving embryo size unchanged.

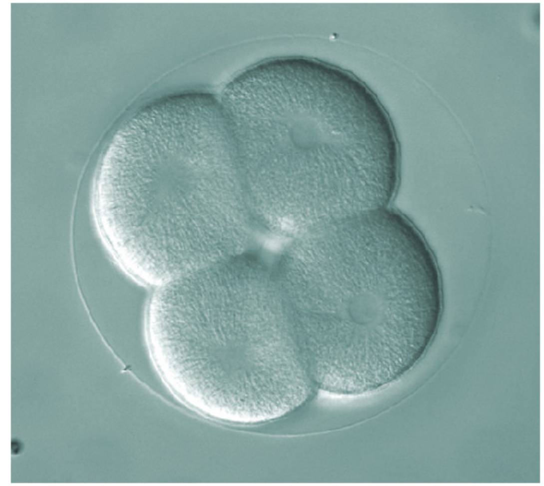
These divisions replenish cells that are needed continuously throughout life, such as blood cells.

Daughter cells take on different fates based on positional information in the embryo.

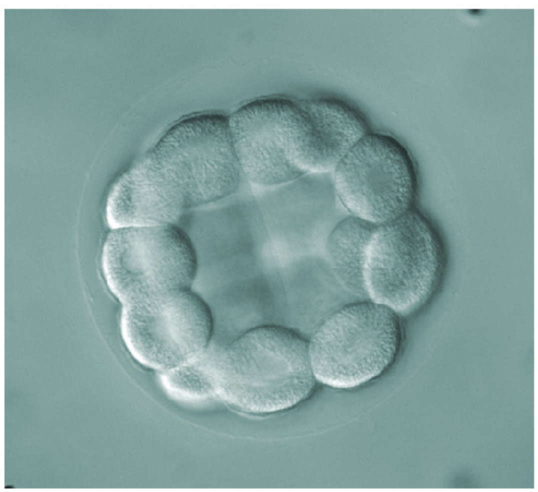
Figure 47.6



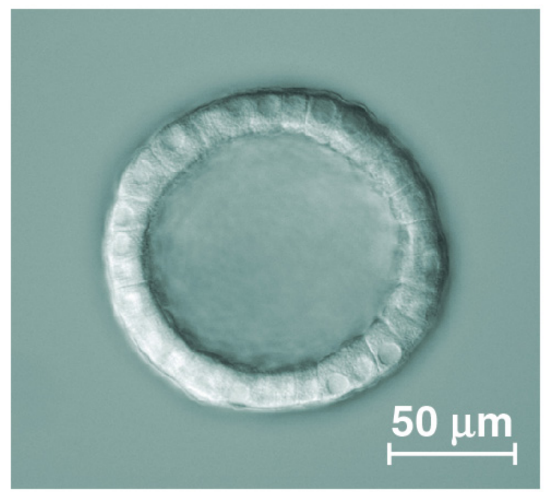
(a) Fertilized egg



(b) Four-cell stage



(c) Early blastula

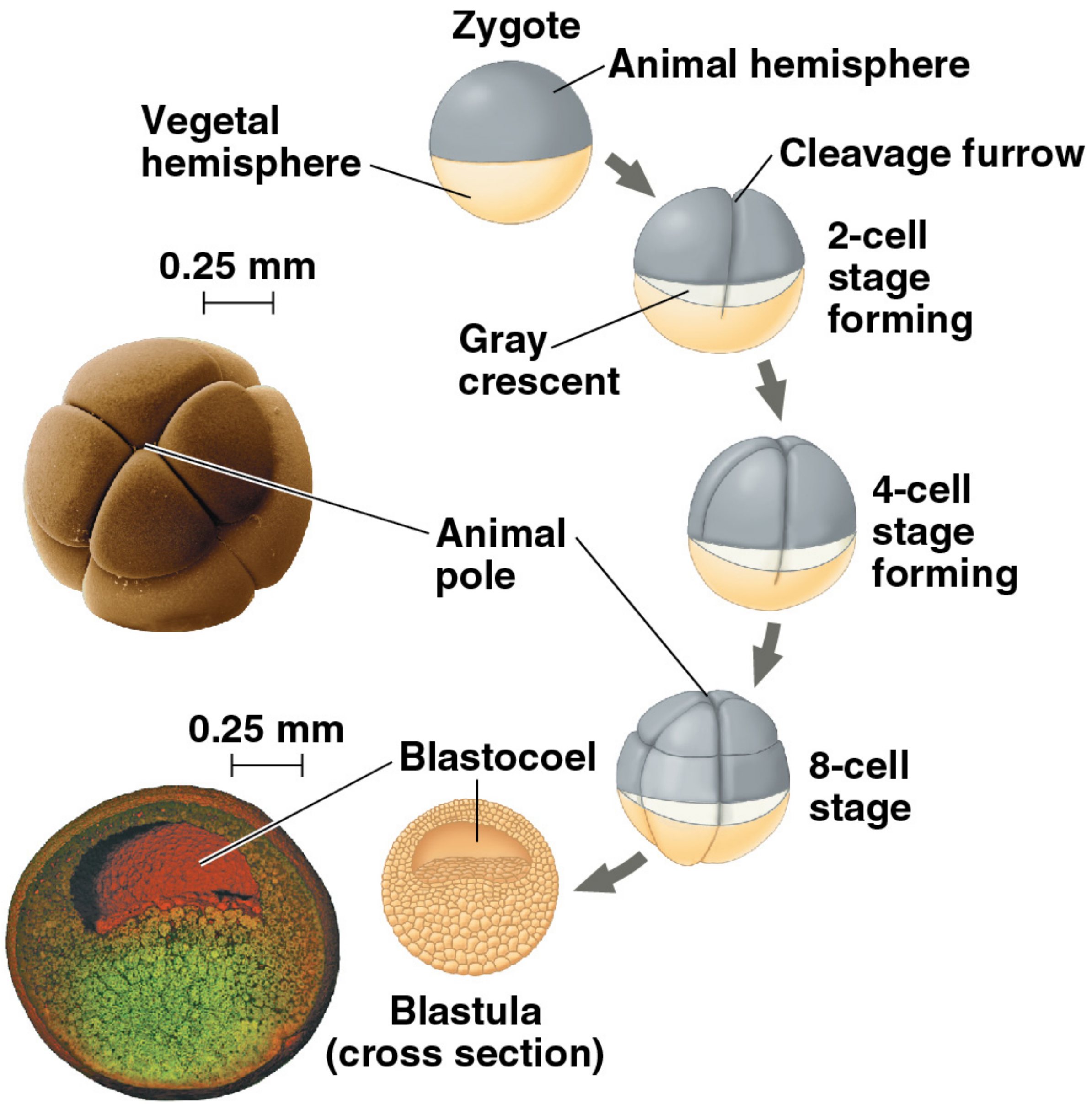


(d) Later blastula

Cleavage Pattern in Frogs

- In frogs and many other land animals, cleavage is asymmetric due to the distribution of **yolk** (stored nutrients)
- The **vegetal pole** has more yolk; the **animal pole** has less yolk
- The yolk greatly affects the pattern of cleavage

Figure 47.7


Zygote
Animal hemisphere
Vegetal hemisphere
Cleavage furrow
2-cell stage forming
Gray crescent
0.25 mm
4-cell stage forming
Animal pole
8-cell stage
0.25 mm
Blastocoel
Blastula (cross section)

- The first two cleavage furrows in the frog form four equally sized blastomeres
- The third cleavage is asymmetric, forming unequally sized blastomeres; this asymmetry is due to the yolk in the vegetal hemisphere

Video: Cleavage of a Fertilized Egg

Cleavage Pattern in Other Animals

- Holoblastic cleavage, complete division of the egg, occurs in species whose eggs have little or moderate amounts of yolk, such as sea urchins and frogs
- Meroblastic cleavage, incomplete division of the egg, occurs in species with yolk-rich eggs, such as reptiles and birds
- In *Drosophila* and other insects, multiple rounds of mitosis occur without cytokinesis

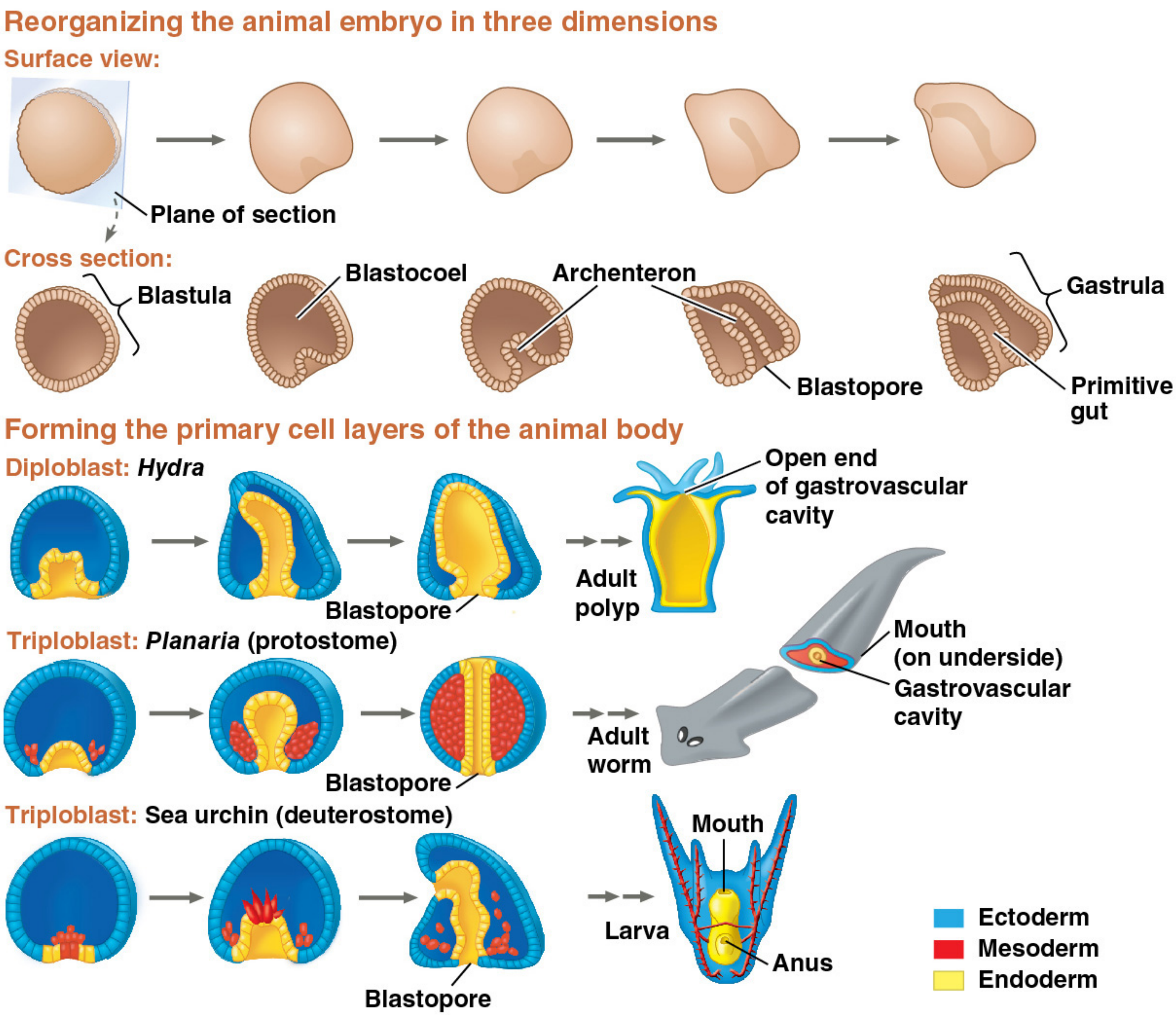
CONCEPT 47.2: Morphogenesis in animals involves specific changes in cell shape, position, and survival

- **Morphogenesis** is the process by which the animal body takes shape over the last two stages of development
  - **Gastrulation**, the movement of cells from the blastula surface to the interior of the embryo
  - **Organogenesis**, the formation of organs

Gastrulation

- Gastrulation rearranges the cells of a blastula into a three-layered embryo called a **gastrula**
- Cells take up new positions and acquire new neighbors

Figure 47.8



Reorganizing the animal embryo in three dimensions
Surface view:
Plane of section
Cross section:
Blastula
Blastocoel
Archenteron
Gastrula
Blastopore
Primitive gut
Forming the primary cell layers of the animal body
Diploblast: Hydra
Open end of gastrovascular cavity
Blastopore
Adult polyp
Triploblast: Planaria (protostome)
Mouth (on underside)
Gastrovascular cavity
Blastopore
Adult worm
Triploblast: Sea urchin (deuterostome)
Mouth
Larva
Anus
Blastopore
Ectoderm
Mesoderm
Endoderm

- The three layers produced by gastrulation are called embryonic **germ layers**
  - The **ectoderm** forms the outer layer
  - The **endoderm** lines the digestive tract
  - The **mesoderm** partly fills the space between the endoderm and ectoderm
- Diploblasts have only the first two; triploblasts also have mesoderm

Video: Sea Urchin Embryonic Development (Time Lapse)

Gastrulation in Frogs

- Each germ layer contributes to a distinct set of structures in the adult animal
- Frog gastrulation begins when a group of cells on the dorsal side of the blastula begins to invaginate
- This position is opposite to the position where the sperm entered the egg

Figure 47.9

ECTODERM (outer layer)

- Epidermis of skin and its derivatives (including sweat glands, hair follicles)
- Nervous and sensory systems
- Pituitary gland, adrenal medulla
- Jaws and teeth

