

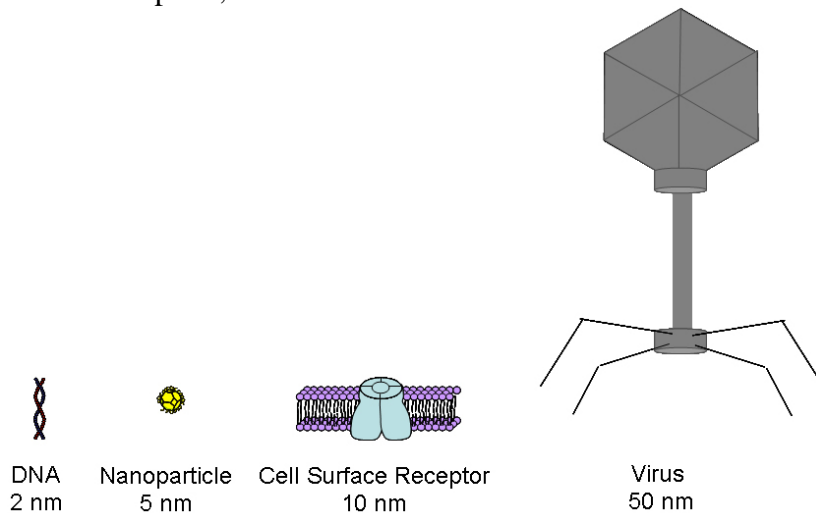
# GOLD NANOPARTICLE BIOSENSORS

Jessica Winter

Rev. 3

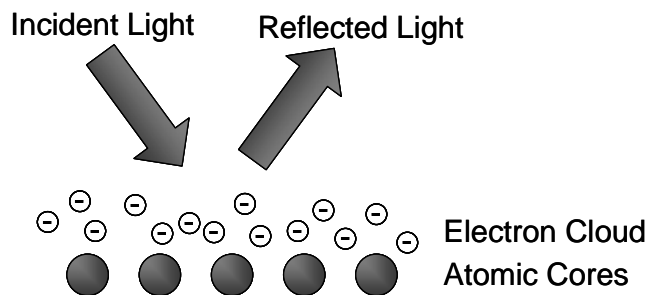
05/23/2007

Gold nanoparticles typically have dimensions ranging from 1-100 nm. From the figure below it is clear that these dimensions are similar to many cellular objects, including DNA, cell surface receptors, and viruses.



*Figure 1: Comparison of nanoparticle size to common biological objects. Reprinted with author's permission (JO Winter) from Tissue, Cell, and Organ Engineering, Ed. Challa Kumar, Wiley VHC, Weinheim, Germany: 2006.*

In addition, gold nanoparticles display many interesting electrical and optical properties. You may be aware that metals (like the gold in the nanoparticles) are good conductors, which is why they are used in electronics and wiring. Metals are good conductors because their electrons are not bound to individual atoms instead forming a “cloud” around the atomic cores (Figure 2). This cloud of electrons is mobile allowing metal to transport charge (electrons) easily. Also, experience tells us that metals are shiny. This is because light is reflected off their surfaces back to the eye. The reason for this reflection has to do with the electron cloud that surrounds metals. Photons (individual units) of light cannot be absorbed by the atomic cores because they are blocked by the electron cloud. Consequently, photons are reflected back to the eye producing the sheen associated with metals.



*Figure 2: Electron cloud in metals. Electrons in metals are not strongly attracted to atomic cores. Light shined at metals is reflected because it is blocked by the electron cloud.*

However, we also know from quantum mechanics that electrons can behave as either a wave or a particle. If we imagine electrons in the electron cloud as a wave with a certain energy value, we can envision a situation where it is possible for light of the same wavelength to be absorbed by the electron cloud, producing resonance. This is similar to what happens on stringed instruments when a vibration occurs that matched the natural length of the string or one of its harmonics.

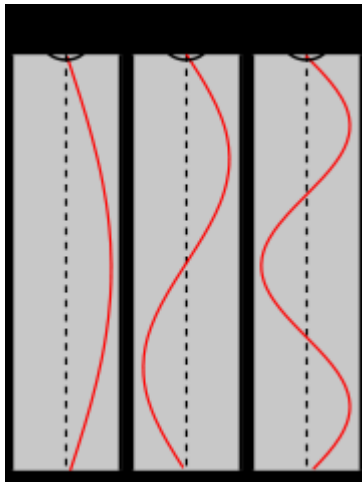


Figure 3: Resonance in stringed instruments. Resonance occurs when a string is vibrated along an even interval. When played, the instrument will have a distinctive sound at resonant intervals.

