Last week we discussed basic forms of self-assembly such as crystal growth. But these cannot create the complexity required for full blown nanotechnology.

However, nature provides solution: Organic Chemistry + Molecular Biology = "life"

(Subjects of this and the lecture to follow)

Classes on organic chemistry spend endless time on memorizing lists of chemical names or on hundreds of alternate synthesis procedures.

I didn't want to be organic chemist myself, but I did have a long and successful collaboration with organic chemists. Experience that led me to an understanding of how to exploit organic chemistry via collaboration - an understanding I now want to share with you.
I also have two other goals:

1) To bring to chemistry what WE have now learned about quantum mechanics

   Chemists allude to the dark mysteries of s & p orbitals, pi bonds . . .

   But they're really just standing-waves, like those in springs and water

   Which, with your new experience, are now readily explained

2) To show how simple organic chemistry explains things affecting your daily life

   Perhaps the chemists got around to this in CHE 300 or Org CHE 200

   But they needn't have waited so long!!

   With very simple chemistry / organic chemistry I can explain:

   free radicals, anti-oxidants, trans-fats . . . and quite a bit more
So, to begin: Demystifying atomic orbitals

Waves trapped in boxes => Standing waves = Atoms

It's that simple and it's what most of Quantum Mechanics is about.

Only becomes hairy if want PRECISE solutions => spherical coordinates . . .

But approximate solutions (treating atoms ~ cubical boxes) are almost intuitive.

Origin of atomic "boxes" = attraction between electrons and nuclear protons.

Potential Energy = \(- q_{\text{electron}} q_{\text{nucleus}} / R\)

Box in sense that electron waves are contained.
But box that gets bigger for outer electrons.
So let's figure out lowest energy electron standing wave:

Plane wave bouncing of opposite walls of a square box => standing wave

$\lambda/2$ standing wave in 1D box:

$\lambda/2$ standing wave in 2D box (i.e. $\lambda/2$ X wave + $\lambda/2$ Y wave = "Superposition"):  

In 3D box: Add similar $\lambda/2$ wave in Z direction => **spherical cloud**:

What your Chemistry teacher called an "s orbital:"
For more energetic electron standing waves: Add oscillations!

More oscillations: \( \lambda \) standing wave in 2D box (i.e. \( \lambda X \) wave + \( \lambda Y \) wave):

\[
\begin{align*}
\n\lambda \text{ standing wave in 2D box} & \Rightarrow \text{2D wave in } X \text{ and } Y \text{ directions} \\
\text{In 3D box: If keep 2D wave (above) but use only } \lambda/2 \text{ wave in } Z \text{ direction} & \Rightarrow \\
\text{What your Chemistry teacher called an "d orbital:"}
\end{align*}
\]

Google images / Winona.edu
But we didn't HAVE to add oscillations in BOTH x and y directions!

In 1D: Full $\lambda$ wave

In 2D box: ONLY add $\lambda/2$ oscillation in perpendicular direction!

Why? Because oscillations $\Rightarrow$ Higher Frequency $\Rightarrow$ Higher Energy

Adding only $\frac{1}{2}$ oscillation in other direction= smallest step up in energy!

Yielding your Chemistry teacher's "p orbital:"
But what about the other possible directions?

That is, why wouldn't the full set of second energy level waves be:

- Each DOES involve simple standing waves
- Only difference is direction of higher frequency wave: X vs. Y vs. Z
- Each arrangement DOES keep charge away from earlier s orbital
- Each arrangement DOES keep charge away from other p orbitals
- So these are indeed three viable alternatives

Derived solely from standing waves / charge repulsion!!
Yielding lowest energy electron waves ($s$, $p_x$, $p_y$, $p_z$):

(Now represented as properly fuzzy clouds)

But what is difference in energy between this set of four trapped electron waves?

Can get the answer directly from our knowledge of waves:

Increased frequency (decreased wavelength) $\Rightarrow$ Increased energy

Three $p$ waves have identical wavelength $\Rightarrow$ identical energy (no surprise)

Earlier "s" cloud only had 1/2 the oscillation, but was down in narrower part of box

So its wavelength (distance for full cycle of oscillation) is not much different

Hence, its frequency was similar $\Rightarrow$ Not that much lower in energy

*A Hands-on Introduction to Nanoscience: WeCanFigureThisOut.org/NANO/Nano_home.htm*
So we've accounted for first 4 electrons? No: 8

The above "orthogonal" waves helped electron waves avoid one another

But electrons have a property beyond their charge, and this is called "spin"

Name from Maxwell's Equation that says spinning blob of charge = electro-magnet

Pairs of magnets ATTRACT: Positioning their poles N-S to S-N

Attraction counters charge repulsion => Electron pairs share same wave pattern

What happens in atoms with MORE than above eight electrons?