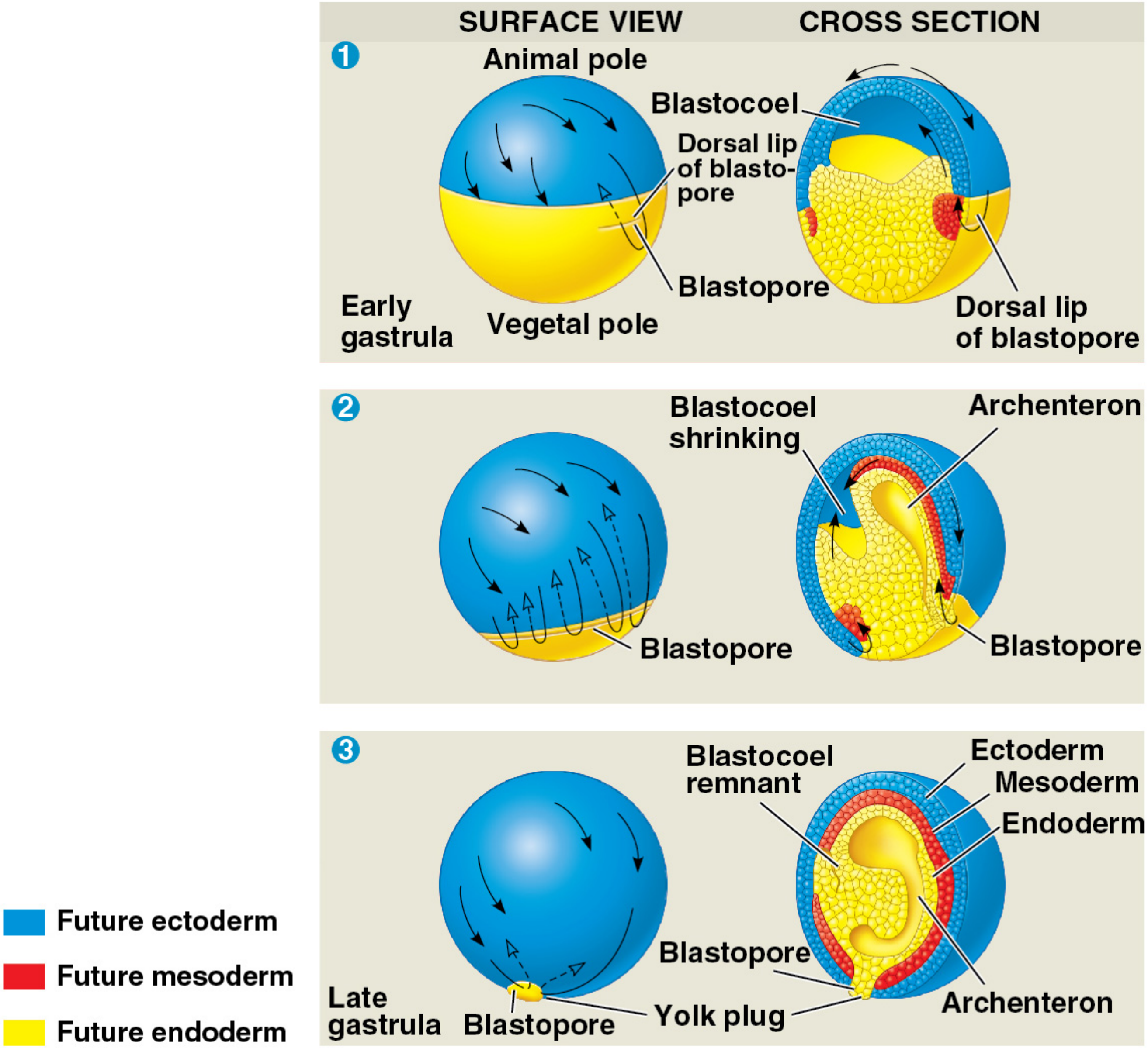
MESODERM (middle layer)

- Skeletal and muscular systems
- Circulatory and lymphatic systems
- Excretory and reproductive systems (except germ cells)
- Dermis of skin
- Adrenal cortex

ENDODERM (inner layer)

- Epithelial lining of digestive tract and associated organs
- Epithelial lining of respiratory, excretory, and reproductive tracts and ducts
- Thymus, thyroid, and parathyroid glands

Figure 47.10

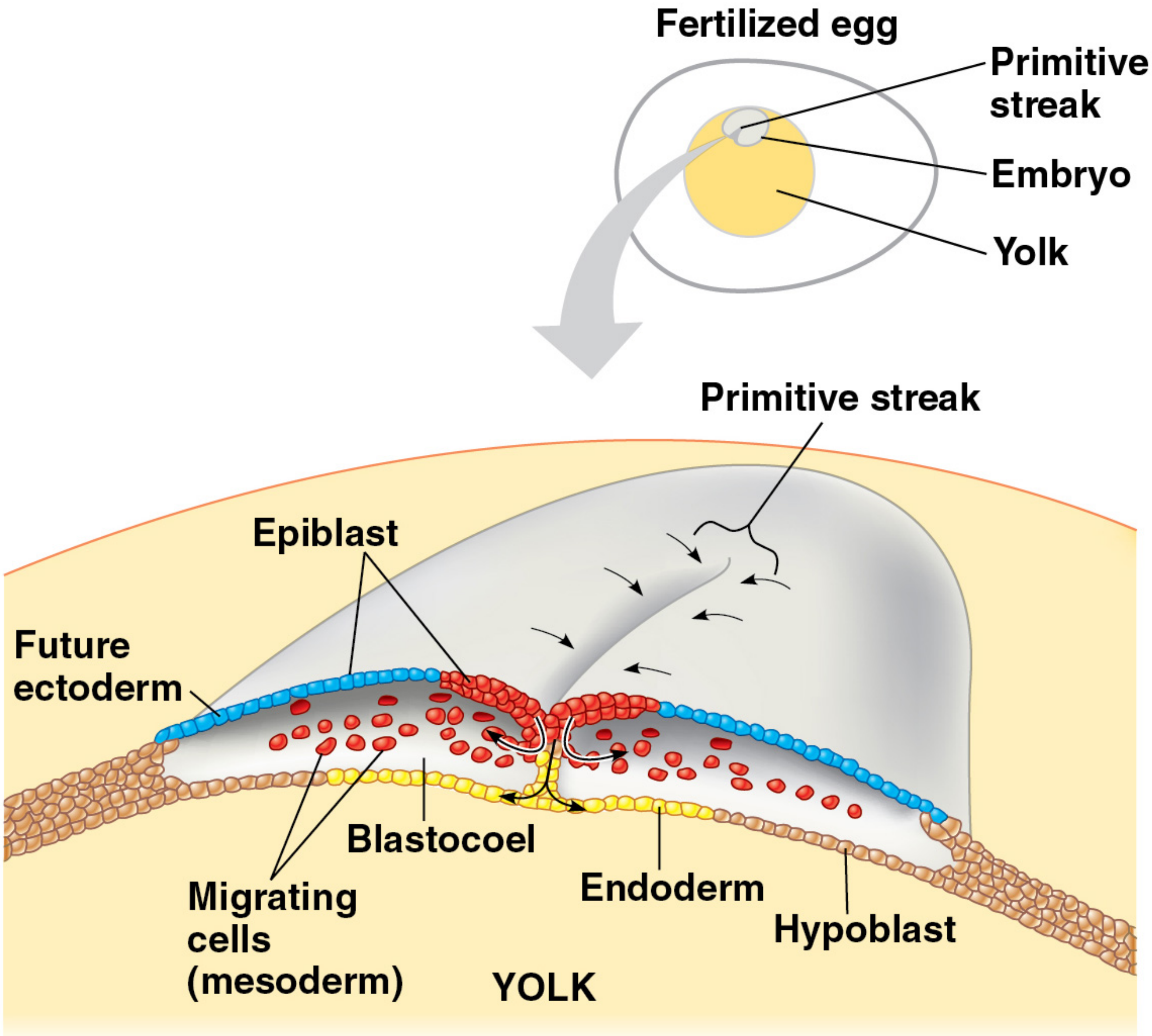

SURFACE VIEW
CROSS SECTION
1
Animal pole
Blastocoel
Dorsal lip of blasto- pore
Blastopore
Dorsal lip of blastopore
Early gastrula
Vegetal pole
2
Blastocoel shrinking
Archenteron
Blastopore
Blastopore
3
Blastocoel remnant
Ectoderm
Mesoderm
Endoderm
Blastopore
Archenteron
Late gastrula
Blastopore
Yolk plug
Future ectoderm
Future mesoderm
Future endoderm

Gastrulation in Chicks

- Prior to gastrulation, the embryo is composed of an upper and lower layer, the epiblast and hypoblast, respectively
- During gastrulation, some epiblast cells move toward the midline of the blastoderm and then into the embryo toward the yolk

- The midline thickens and is called the primitive streak
- The hypoblast cells contribute to the sac that surrounds the yolk and a connection between the yolk and the embryo, but do not contribute to the embryo itself

Figure 47.11



Fertilized egg
Primitive streak
Embryo
Yolk
Primitive streak
Epiblast
Future ectoderm
Blastocoel
Migrating cells (mesoderm)
Endoderm
Hypoblast
YOLK

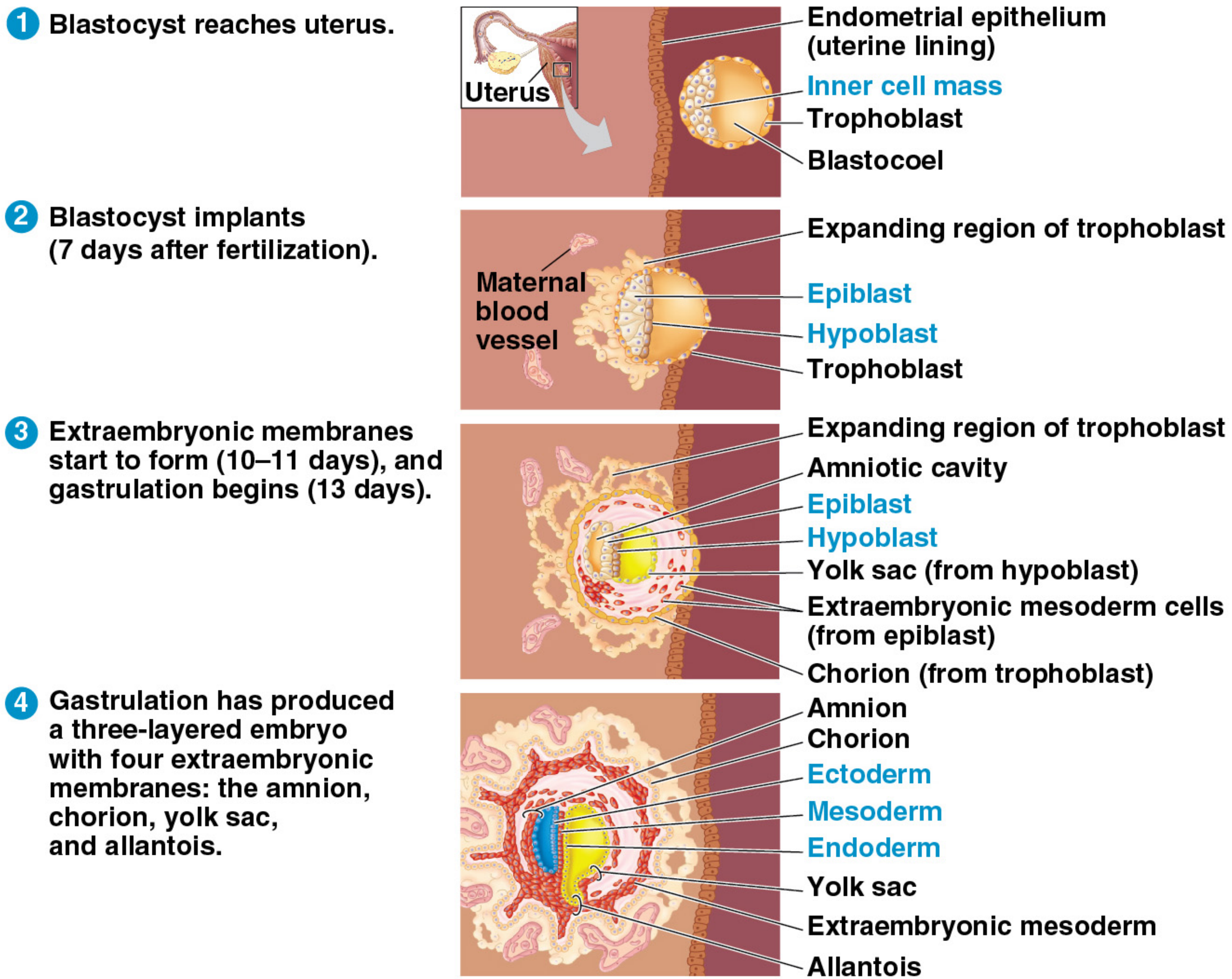
Gastrulation in Humans

- Human eggs are small, with very little yolk
- Fertilization takes place in the oviduct and development begins while the embryo moves through the oviduct to the uterus

- A **blastocyst** is the human equivalent of the blastula
- The **inner cell mass** is a cluster of cells at one end of the blastocyst
- The **trophoblast** is the outer epithelial layer of the blastocyst and does not contribute to the embryo, but instead initiates implantation
- The inner cell mass then forms a disk with an inner layer of cells, the epiblast, and an outer layer called the hypoblast

- Following implantation, the trophoblast continues to expand, and a set of **extraembryonic membranes** is formed
- These enclose specialized structures outside of the embryo
- Gastrulation involves the inward movement from the epiblast through a primitive streak, similar to the chick embryo
- After gastrulation, the embryonic germ layers have formed