Figure from: [http://en.wikipedia.org/wiki/Acoustic\\_resonance](http://en.wikipedia.org/wiki/Acoustic_resonance)

When a metal absorbs light of a resonant wavelength it causes the electron cloud to vibrate, dissipating the energy. This process usually occurs at the surface of a material (as metals are not usually transparent to light) and is therefore called **surface plasmon resonance**. Plasmons are the name for the oscillations of the electron cloud.

What this means in real terms is that there are certain wavelengths for metal where photons are not reflected, but instead are absorbed and converted into surface plasmon resonance (electron cloud vibrations). For “normal” metals, like gold jewelry, these wavelengths occur in the infrared portion of the spectrum (Figure 4, wavelength > 800 nm). These wavelengths fall outside the visible range that can be seen with the eye, and the metal therefore appears to reflect most light and is shiny.

But nanoparticles have extremely high proportions of their substance at their surfaces. If you were to compare the proportion of surface in a nanoparticle to a gold stud earring you would find that it has two million times more surface area compared to its volume than the earring. More surface area means more potential for surface plasmon resonance.

Nanoparticles can experience surface plasmon resonance in the visible portion of the spectrum. This means

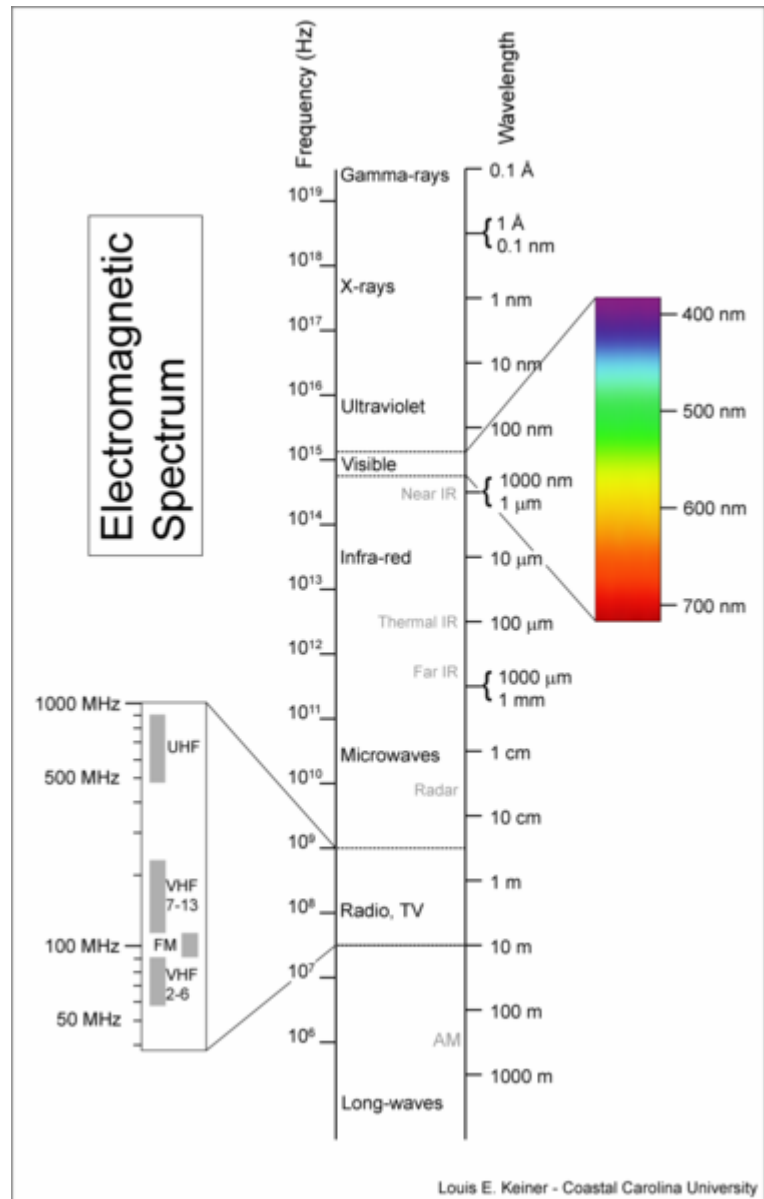


Figure 4: Electromagnetic Spectrum.

Figure from: <http://en.wikipedia.org/wiki/Image:Electromagnetic-Spectrum.png>

that a certain portion of visible wavelengths will be absorbed, while another portion will be reflected. The portion reflected will lend the material a certain color. Small nanoparticles absorb light in the blue-green portion of the spectrum (~400-500 nm) while red light (~700 nm) is reflected, yielding a deep red color (Figure 5, left). As particle size increases, the wavelength of surface plasmon resonance related absorption shifts to longer, redder wavelengths. This means that red light is now adsorbed, and bluer light is reflected, yielding particles with a pale blue or purple color (Figure 5, center). As particle size continues to increase toward the bulk limit, surface plasmon resonance wavelengths move into the IR portion of the spectrum and most visible wavelengths are reflected. This gives the nanoparticles clear or translucent color (Figure 5, right).