Possibility 1) Add more complex "d" waves (standing waves with more oscillations)

Possibility 2) Use stretched out versions of s and p waves that exploit enlarging box
Nature ultimately uses both possibilities

But for organic chemistry (~ first few rows of periodic table) => Possibility 2

Nature just adds enlarged versions of s and p waves:

One set of orbitals in narrow part of box:  
Next set of orbitals in wider part of box:

New expanded set of 8 electron waves largely avoid earlier (lower energy versions)

But because outer electron structure is similar, new set acts similarly =>

**PERIODIC TABLE** with repeated rows of 8 atoms. **But what about first row?**

Tiny p orbitals are too close to other electron clouds => too energetic => deleted
Leading to my "standing wave" version of the Periodic Table

Modified "Periodic Table" that leaves out atoms in middle part:

After the first (lone) energy level (→ H and He) we get
tight groups of four energy levels (capable of holding 8 electrons)
Now, before continuing, we must answer a BIG QUESTION:

Why does "organic" chemistry = carbon chemistry

Are we just being parochial? Failing to see other "paths not taken" (on earth)?

**Reasons why Carbon might indeed be special:**

1) Carbon has four bonding (valence) electrons = perfect number of bonds for 3D assembly

Bonds = electrons → which naturally repel on another

1 bond → line (1D):

2 bonds → chain (1D):

3 bonds w/ max separation → Plane (2D):

4 bonds w/ max separation → Tetrahedron (3D):
But ALL Column IV atoms have four bonding electrons!

So, as suggested by Sci-Fi, why couldn't "organic" life be based on Silicon?

Covalent Bonds = Pairs of electrons, coupled by magnetic "spin"

Strength of magnetic paring increases with distance over which the pair overlaps

Carbon is at the TOP of periodic table's Column IV → Smallest nucleus

Carbon Nucleus  Nucleus + electrons  C - C pair

Small core → Snuggle closely → Long overlap → SHORT (1.54 Å) STRONG (3.6 eV) bond
As compared to silicon:

Much larger core (14/6 times more protons, neutrons, electrons):

Silicon Nucleus  Nucleus + electrons  Si - Si pair

Much bigger separation: 2.35 Å (versus carbon's 1.54 Å)

And WEAKER bond: 2.3 eV (versus carbon's 3.6 eV)
And compare non-self bonding energies:

Bond energies in units of eV (1 kcal/mole = 0.04336 eV):

<table>
<thead>
<tr>
<th></th>
<th>H</th>
<th>C</th>
<th>N</th>
<th>O</th>
<th>F</th>
<th>Cl</th>
<th>Br</th>
<th>I</th>
<th>Si</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>4.5</td>
<td>4.3</td>
<td>4</td>
<td>4.8</td>
<td>5.9</td>
<td>4.5</td>
<td>3.8</td>
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<tr>
<td>C</td>
<td>4.3</td>
<td>3.6</td>
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<td>4.7</td>
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<tr>
<td>F</td>
<td>5.9</td>
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<td>5.9</td>
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<tr>
<td>Cl</td>
<td>4.5</td>
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<tr>
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<tr>
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<td>3.9</td>
<td>3.2</td>
<td>2.4</td>
<td>2.3</td>
<td></td>
</tr>
</tbody>
</table>

Row 3) C-C bonds are stronger than most C-X bonds (big exceptions are bonds to H & F)

Row 10) Si-Si bonds are MUCH weaker than ALL Si-X bonds in table!!

Silicon very much WANTS to bond with something OTHER than itself

Carbon PREFERENCES to bond with itself => C chains, rings . . . = "Organic" chemistry
So now let's explore carbon bonding more deeply:

In Periodic Table's 1st row, all atoms **could** support two electron standing waves.

Beyond first row, all atoms **could** support full set of 8 electron standing waves.

But they won't add electrons above number of charge-balancing nuclear protons.

In order to add **BOTH** electrons and protons => They must bond to another atom.

As implemented in first row of periodic table by hydrogen:

Or, using the surprisingly powerful **Lewis Representation**:

Core of atom (nucleus + inner non-bonding electrons) = Atom's letter symbol.

Bonding electrons = dots (max of 2 for H/He, max of 8 for other atoms).

Reaction of hydrogen bonding then becomes: 

\[ \cdot H + \cdot H \rightarrow H: H \]
Extending Lewis representation to other atoms:

- Number of bonding (valence) electrons = Column number = number of dots

- Atoms in right section have max of eight closely spaced energy levels

- Electrons like to pair

Eight possible electrons + pairing → 4 likely bond directions

Note semi-standard color code used for atoms above
Start to do some chemistry with this "Lewis" notation:

For instance, how would Boron and Fluorine form a compound?

After first spreading Boron's electrons out in different directions

\[ \text{B} + 3 \text{F} = \text{BF}_3 \]

Only way all electrons pair!