Figure 47.12



1 Blastocyst reaches uterus.
Uterus
Endometrial epithelium (uterine lining)
Inner cell mass
Trophoblast
Blastocoel
2 Blastocyst implants (7 days after fertilization).
Maternal blood vessel
Expanding region of trophoblast
Epiblast
Hypoblast
Trophoblast
3 Extraembryonic membranes start to form (10–11 days), and gastrulation begins (13 days).
Expanding region of trophoblast
Amniotic cavity
Epiblast
Hypoblast
Yolk sac (from hypoblast)
Extraembryonic mesoderm cells (from epiblast)
Chorion (from trophoblast)
4 Gastrulation has produced a three-layered embryo with four extraembryonic membranes: the amnion, chorion, yolk sac, and allantois.
Amnion
Chorion
Ectoderm
Mesoderm
Endoderm
Yolk sac
Extraembryonic mesoderm
Allantois

Video: Ultrasound of Human Fetus 1

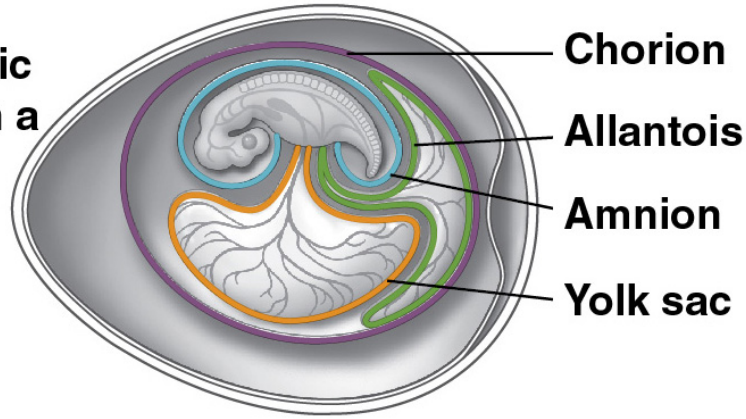
Video: Ultrasound of Human Fetus 2

Developmental Adaptations of Amniotes

- Land vertebrates form four extraembryonic membranes: the chorion, allantois, amnion, and yolk sac
- These provide a life-support system for the further development of the embryo
- Reproduction outside of aqueous environments required development of
  – The shelled egg of birds, other reptiles, and the monotremes
  – The uterus of marsupial and eutherian mammals

Figure 47.13

(a) The four extraembryonic membranes in a reptile egg



(b) A baby red-tailed racer snake (*Gonyosoma oxycephala*) hatching from its protective egg

- In both adaptations, embryos are surrounded by fluid in a sac called the amnion
- This allows reproduction on dry land
- Mammals and reptiles including birds are called **amniotes** for this reason

- The four extraembryonic membranes that form around the embryo have specific functions
  - The chorion functions in gas exchange
  - The amnion encloses the amniotic fluid
  - The allantois disposes of waste products and contributes to gas exchange
  - The yolk sac encloses the yolk

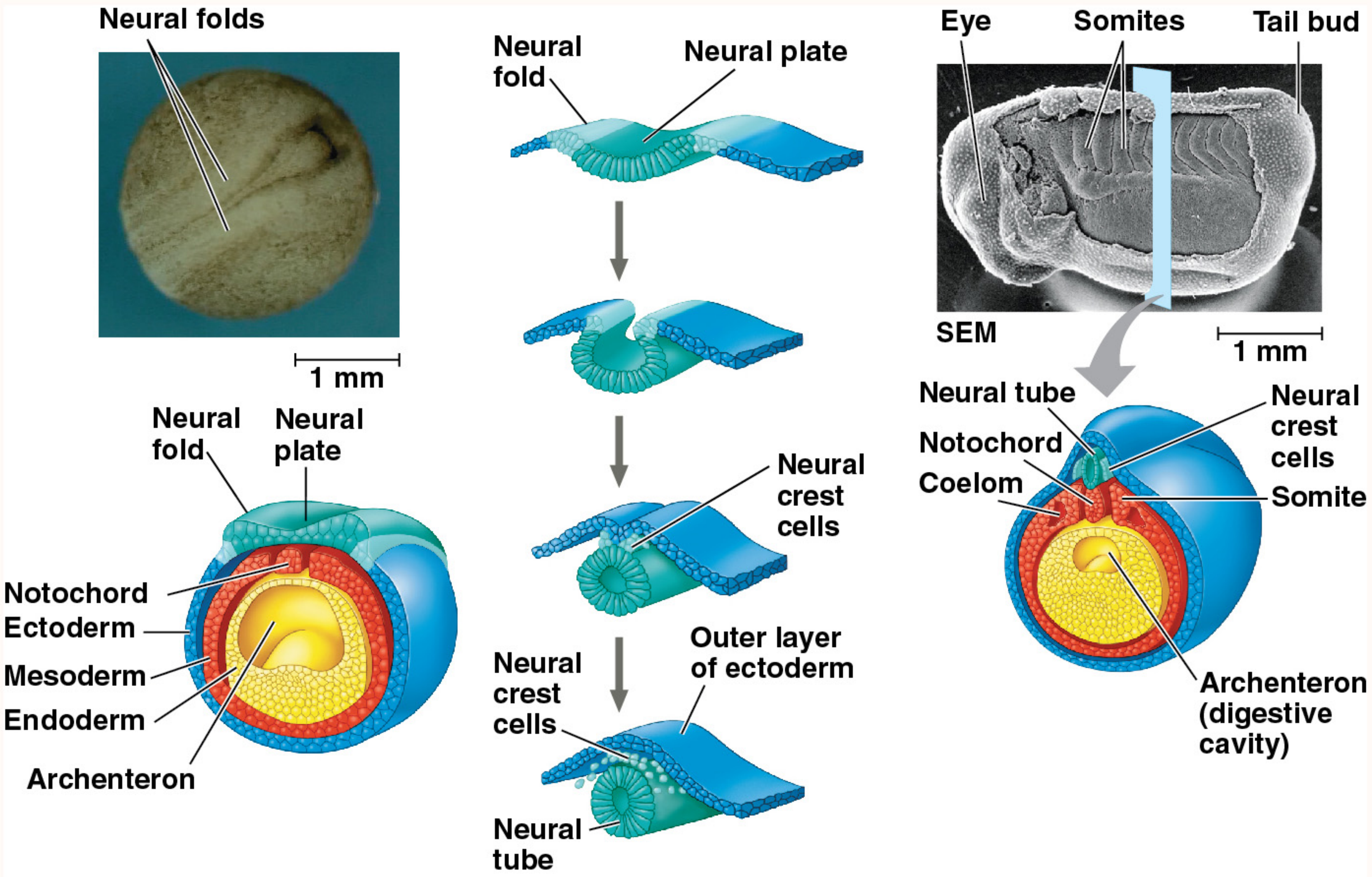
Organogenesis

- During organogenesis, various regions of the germ layers develop into rudimentary organs
- Adoption of particular developmental fates may cause cells to change shape or even migrate to a new location in the body
- Neurulation is the formation of the brain and spinal cord in vertebrates

Neurulation

- Neurulation begins as cells from the dorsal mesoderm form the **notochord**, a rod extending along the dorsal side of the embryo
- Signaling molecules secreted by the notochord and other tissues cause the ectoderm above to form the neural plate
- This is an example of **induction**, when cells or tissues cause a developmental change in nearby cells

- The neural plate rolls itself into the **neural tube**
- The neural tube will become the central nervous system (brain and spinal cord)
- The notochord disappears before birth, but contributes to parts of the disks between vertebrae



(a) Neural plate formation (b) Neural tube formation (c) Somites

Cell Migration in Organogenesis

- **Neural crest** cells develop along the neural tube of vertebrates and migrate in the body, eventually forming various parts of the embryo (nerves, parts of teeth, and skull bones)
- Mesoderm lateral to the notochord forms blocks called **somites**
- Parts of the somites dissociate to form mesenchyme cells, which form the vertebrae and the ribs and muscles associated with the vertebral column

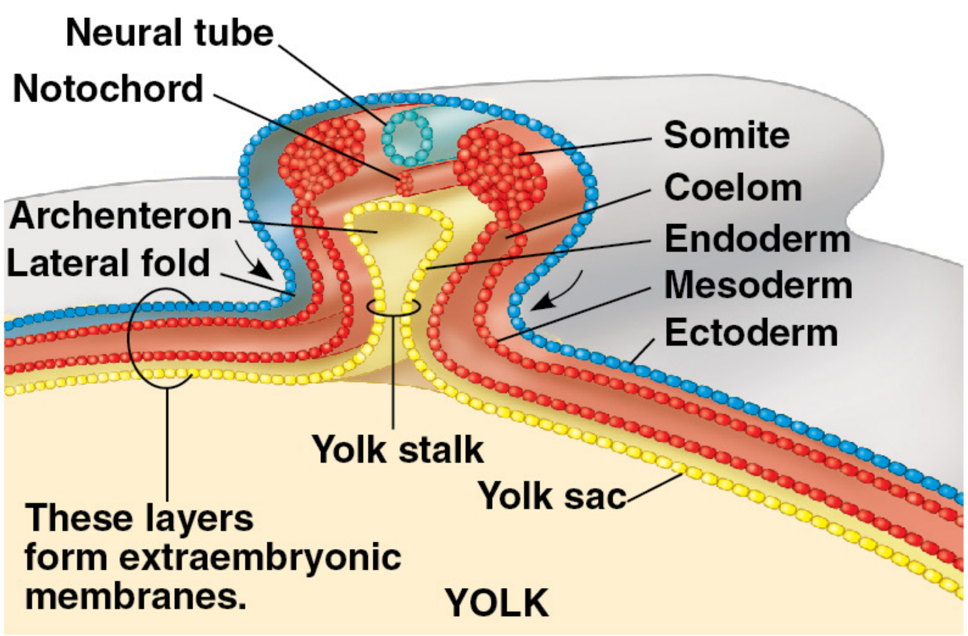
Video: Frog Embryo Development

[redacted]

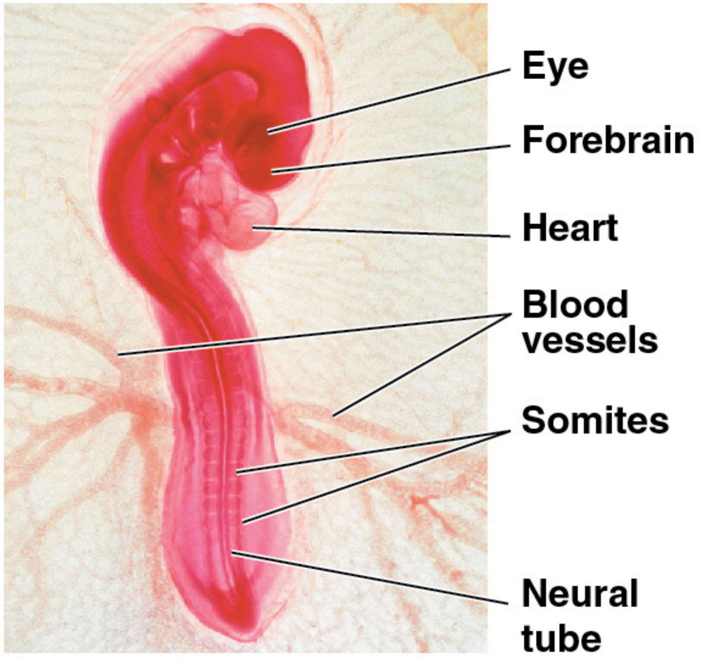
Organogenesis in Chick and Insects

- Early organogenesis in the chick is quite similar to that in the frog
- By the time the embryo is 56 hours old, rudiments of the major organs are readily apparent
- Pattern and appearance of organogenesis in invertebrates are different from that in vertebrates
- However, the mechanisms of organogenesis, such as neurulation, are quite similar

