Let's quickly return to that silicon-based life form, since we didn't have time on Friday with the exam review.

- Since many silicon compounds are quite unstable in water environments without lots of sulfuric acid, and . . .
- Since oxygen based metabolism with silicon produces insoluble silicon dioxide except at extremely high temperatures, and since . . .
- Ammonia versus water gets around some of these problems, but oxidizes very rapidly.
- It is highly unlikely that there would be enough oxygen gas around, and even if there was, it would be present in an atmosphere of strong sulfuric acid vapor and/or ammonia vapor at very high temperatures! Therefore, no, there's not much of a chance that a silicon-based life form and us could share the same atmosphere. One of us would need a very sophisticated life support suit.
On to ... the cell cycle and mitosis

Now that we've seen how DNA replicates, let's put it in context — within the cell.
Cells divide and cells die.

Each of an organism's cells (except red blood cells) retains the genetic information present in the fertilized egg (or parental cell for asexual reproduction). That is — every cell in an organism has all the same DNA!

Every cell in an organism results from countless rounds of cell division.

Cells death also happens — from outside causes, as well as in predictable, internal ways. This is known as apoptosis (or programmed cell death).

Cell death is a normal part of development; a necessary part of life.

Cell division and cell death must be in balance, or the organism dies!
Chromosome duplication

* An organism’s entire genome must be duplicated before cell division can occur.

* As we’ve seen, in Bacterial and Archaeal cells, the genome is usually a single circular DNA molecule. However, . . .

* In eukaryotic cells, the genome is divided and packaged among multiple chromosomes, all housed in the nucleus.

* For example, humans have 46 (23 pair), chickens 78 (39 pair, including ‘microchromosomes’), rice 24 (12 pair), and zebrafish 50 (25 pairs) chromosomes.
Eukaryotic chromosomes

* Stretched end to end and unpackaged all of the DNA in a human cell would be over two yards long. That’s a lot of DNA!

* Chromatin — DNA plus histone packaging and other associated proteins.

* Nucleosomes — stretch of DNA wrapped around histones (‘beads on a string’).

* Chromatin is barely visible when the cell is not dividing and the chromosomes have not condensed. Therefore, much of the time . . .

* DNA is loosely packed and accessible for cellular activities like making RNA and more DNA.
What's a nucleosome?

One more time: http://molbio.info.nih.gov/cgi-bin/moldraw?1EQZ
And in preparation for cell division, it all packages up into chromosomes.

- DNA condenses into visible chromosomes before cell division.
- Chromatid – one of two identical copies of a replicated chromosome.
- Sister chromatids – pair with identical DNA sequences.
- Centromere – point of attachment.
Know the vocabulary.

Really! Know this stuff.

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromatin</td>
<td>Nucleic acids and associated proteins in the nucleus</td>
</tr>
<tr>
<td>Chromosome</td>
<td>A discrete, continuous molecule of DNA wrapped around protein. Eukaryotic cells contain multiple linear chromosomes, whereas prokaryotic cells each contain one circular chromosome.</td>
</tr>
<tr>
<td>Chromatid</td>
<td>One of two identical attached copies of a replicated chromosome</td>
</tr>
<tr>
<td>Centromere</td>
<td>A small part of a chromosome that attaches sister chromatids to each other</td>
</tr>
</tbody>
</table>
Karyotype

Most human cells have 46 chromosomes, with...

- 23 from each parent:
  - 22 Autosomes, plus a pair of sex ones.

- Diploid – two full sets of genetic information.
  - Pair members look alike (but are not genetically identical).
  - Except the sex chromosomes, X and Y.
  - All produced by mitosis.

However, sperm and egg cells (called gametes) are haploid.

- They only have 23 chromosomes...
- And are produced by meiosis in germ cells in the testes and ovaries.
The Cell Cycle...

Includes all the events between one cell division and the next.

Two major stages:
- Interphase - cell not dividing but it is very active.
- Cell division - mitosis and cytokinesis.
No stage is discrete; they all blend from one to the next.

http://www.valdosta.edu/~stthompson/animations/Chapter08/the_cell_cycle.swf
And an animation . . .

Most eukaryotic cells follow a process of growth and division called the cell cycle. These events include a growth stage, mitosis or nuclear division and cytokinesis or division of the cytoplasm.

http://highered.mcgraw-hill.com/sites/0072495855/student_view0/chapter2/animation__how_the_cell_cycle_works.html
Interphase . . .