*Figure 5: Gold Nanoparticles of different sizes. As gold nanoparticles increase in size they change from red to blue (from left, 30 nm, 60 nm, and 90 nm gold nanoparticles.)*

These properties have been used to create biosensors. Individual small gold nanoparticles appear red; however, when particles aggregate together the plasmon resonances can combine. The particle will appear as one large particle rather than two separate ones. Plasmon resonance associated-absorption wavelengths will shift from blue to red, and reflected light will shift from red to blue. Therefore particle color will change from red to blue on aggregation.

The most familiar example of nanoparticles in sensing is the home pregnancy test. Certain brands use gold nanoparticle aggregation to create a colorimetric response. Nanoparticles (< 50 nm) are bound to antibodies complementary to a hormone produced by pregnant women (Figure 6). Latex microspheres are also bound to antibodies for the hormone. When the stick is submerged in urine flow, if the hormone is present it will bind to the microspheres (~ 500  $\mu$ m) and nanoparticles causing aggregates to form. The solution then passes through a paper filter. If the pregnancy hormone is present, the aggregates will be trapped by the filter producing a colored product. If the pregnancy hormone is not detected, the nanoparticles will pass through the filter because of their small size.

Although this test does not rely explicitly on plasmon resonance to create the signal, the deep red color of the nanoparticles employed results directly from this feature. Other tests that do take advantage of surface plasmon resonance changes include tests for DNA detection. For example, one kind of DNA test looks for certain bases. In this test, nanoparticles start out as large aggregates that are blue. If the complementary DNA base is present, the nanoparticles will bind to that base instead of each other and the aggregates will dissolve producing a deep red color (Figure 7). This can be followed using an instrument called a spectrophotometer that measures

light absorption at different wavelengths. The graph in Figure 7 tells us that we can detect the color changes associated with DNA binding in about 2 minutes, making for a rapid assay.