Figure 47.15



(a) Early organogenesis



(b) Late organogenesis

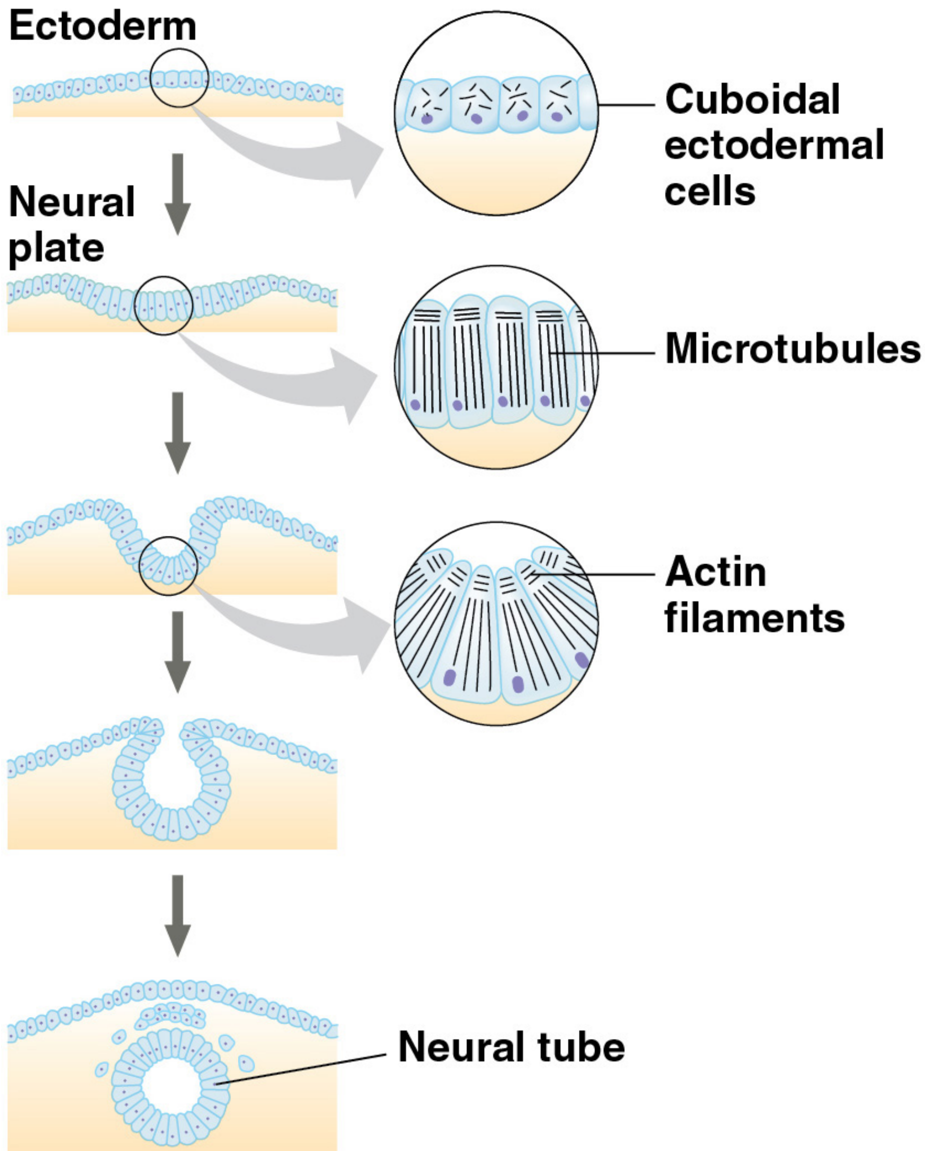
The Cytoskeleton in Morphogenesis

- In animals, movements of parts of a cell can bring about cell shape changes or can enable a cell to migrate to a new location
- The microtubules and microfilaments of the cytoskeleton are essential to these events

Cell Shape Changes in Morphogenesis

- Reorganizing the cytoskeleton is a major force in changing cell shape during development
- For example, the contraction of actin filaments at the apical end of cells causes them to become wedge shaped
- This is a common mechanism for invaginating a cell layer

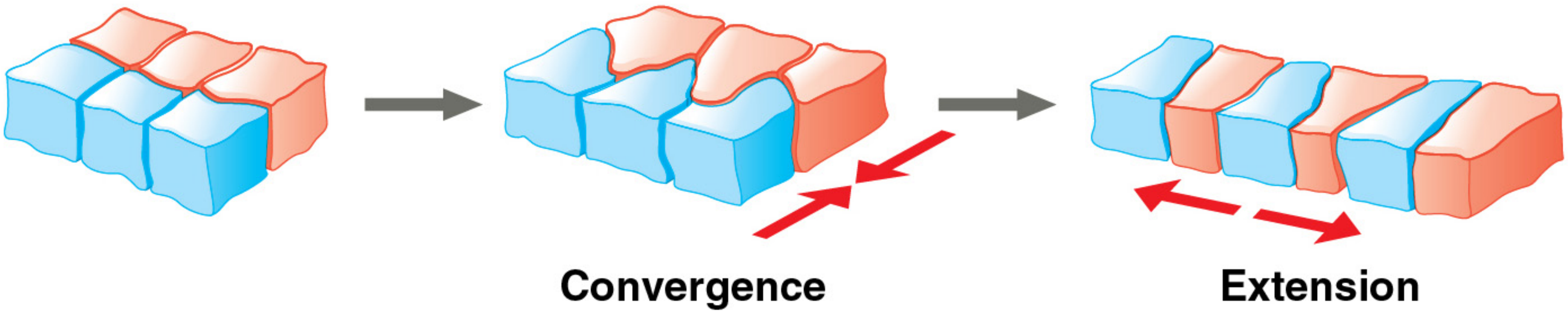
Figure 47.16



Ectoderm
Cuboidal ectodermal cells
Neural plate
Microtubules
Actin filaments
Neural tube

- The cytoskeleton also directs **convergent extension**
- In convergent extension, a sheet of cells undergoes rearrangement to form a longer and narrower shape
- Cells elongate and wedge between each other to form fewer columns of cells

Figure 47.17



Cells elongate and crawl between each other.

The sheet of cells becomes longer and narrower.

Cell Migration in Morphogenesis

- The cytoskeleton is also responsible for cell migration
- Transmembrane glycoproteins called cell adhesion molecules play a key role in migration
- Migration also involves the extracellular matrix (ECM), a meshwork of secreted glycoproteins and other molecules lying outside the plasma membrane of cells

Programmed Cell Death

- Programmed cell death is also called **apoptosis**
- At various times during development, individual cells, sets of cells, or whole tissues stop developing, die, and are engulfed by neighboring cells
- For example, many more neurons are produced in developing embryos than will be needed
- Extra neurons are eliminated by apoptosis

- In some cases, a structure functions in early stages and is eliminated during later development
- For example, the tail of the tadpole undergoes apoptosis during frog metamorphosis

CONCEPT 47.3: Cytoplasmic determinants and inductive signals contribute to cell fate

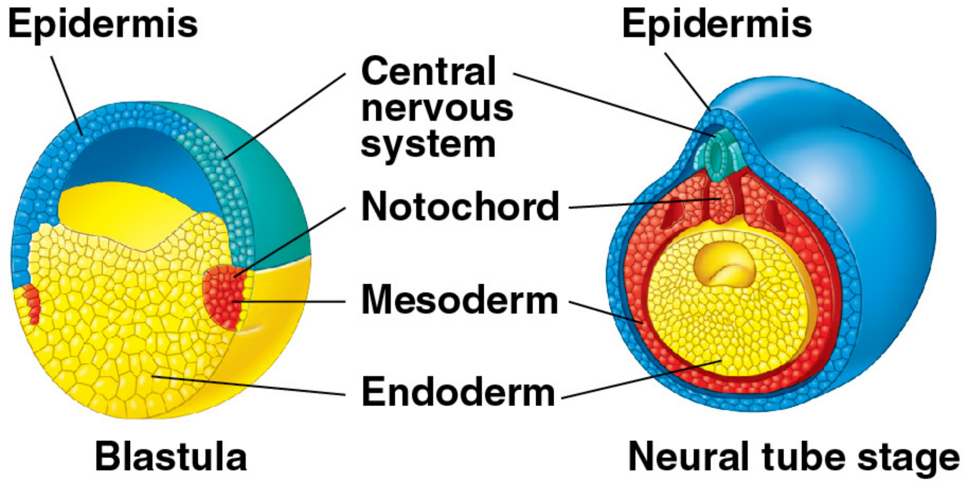
- **Determination** is a term referring to the process by which a cell or group of cells becomes committed to a particular fate
- **Differentiation** refers to the resulting specialization in structure and function

- Cells in a multicellular organism share the same genome
- Differences in cell types are the result of the expression of different sets of genes

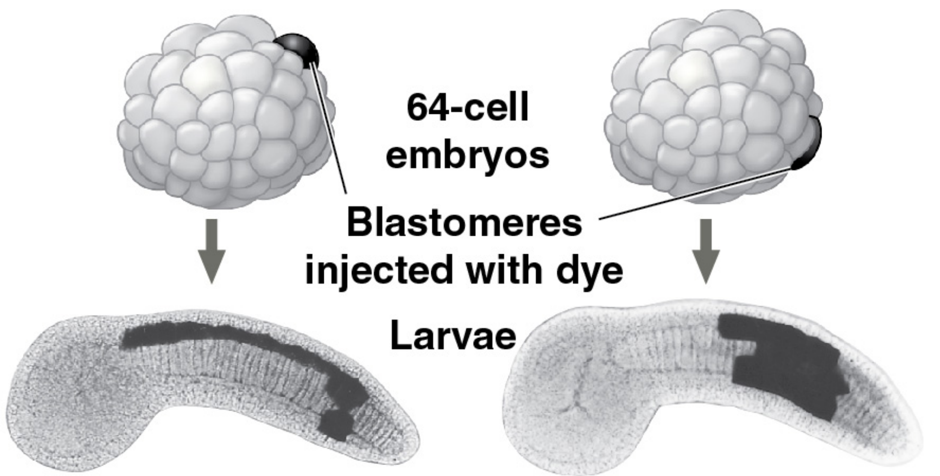
Fate Mapping

- **Fate maps** are diagrams showing organs and other structures that arise from each region of an embryo
- Researchers developed techniques to mark an individual blastomere during cleavage, and follow the marker in the descendants of that cell

Figure 47.18



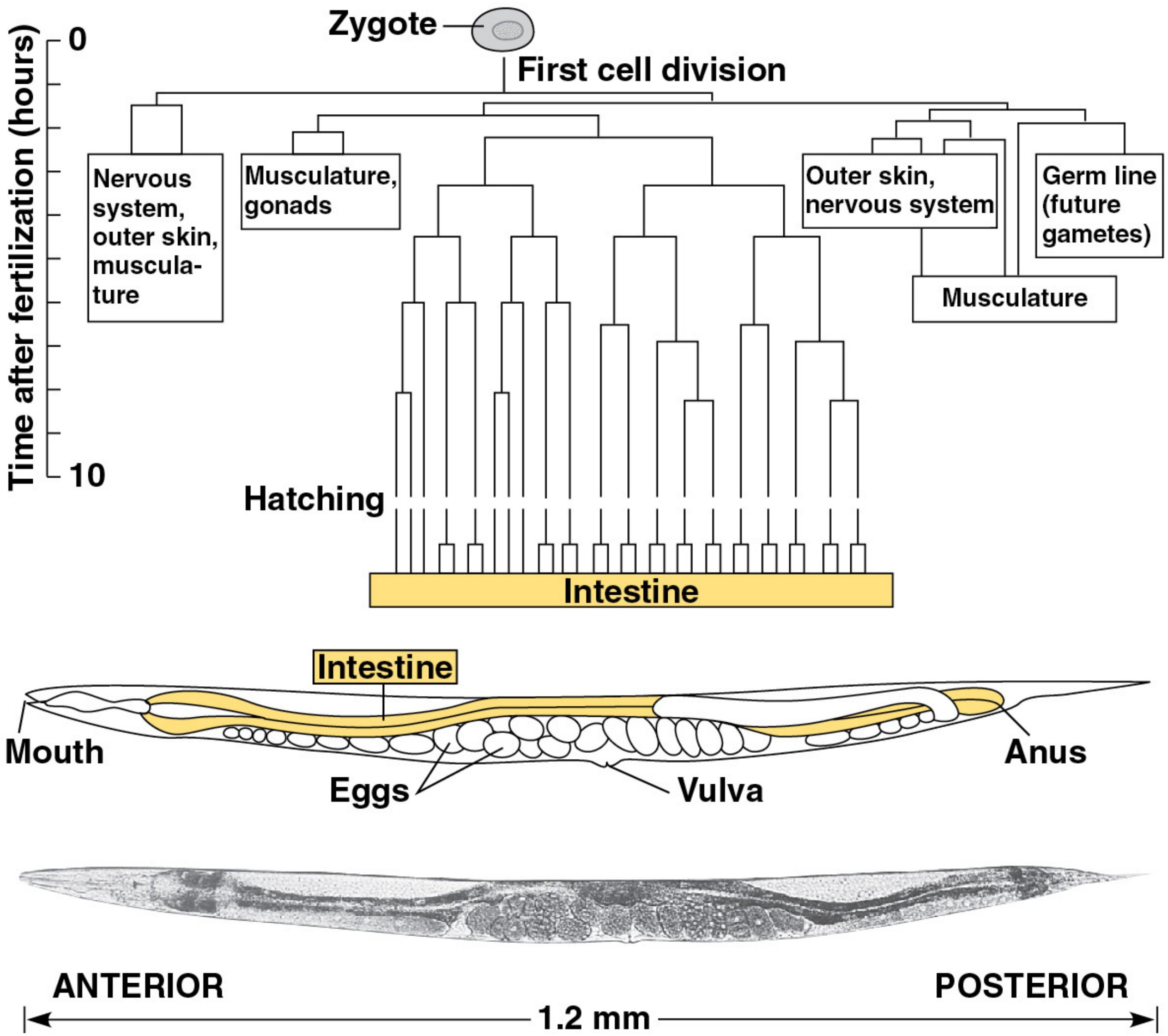
(a) Fate map of a frog embryo



(b) Cell lineage analysis in a tunicate

- Studies of the nematode *Caenorhabditis elegans* used the ablation (destruction) of single cells to determine the structures that normally arise from each cell
- The researchers were able to determine the lineage of each of the 959 somatic cells in the worm