* Is a very active time in the cell cycle.

* $G_1$ (gap 1) — cell grows and carries out basic functions. Various . . .

* Signals tell the cell to divide, to stop for repair of its DNA, to die, or to enter $G_0$, a quiescent stage.

* $S$ (synthesis) — the genetic material (DNA) replicates!

* $G_2$ (gap 2) — the cell prepares to divide and chromosomes begin to condense.
Mitosis . . .

* Overall, it separates the replicated genetic material from the S phase evenly between the two daughter cells. A pretty amazing thing.

* The mitotic spindle (cytoskeleton) pulls each half to each new cell.

* Centrosomes organize the mitotic spindle in many animal cells.

* Kinetochore attaches the chromosomes to the spindle.
Again, the vocabulary does matter. These really are terms you need to know. OK, kinetochore and centrosome’s not that big of a deal, but everything else is!

### Table 8.2 Miniglossary of Cell Division Terms

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diploid</td>
<td>Containing two sets of chromosomes, one from each parent; somatic cells are diploid</td>
</tr>
<tr>
<td>Haploid</td>
<td>Containing one set of chromosomes; gametes are haploid</td>
</tr>
<tr>
<td>Meiosis</td>
<td>Division of a diploid nucleus into four genetically different haploid nuclei</td>
</tr>
<tr>
<td>Mitosis</td>
<td>Division of a nucleus into two identical nuclei</td>
</tr>
<tr>
<td>Cytokinesis</td>
<td>Distribution of cytoplasm to daughter cells following division of a cell’s nucleus</td>
</tr>
<tr>
<td>Mitotic spindle</td>
<td>Part of the cytoskeleton that moves chromosomes during mitosis</td>
</tr>
<tr>
<td>Kinetochore</td>
<td>Part of the centromere to which the mitotic spindle attaches</td>
</tr>
<tr>
<td>Centrosome</td>
<td>Structure that organizes the mitotic spindle; it consists of tubulin and other proteins, and sometimes centrioles</td>
</tr>
</tbody>
</table>
Here are the parts...
And an animation...

The steps (but, remember, they’re really not discrete).

* Prophase – the chromosomes condense, the mitotic spindle begins to form.
* Prometaphase – kinetochores grow on centromeres, the nuclear envelope breaks down (often not named).
* Metaphase – the chromosomes line up on the mitotic spindle along the “equator” of the cell.
* Anaphase – the centromeres split, one chromatid of each pair is pulled to the opposite pole.
* Telophase – the mitotic spindle disassembles, the chromosomes begin to unwind, and the nuclear envelope reforms.

And the silly way I memorized it way back when: “Prophase meta Anaphase, and called her up on the Telophase, and said ‘Hey, let’s Interphase!’”
And in more detail, check this out . . .
Continued...

ANAPHASE
Sister chromatids separate and move to opposite poles of cell.

TELOPHASE
Nuclear membranes assemble around two daughter nuclei. Chromosomes decondense. Spindle disappears.

CYTOKINESIS
Division of the cytoplasm into two cells. Cells resume normal functions or enter another division cycle.

G₁, early interphase of daughter cells

Top all: © Ed Reschke; bottom all: © Dr Alexey Khodjakov/Photo Researchers, Inc.
And cytokinesis is . . .

- **Animal cells** — a cleavage furrow results from a contractile ring.
- **Plant cells** construct a brand new cell wall each time.
Let’s review this with another animation.

http://www.valdosta.edu/~stthompson/animations/Chapter08/mitosis.swf

When metaphase is completed, anaphase begins. The sister chromatids separate and each chromatid is now linked to only one pole via a kinetochore microtubule.
Cell cycle regulation is vital!

* Some cells divide more or less constantly, e.g. the stem cells in your bone marrow.
* But, cells need to ‘know’ whether to divide or not. That’s not an easy decision . . .
* The chemical signals to divide usually come from outside a particular cell. Often it’s . . .
* Growth factors — proteins that stimulate cell division, often from outside that cell.
* Checkpoints — ensure that the cell does not enter the next stage until the previous stage is complete. But how . . .?
Here's some of the most important checkpoints in the cell cycle.

- **S phase checkpoint**
  - Is DNA replicating correctly?

- **G₂ checkpoint**
  - Has all DNA replicated?
  - Can damaged DNA be repaired?
  - Is spindle-making machinery in place?

- **G₁ checkpoint**
  - Is DNA damaged?