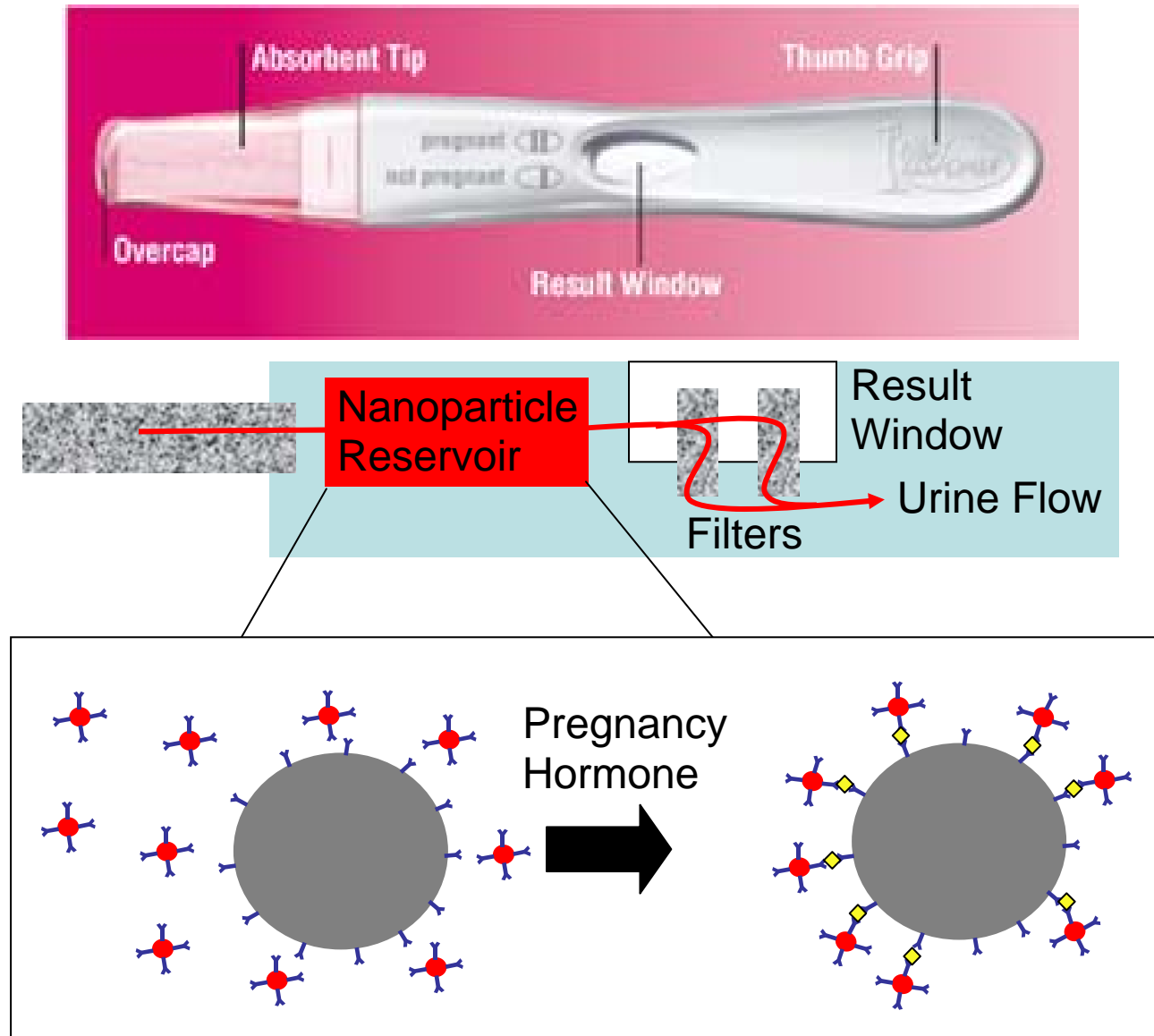


Figure 6: (Top) Photo of First Response <sup>®</sup> Early Pregnancy Test (Carter-Wallace, <http://www.firstresponse.com/products/earlyResultInsert.asp#use>) (Middle) Conceptual diagram of home pregnancy test. Urine passes from the flow stick to a central reservoir containing gold nanoparticles and latex microparticles. If pregnancy hormone is present particles aggregate and are prevented from passing through a downstream filter. This produces a red signal in the viewing window. (Bottom) Nano- and micro- particles are modified with antibodies (blue) that bind to pregnancy hormone. If pregnancy hormone (yellow) is present in urine, particles will aggregate and are unable to pass through the downstream filter.

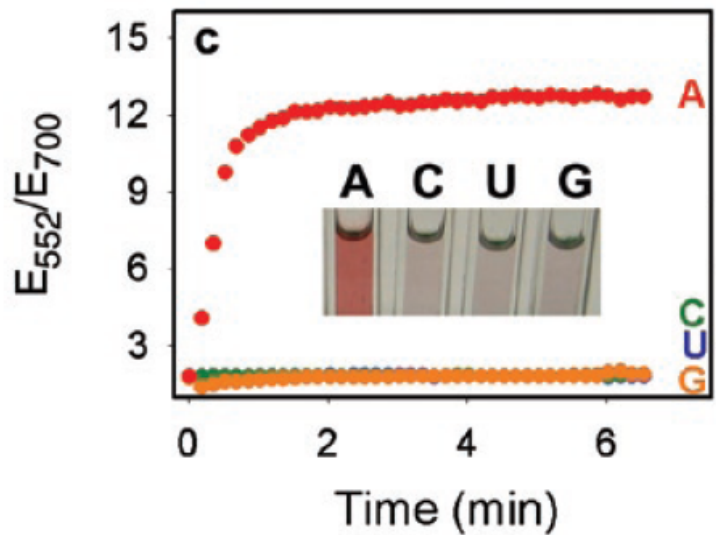


Figure 7: Gold nanoparticles for DNA detection. Nanoparticles are assembled into large complexes (blue). When DNA with the complementary base is added; the aggregates disassemble to create a deep red signal. The signal can be detected with light spectroscopy. (Y axis = Fluorescence at wavelength 552 nm / background at 700 nm) [Liu, Nat Protocols, 1, 2006, 246]

### QUESTIONS FOR THOUGHT

1. What kinds of biological objects have sizes similar to nanoparticles?
2. Describe why gold is shiny.
3. What is surface plasmon resonance and how does it change the color of nanoparticles? Why do they have different colors than bulk materials like gold earring studs?
4. Describe how gold nanoparticles are used in home pregnancy tests? Why are latex microspheres also used in the test? Why not gold nanoparticles alone?
5. How can surface plasmon resonance be used to create DNA sensors?

### ADDITIONAL RESOURCES

<http://mrsec.wisc.edu/Edetc/nanolab/gold/index.html>- Site maintained by the University of Wisconsin Materials Research Science and Engineering Center. Contains videos and detailed instructions of gold nanoparticle synthesis, plus additional experiments on nanoparticle light diffraction and creating your own sensor.