Figure 47.19

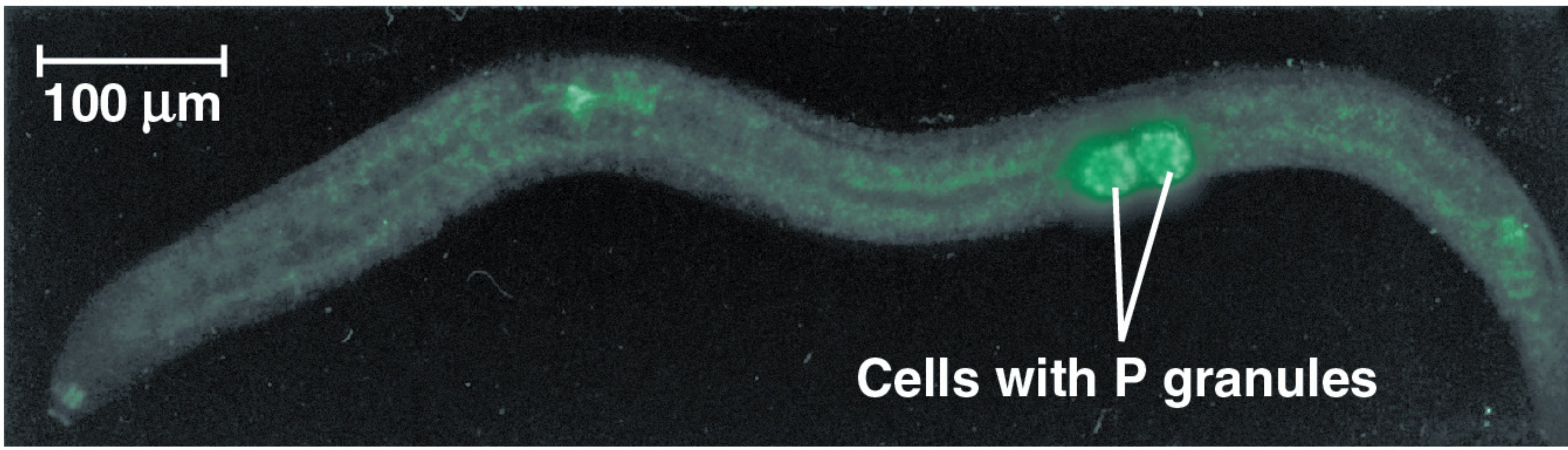


Time after fertilization (hours)
0
10
Zygote
First cell division
Nervous system, outer skin, muscula-ture
Musculature, gonads
Outer skin, nervous system
Germ line (future gametes)
Musculature
Hatching
Intestine
Intestine
Mouth
Eggs
Vulva
Anus
ANTERIOR
POSTERIOR
1.2 mm

Video: C. *elegans* Embryo Development (Time Lapse)

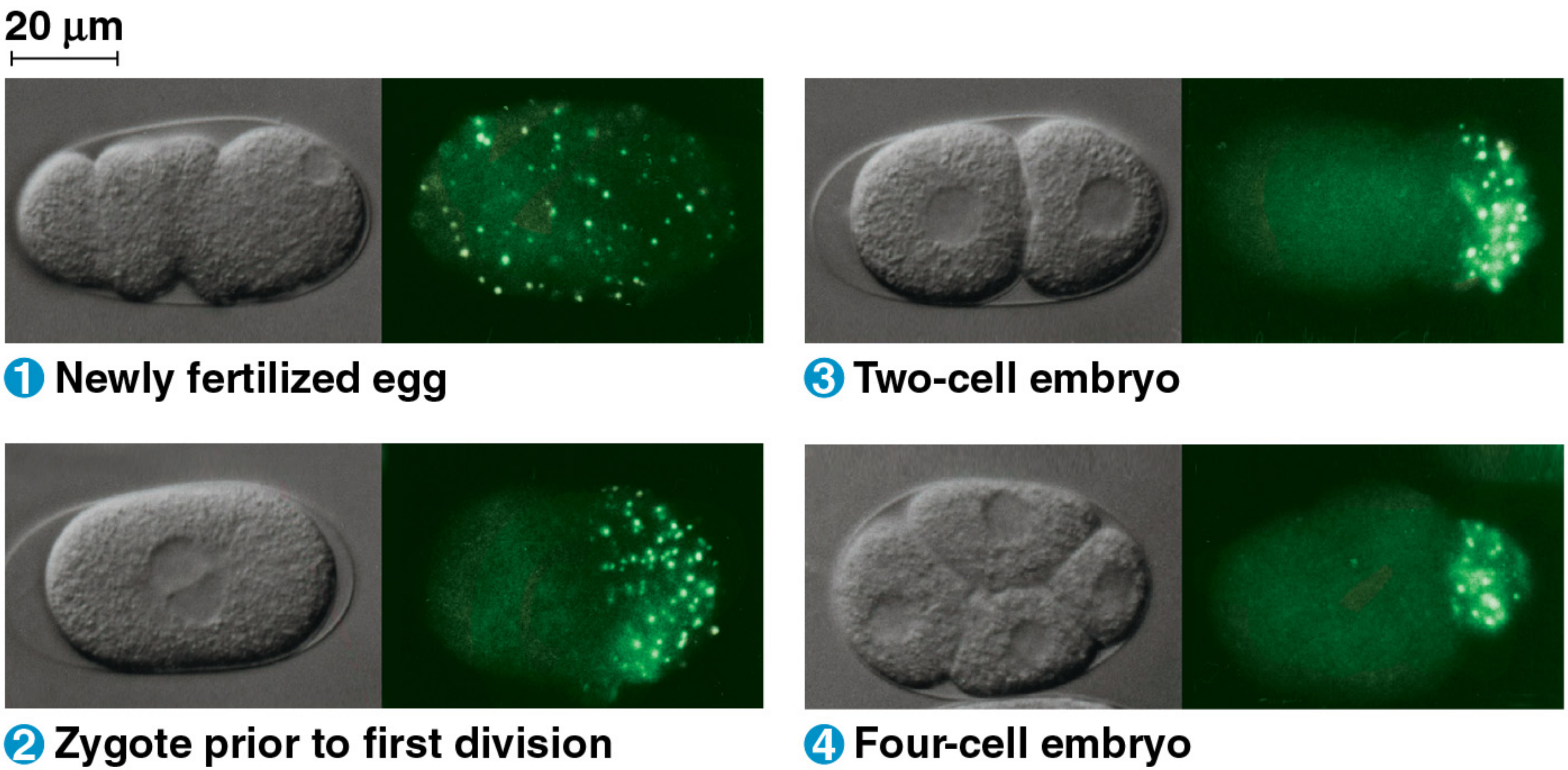
- Germ cells are the specialized cells that give rise to eggs or sperm
- Complexes of RNA and protein are involved in the specification of germ cell fate
- In *C. elegans*, such complexes are called P granules, persist throughout development, and can be detected in germ cells of the adult worm

Figure 47.20



- P granules are distributed throughout the newly fertilized egg and move to the posterior end before the first cleavage division
- With each subsequent cleavage, the P granules are partitioned into the posterior-most cells
- P granules act as cytoplasmic determinants, fixing germ cell fate at the earliest stage of development

Figure 47.21


20 µm
1 Newly fertilized egg
3 Two-cell embryo
2 Zygote prior to first division
4 Four-cell embryo

Axis Formation

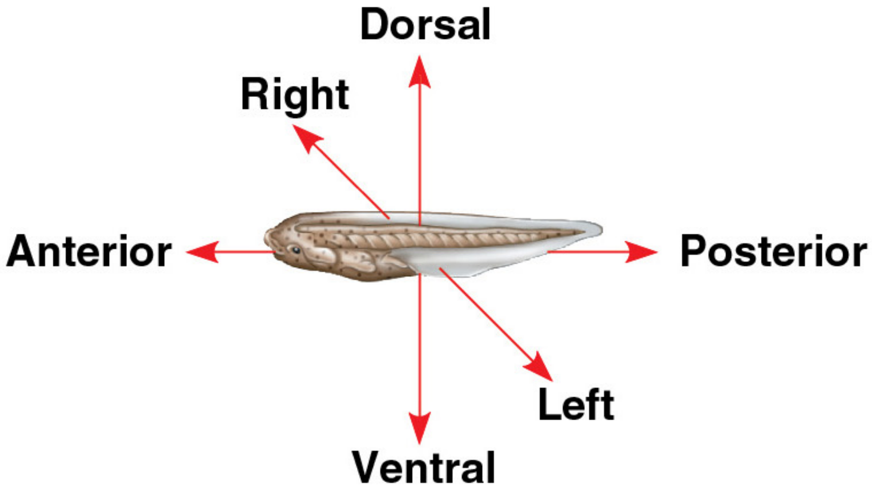
- A body plan with bilateral symmetry is found across a range of animals
- This body plan exhibits asymmetry across the dorsal-ventral and anterior-posterior axes
- The right-left axis is largely symmetrical

Axis Formation in the Frog

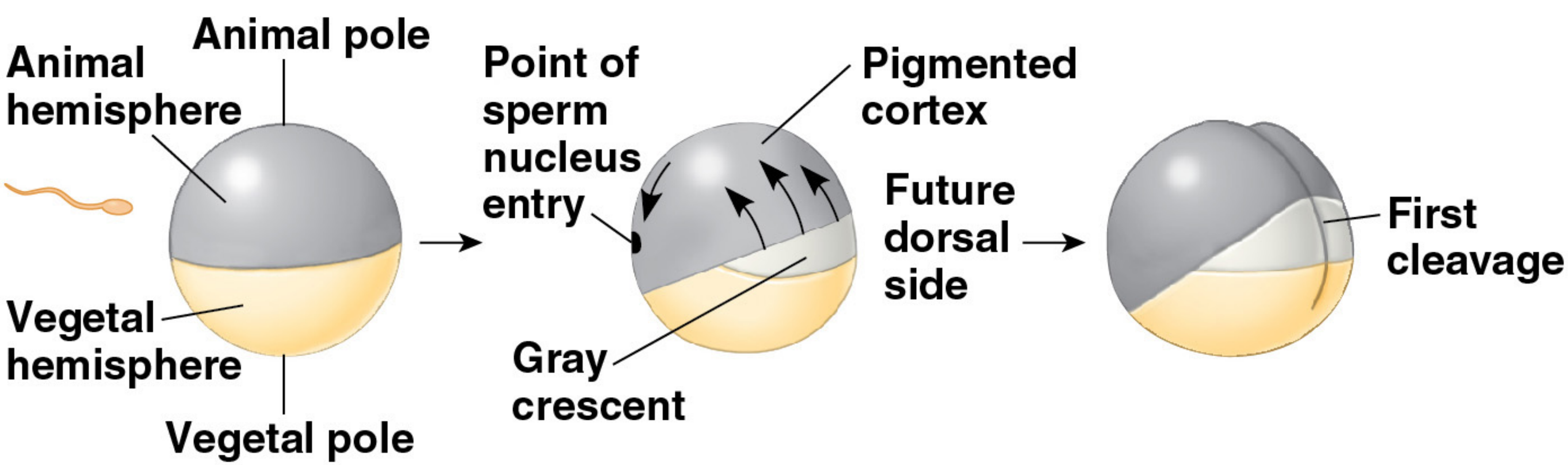
- The anterior-posterior axis of the frog embryo is determined during oogenesis
- The animal-vegetal asymmetry dictates where the anterior-posterior axis forms
- The dorsal-ventral axis is determined at random
- Wherever the sperm enters in the animal hemisphere determines the position of the dorsal-ventral axis

- Upon fusion of the egg and sperm, the egg surface rotates with respect to the inner cytoplasm
- This cortical rotation brings molecules from one portion of the vegetal cortex to interact with molecules in the inner cytoplasm of the animal hemisphere
- This leads to expression of dorsal- and ventral-specific genes

Figure 47.22



(a) The three axes of the fully developed embryo



(b) Establishing the axes

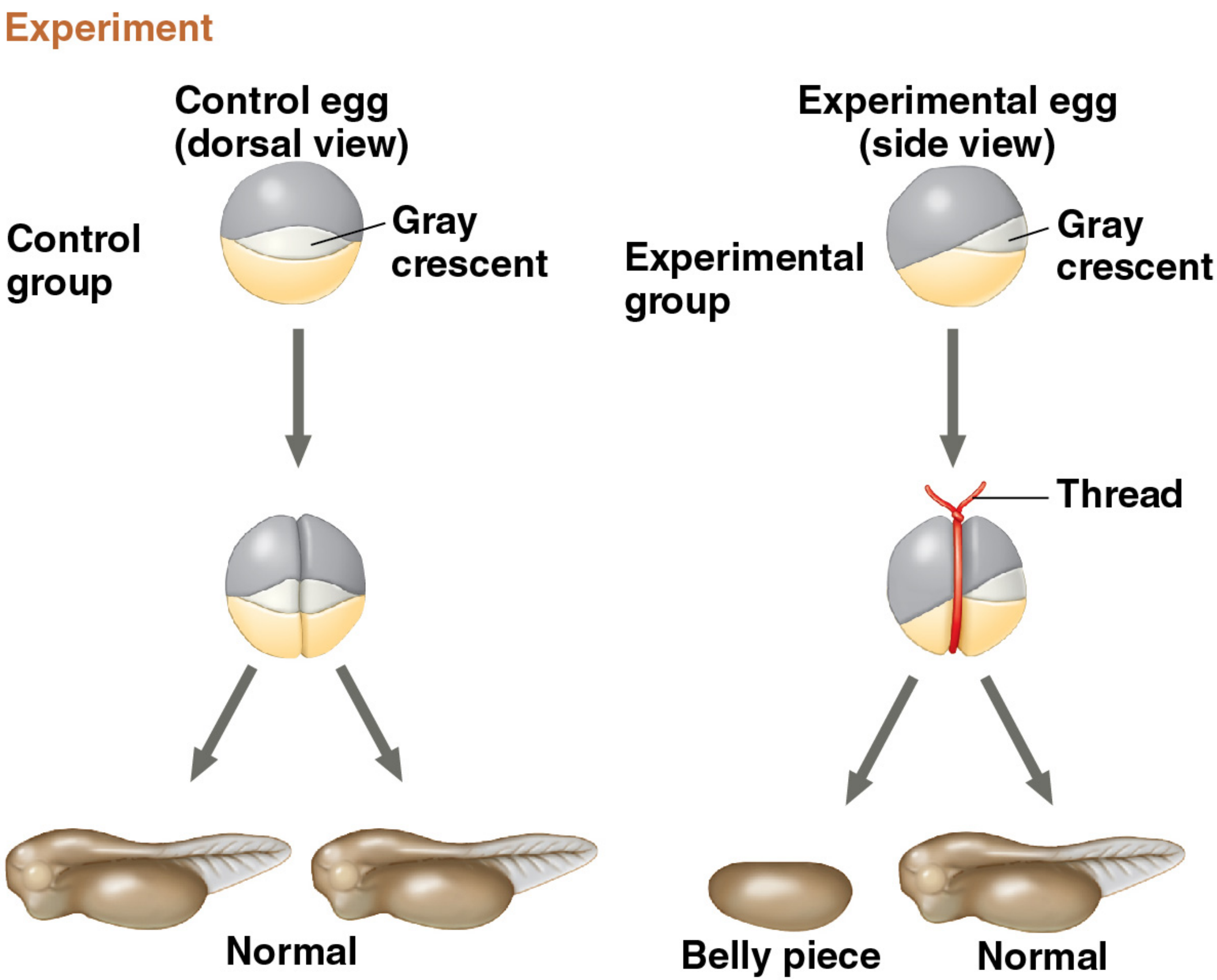
Axis Formation in Birds, Mammals, and Insects

- In chicks, gravity is involved in establishing the anterior-posterior axis
- Later, pH differences between the two sides of the blastoderm establish the dorsal-ventral axis
- In zebrafish, signals in the embryo gradually establish the anterior-posterior axis over the course of a day
- In insects, morphogen gradients establish the anterior-posterior and dorsal-ventral axes

Restricting Developmental Potential

- Hans Spemann performed experiments to determine a cell's developmental potential (range of structures to which it can give rise)
- The first two blastomeres of the frog embryo are **totipotent** (can develop into all the possible cell types)

Figure 47.23



Data from H. Spemann, *Embryonic Development and Induction*, Yale University Press, New Haven, CT (1938).