- **Metaphase checkpoint**
  - Is spindle built?
  - Do chromosomes attach to spindle?
  - Are chromosomes aligned down equator?
And in animation . . .

The process of cell growth and division in eukaryotes is called the cell cycle. This cycle is divided into phases based on what is happening in the cell at a given time. A cell grows during the G1 phase.

http://www.valdosta.edu/~stthompson/animations/Chapter08/control_cell_cycle.swf
Telomeres – a cellular ‘clock’

* Located at tips of eukaryotic chromosomes.
* They lose nucleotides and become shorter with each cell division.
* Cell division stops after about 50 cell divisions due to telomere loss.
* Some cell types express telomerase; it adds DNA to the telomeres, which...
* Allows cells to go beyond 50 divisions.
* It’s present in some normal cells, e.g. sperm germ cells, intestinal lining cells, plant meristem tissue, and in most cancer cells.
Here's what happens:

For a recent story related to this see: http://abcnews.go.com/Health/Alzheimers/aging-reversed-mice/story?id=12269125

a. From L. Chong “A Human Telomeric Protein”, Science, 270: 1663-1667, © American Association for the Advancement of Science, Photo courtesy Dr. Tita De Lange
Cancer!

* Has affected almost everybody's lives.
* Tumor — an abnormal mass of tissue.
* It forms when the body somehow loses control of the balance between cell division and cell death.
* Benign tumor — is usually slow-growing and harmless.
* Malignant tumor — invades other tissues (metastasizes) — cancer.
Cancer cells are way different.

They:

* Are not normal cells; they . . .
* Look different; and are . . .
* Essentially immortal; and . . .
* May produce their own signals to divide.
* They lack contact inhibition; and . . .
* May not undergo apoptosis when damaged; and . . .
* Send signals to stimulate the growth of blood vessels.
Normal marrow cells on the right versus leukemia cells on the left.
Causes of cancer...

- It is NEVER contagious, though some viruses can cause cancer, e.g. HPV (human papilloma virus).
- Oncogenes – are abnormal variants of genes that normally control cell division. You may inherit them, or they may mutate within your body due to carcinogens.
  - They may accelerate the cell cycle and cause cancer.
- Tumor suppressor genes – encode proteins that normally block cancer development, e.g. BRCA1 & 2 (breast cancer 1 & 2).
  - They promote normal cell death or prevent cell division.
- Inactivation, deletion, or mutation can cause loss of function. Again, this can be inherited or a somatic mutation.
- Harmful chemicals, radiation, and viruses can all alter DNA.
- There are many risk factors, such as poor diet, lack of exercise, sun overexposure, and smoking, can all increase the chance of getting cancer.
Here's a schematic of two genetic pathways towards cancer.

And a pretty nice video overview from the M.D. Anderson Cancer Center:
http://www.youtube.com/watch?v=CC4WgtGheac

Oncogene DNA sequence mutates.
The altered DNA sequence results in production of abnormal and excessive proteins, and accelerates the cell cycle.
Accelerated replication continues.

Tumor suppressor gene DNA sequence mutates.
If both copies of the tumor suppressor gene are damaged, production of growth-inhibiting proteins stops.
Left unchecked, the cancer cell survives and replicates.
Cancer treatments . . .

* Include:
  * Selective surgical tumor removal.
  * Chemotherapy and radiation, which target ALL rapidly dividing cells – both cancerous and healthy.
  * The death of healthy cells causes all the side effects. And they are nasty!
  * New more targeted drugs home in on the receptors for growth factors.
  * Early detection is the absolute key to successful treatment!
Has two main functions:
- It eliminates excess cells to carve out functional structures like fingers and toes.
- And it weeds out cells that might harm the organism.

Apoptosis must be overcome for mitosis to occur.

For example, many critters lose the webbing between their toes, others don’t.
‘Killer’ enzymes dismantle the cells destined for death.

* Caspases – are apoptosis specific enzymes. And are...

* Triggered when a “death receptor” protein receives a signal. This...

* Cuts apart the cell’s proteins and destroys the cell.

1. Death receptor on doomed cell binds signal molecule. Caspases are activated within.

2. Caspases destroy proteins and other cell components.

3. Immune system cell attacks and engulfs cell remnants. Cell components are degraded.
That's it for the cell cycle and mitosis.

We'll split the next lecture into two parts as well. They'll cover the how's, what's, and why's of sex — why it evolved at all, what it takes to make nuclei with half the chromosomes of most, and how those nuclei are packaged into special sex cells.