- In mammals, embryonic cells remain totipotent until the eight-cell stage, much longer than many other organisms
- This is likely due to the ability of the cells to regulate their fate in response to their environment
- Progressive restriction of developmental potential is a general feature of development in all animals
- In general, tissue-specific fates of cells are fixed by the late gastrula stage

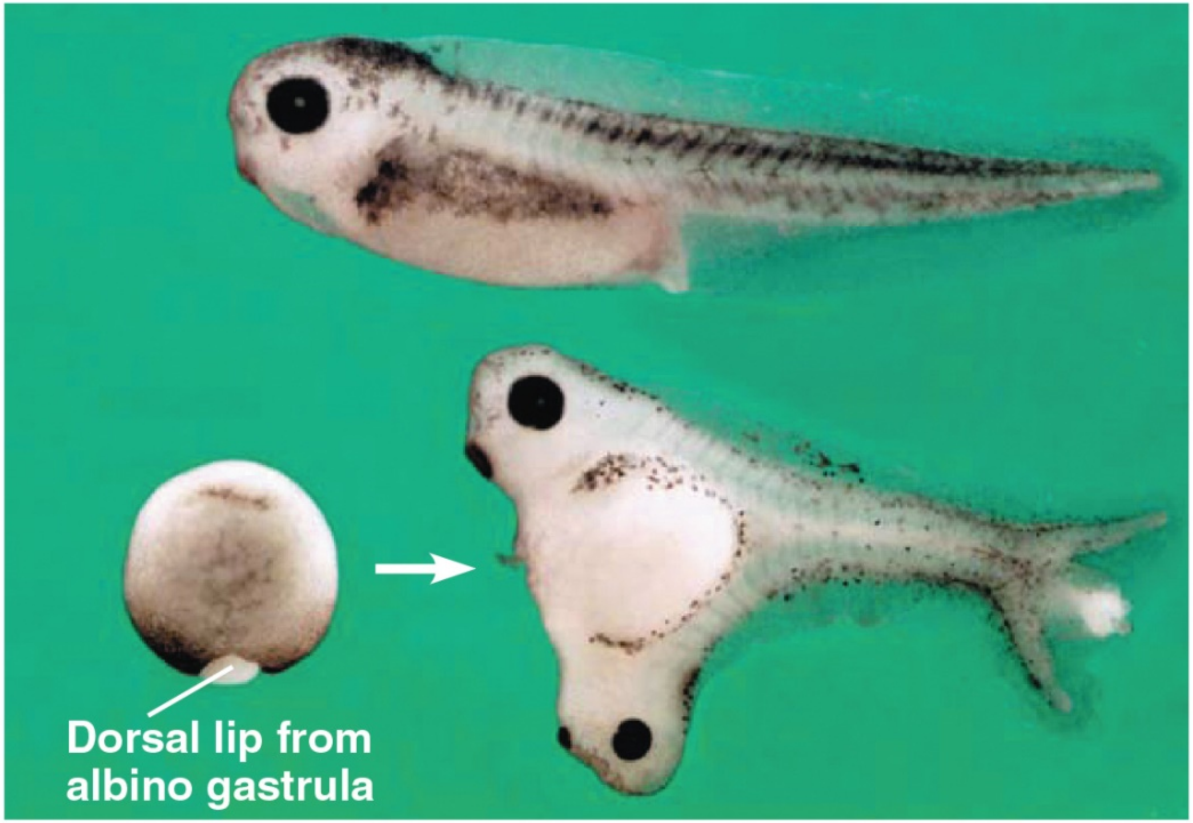
Cell Fate Determination and Pattern Formation by Inductive Signals

- As embryonic cells acquire distinct fates, they influence each other's fates by induction
- The response to an inductive signal is usually to switch on a set of genes that make the cells differentiate into a specific cell type

The "Organizer" of Spemann and Mangold

- Spemann and Mangold transplanted tissues between early gastrulas and found that the transplanted dorsal lip of the blastopore triggered a second gastrulation in the host
- The dorsal lip functions as an organizer of the embryo body plan, inducing changes in surrounding tissues to form the notochord, neural tube, and so on

Results



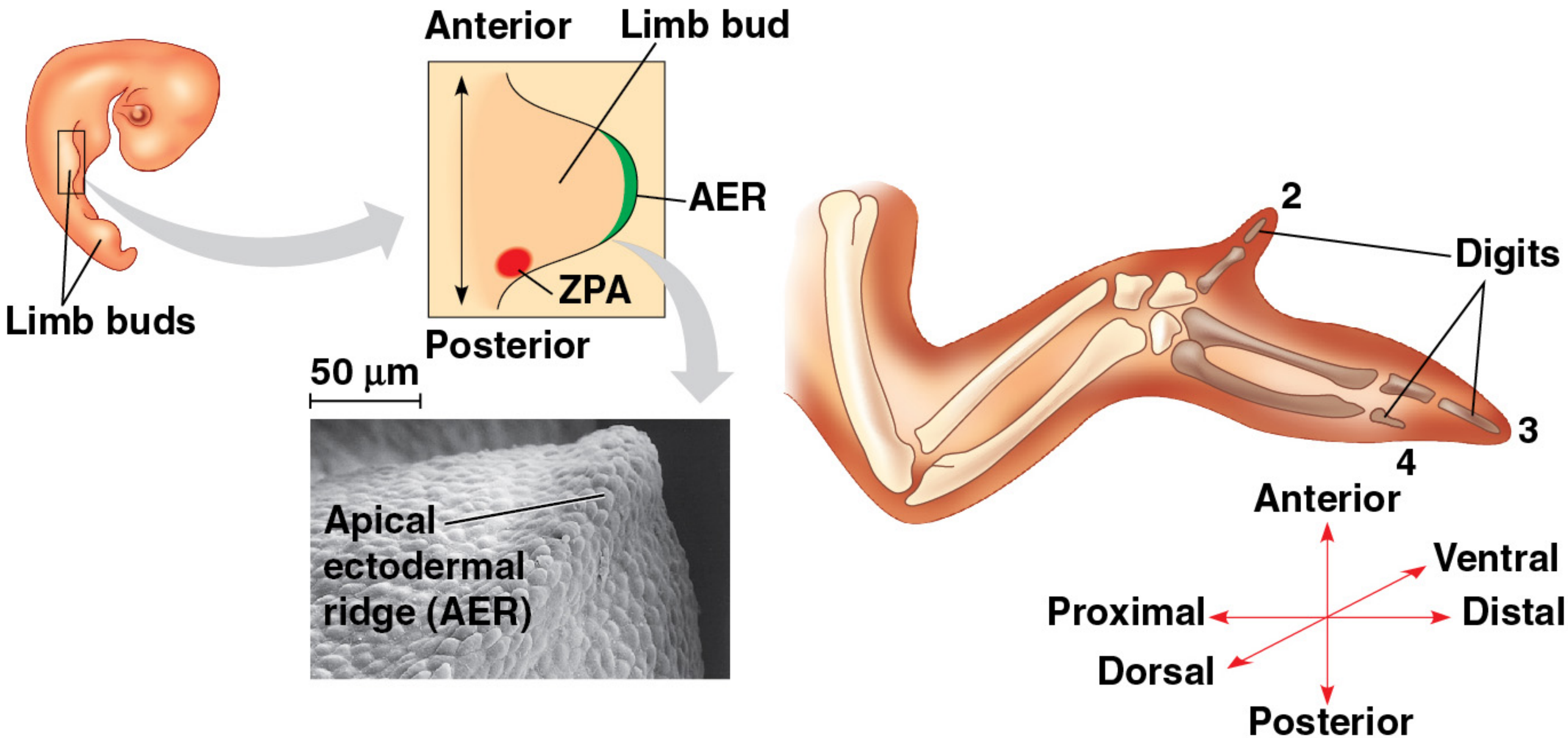
Data from H. Spemann and H. Mangold, Induction of embryonic primordia by implantation of organizers from a different species, Trans. V. Hamburger (1924). Reprinted in *International Journal of Developmental Biology* 45:13–38 (2001); and E. M. De Robertis and H. Kuroda, Dorsal-ventral patterning and neural induction in *Xenopus* embryos, *Annual Review of Cell and Developmental Biology* 20:285–308 (2004).

Formation of the Vertebrate Limb

- Inductive signals play a major role in **pattern formation**, the process governing the arrangement of tissues and organs
- The molecular cues that control pattern formation are called **positional information**
- This information tells a cell where it is with respect to the body axes
- It determines how the cell and its descendants respond to future molecular signals

- The wings and legs of chicks, like all vertebrate limbs, begin as bumps of tissue called limb buds
- The embryonic cells in a limb bud respond to positional information indicating location along three axes
  - Proximal-distal axis
  - Anterior-posterior axis
  - Dorsal-ventral axis

Figure 47.25



(a) Organizer regions

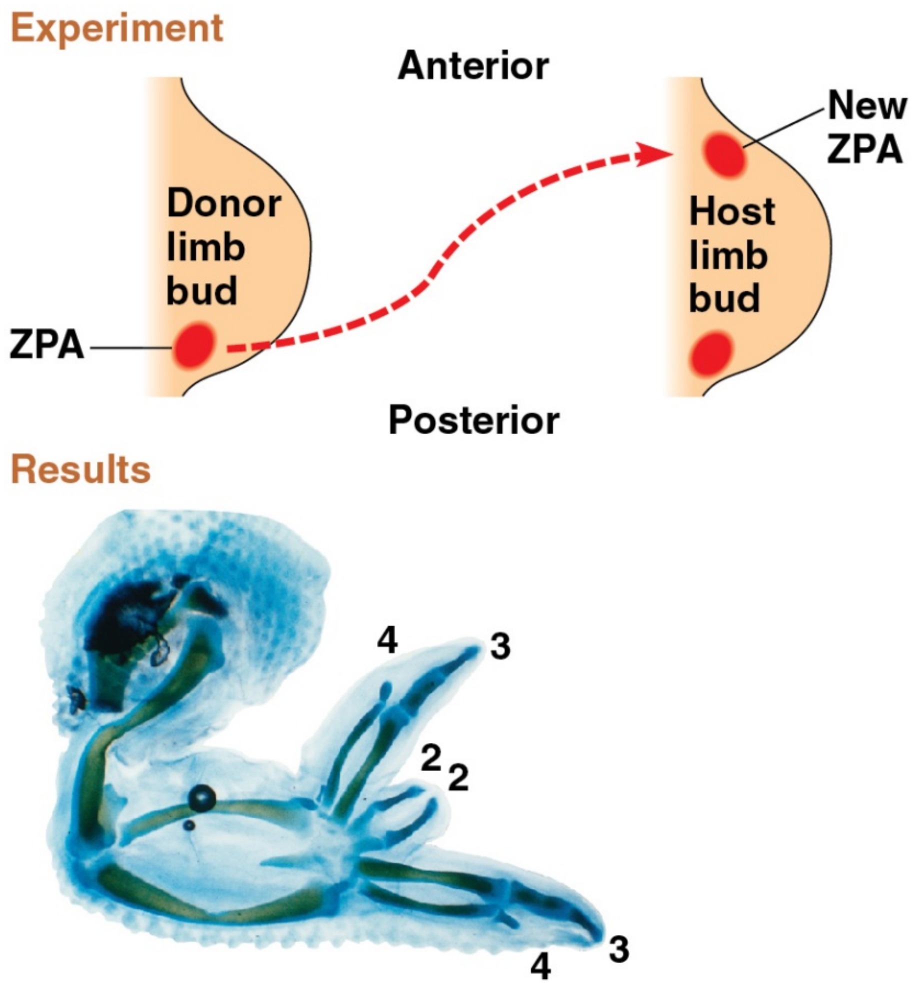
(b) Wing of chick embryo

- One limb bud–regulating region is the **apical ectodermal ridge (AER)**
- The AER is thickened ectoderm at the bud’s tip
- The AER secretes a protein signal called fibroblast growth factor (FGF) that promotes limb-bud outgrowth

- The second region is the **zone of polarizing activity (ZPA)**
- The ZPA is mesodermal tissue under the ectoderm where the posterior side of the bud is attached to the body
- The ZPA regulates development along the anterior-posterior axis of the limb
- Cells nearest the ZPA form posterior structures, and those furthest away form anterior structures

- Sonic hedgehog is a secreted signal produced by the ZPA
- Implanting cells that produce Sonic hedgehog into the anterior part of a developing limb bud results in a mirror-image limb
- Production of Sonic hedgehog in parts of the limb bud where it is not usually found results in extra toes

Figure 47.26



Data from L. S. Honig and D. Summerbell, Maps of strength of positional signaling activity in the developing chick wing bud, *Journal of Embryology and Experimental Morphology* 87:163–174 (1985).

- The production of a forelimb or a hindlimb depends on patterns of *Hox* gene expression
- BMP-4, FGF, hedgehog, and Hox proteins are examples of a larger set of molecules governing cell fates in animals

Cilia and Cell Fate

- Cilia are essential for proper specification of cell fate in the human embryo
- Monocilia (stationary primary cilia) jut from the surfaces of nearly all cells, one per cell
- Motile cilia are restricted to cells that propel fluid over their surfaces, such as epithelial cells of airways
- Motile cilia are also found on sperm, as flagella that propel movement

- Monocilia act as antennae on the cell surface, receiving signals from multiple signaling proteins, including Sonic hedgehog
- When monocilia are defective, signaling is disrupted

- Kartagener's syndrome is a set of medical conditions that often appear together
- These include immotile sperm, infections of nasal sinuses and bronchi, and situs inversus, a reversal of normal left-right asymmetry
- All of the associated conditions result from a defect that makes cilia immotile

Figure 47.27

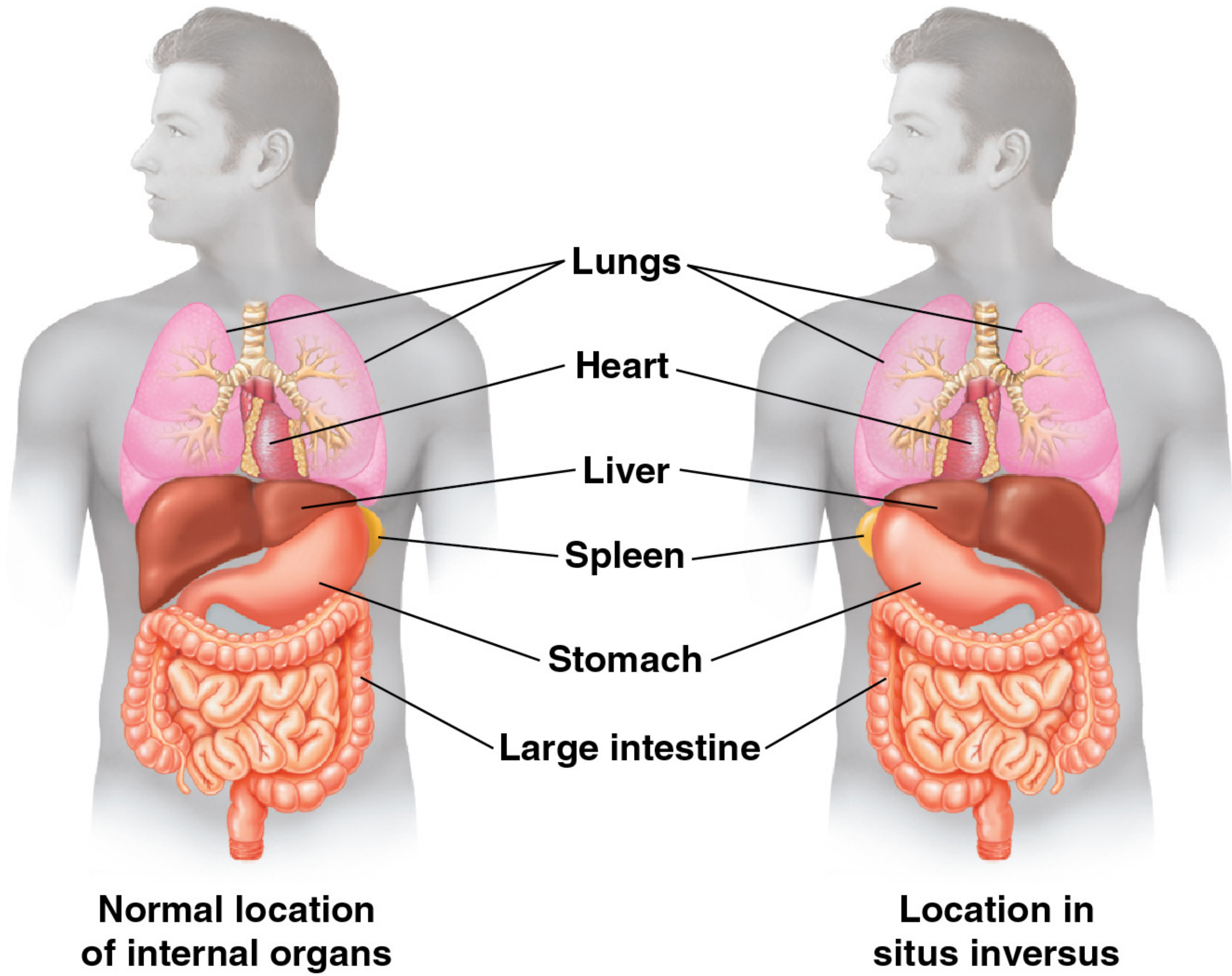
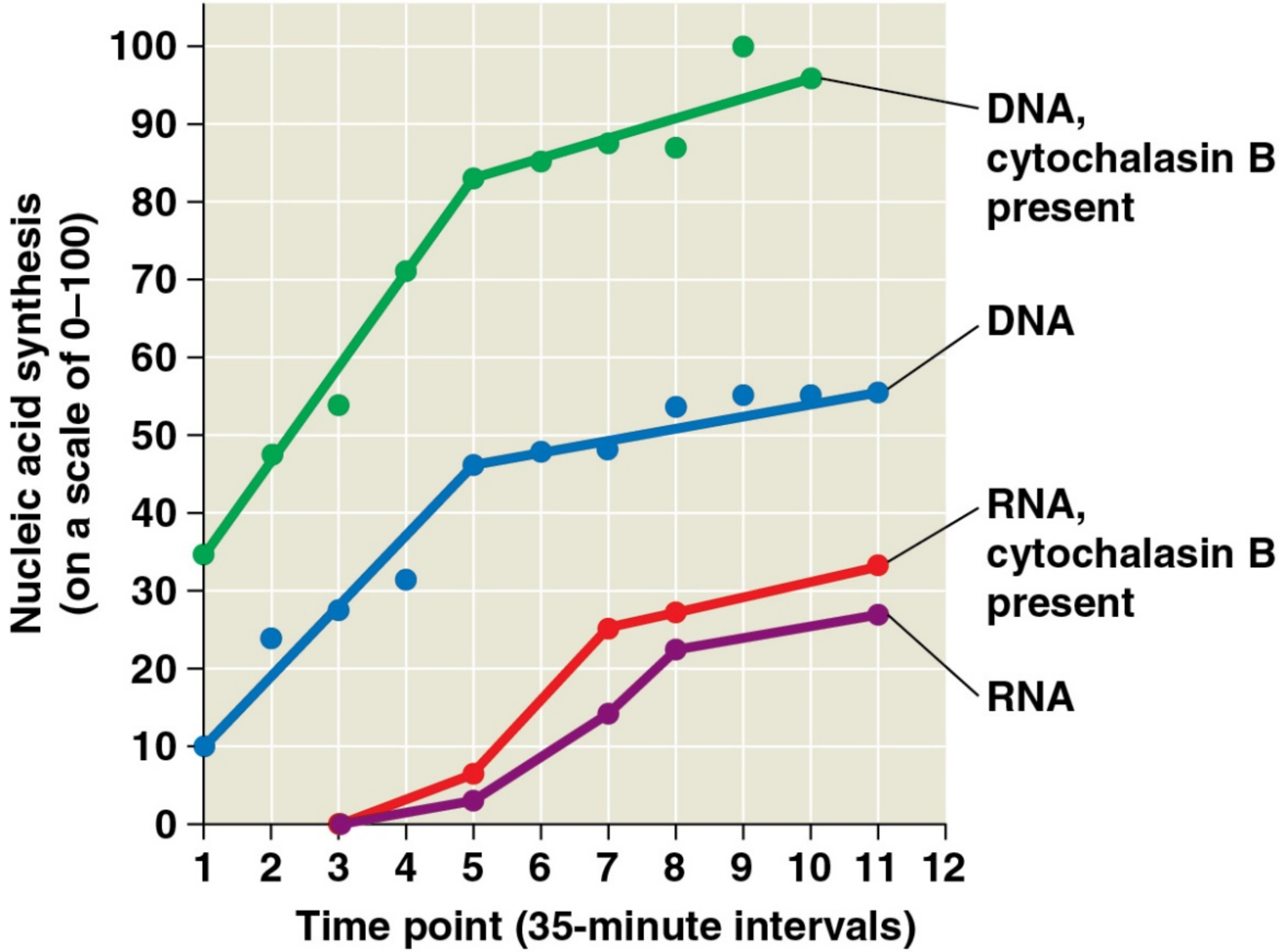

Lungs
Heart
Liver
Spleen
Stomach
Large intestine
Normal location of internal organs
Location in situs inversus

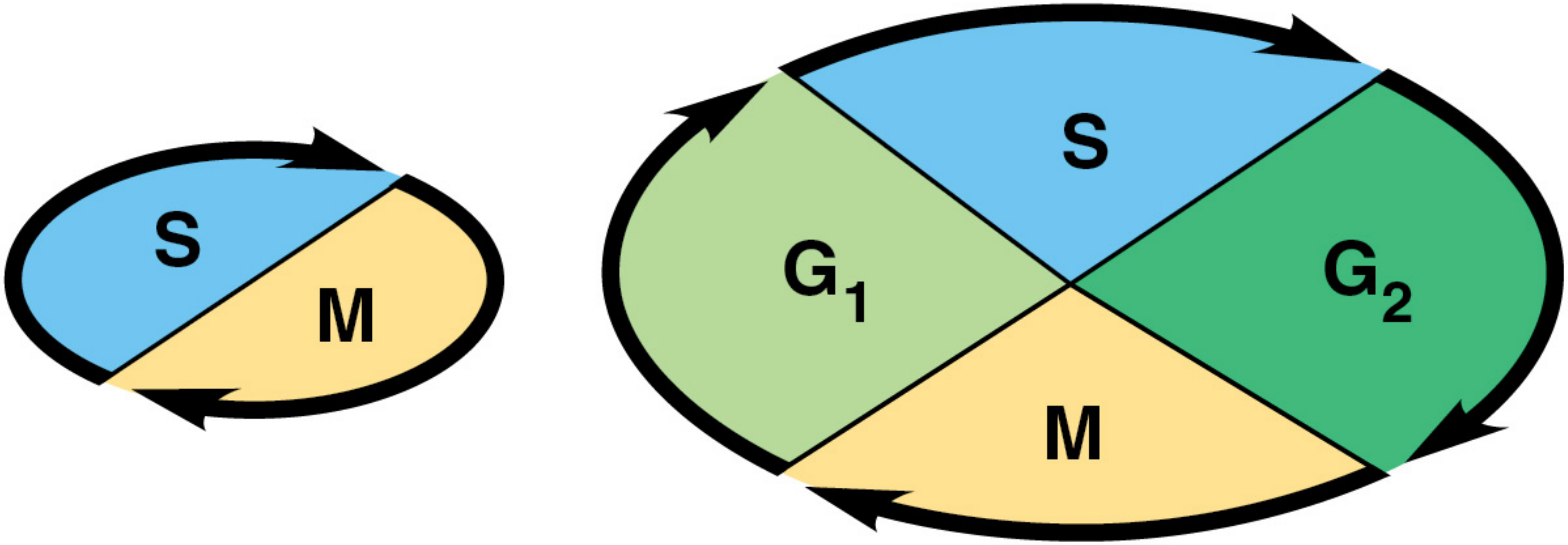
Figure 47.UN01

Data from the Experiments



Data from J. Newport and M. Kirschner, A major developmental transition in early Xenopus embryos: I. Characterization and timing of cellular changes at the midblastula stage, *Cell* 30:675–686 (1982).

Figure 47.UN02



Cell cycle during cleavage stage

Cell cycle after cleavage stage

Figure 47.UN03

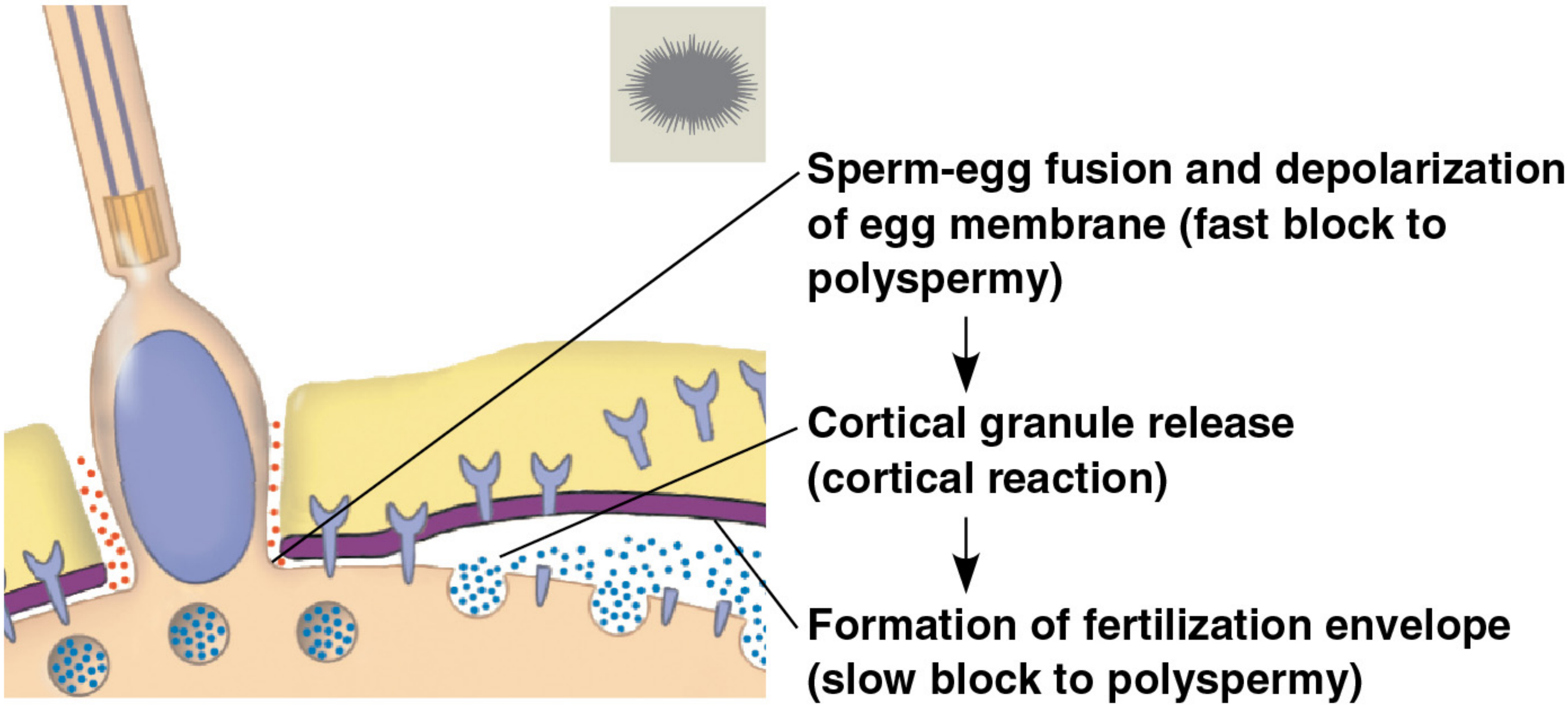


Figure 47.UN04

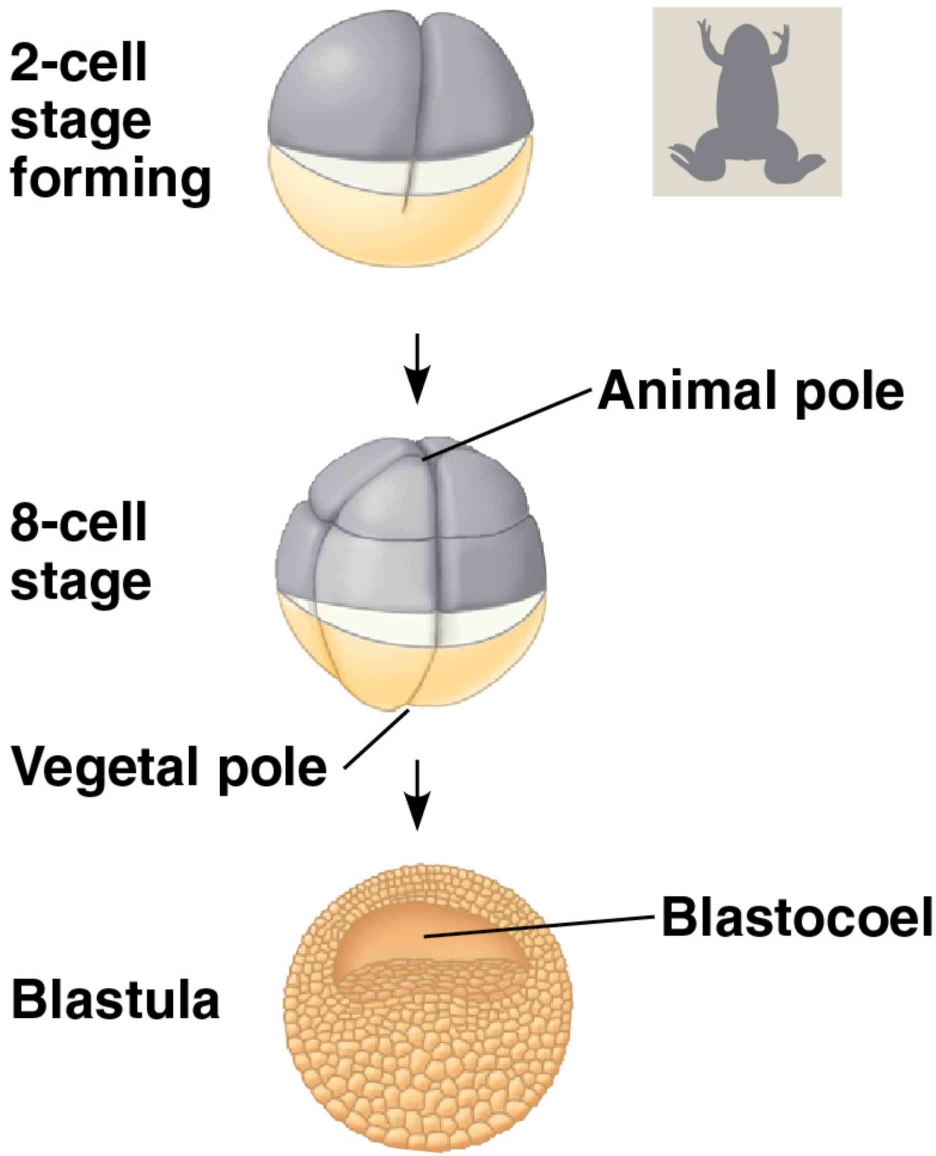


Figure 47.UN05

Figure 47.UN06

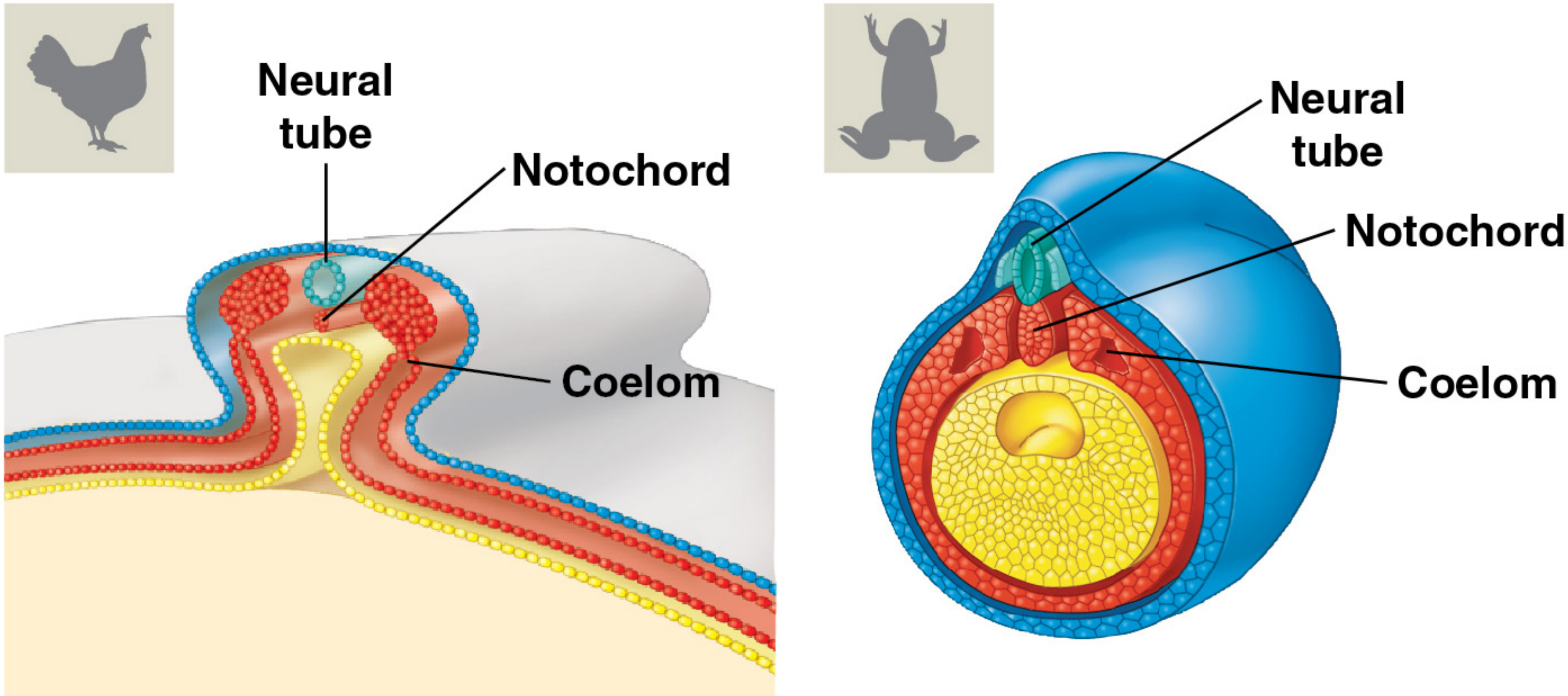


Figure 47.UN07

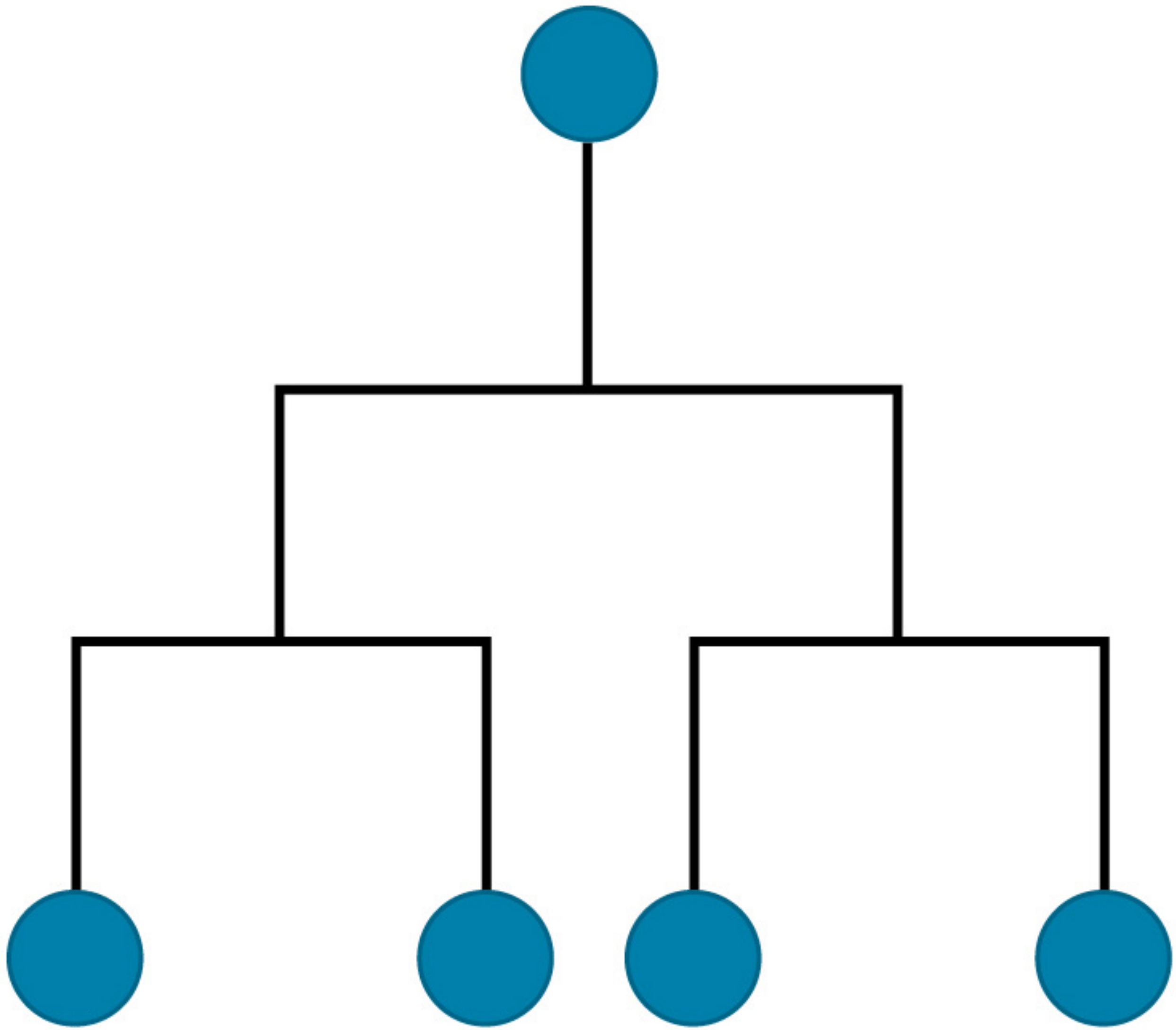


Figure 47.UN08