What about carbon bonding with hydrogen?

\[ \text{C} + 4 \text{H} = \text{CH}_4 \]

Again, just spread an atom's electrons out, then pair them into bonds
Oxygen plus two hydrogens: \( \text{O} + 2 \cdot \text{H} = \text{H} \cdot \text{O} \cdot \text{H} \)

But what if add 3rd H? \( \text{O} + 3 \cdot \text{H} = \text{H} \cdot \text{O} \cdot \text{H} \rightarrow \text{H} \cdot \text{O} \cdot \text{H} + \cdot \cdot \cdot \)

Self-bonding? \( \cdot \text{O} = \text{O} \cdot \text{O} \) Double bond = 2 sets of paired electrons

Or begin to mix things up a bit:

\( \text{O} \cdot \text{C} \cdot \text{O} \) \hspace{2cm} \( \text{H} \cdot \text{C} \cdot \text{N} \)

\( \text{CO}_2 \) \hspace{2cm} \text{Hydrogen Cyanide}
OK, but teach me something I don't sort of already know!

- DNA is incredibly floppy, and yet it maintains a taught double helix structure
- DNA bases are hydrogen bonded, and yet DNA splits apart at just 90°C
- DNA fingerprinting is based upon the movement of CHARGES in electric fields

All explained by the Lewis structure of DNA's phosphate groups and the negative charge that drives them apart:

Unpaired electron

"Withdraws" (steals) partner from elsewhere
Onward: We also need to figure out the SHAPE of molecules

For that, key fact is:

**Pairs of electrons, even if unbonded, act in same way as bonded pairs**

Prime example is in $\text{H}_2\text{O}$:

Is this, in fact, a linear molecule?

NO, there are 4 pairs of electrons: Two bonded pairs, two unbonded pairs

Four independent repelling groups $\rightarrow$ tetrahedron

**Pedantic chemistry teacher:** "It's not an **exact** tetrahedron!

**John:** "Show me where 1-2 degrees matters and I'll care!"

Gray lumps = unbonded pairs
Leading to bonding structure of more complex molecules:

Carbon: Comes with 4 bonding electrons - But has 8 easy places to put electrons

Simplest self-assembly = singly bonded chain ("alkane"):

But that leaves LOADS of unbonded, unpaired electrons:

Solution = Add hydrogens

But is this really accurate? Are bonds all at right angles, in a single plane?

Of course not! We have four naturally repelling electron pairs →
So real singly bonded carbon chain must look more like:

4 independent repelling bonds $\rightarrow$ Tetrahedra

Figure out number of independent bonds $\rightarrow$ Spread them out at far as possible

Physicists and chemists go on and on about sp2, sp3 . . . hybridization

But that is just the mathematical process of doing the same thing!!

Example: What if carbon chain had alternating single and double bonds:

Added enough H's to give each C necessary 4 bonds

$\Rightarrow$ only 3 independent bonds: 2 single $+ 1$ double
Three independent bonds repelling one another:

Planar, 120 degrees apart

So true structure of single-doubly bonded chain must be planar:

Then what about a single-triple bonded chain: $\text{H-C\equivC-C\equivC-H}$

Well, every C now has two independent bonds: 1 single + 1 triple

Will spread in opposite directions = a line: **Exactly as in formula: H-C\equivC-C\equivC-H**
Everyday Application: “Free Radicals” & “Antioxidants”

These terms are all over the news (or at least in “health food” advertising)!

Radicals also come up in discussion of possible nanoscience hazards

What’s it all about?

Oxygen tends to steal electrons => “Oxidation” is defined as loss of electrons

For organics, this can be the same as losing Hydrogens:
Representing bonds as lines, restructuring of the molecule is more obvious:

But what might make Hydrogens suddenly leave? FREE RADICALS

Molecule (“R”) with atom ("X") having unpaired electron: 

Possible source of radicals? Surface of Nanotubes & C60 (more on this later)

How would these “Free Radicals” promote loss of Hydrogen (a.k.a. oxidation)?
Free Radical Induced Oxidation

Free Radical approaching organic molecule:

If Hydrogen bond to radical is stronger, it can “steal” a hydrogen!

As organic loses electrons it will be driven to reconfigure its bonds

Oxidation => Major restructuring of molecules = Change in their biological function
Oxidation could, for instance, convert chains to rings:

- Oxidizing two hydrogens on ends of chain
- Connect now radicalized end carbons
**Antioxidant? = Molecules that can SUPPLY electrons**

Or, supply Hydrogens that bring along their electrons

Classic example is VITAMIN C (ascorbic acid):

Normal configuration:  After giving up two Hydrogens:

So “antioxidants” don’t STOP oxidation. They undergo oxidation!

Acting as sacrificial volunteers!
Cyclohexane:

- Cyclo = it's a ring
- hex = with six atoms
- ane = singly bonded

But notice how electrons/bonds are still in an almost undistorted tetrahedral geometry:

Figures on this (and the six pages to follow) are screenshots of interactive / manipulatable 3D models on WeCanFigureThisOut.org: [WeCanFigureThisOut.org/VL/Nanocarbon.htm](http://WeCanFigureThisOut.org/VL/Nanocarbon.htm)
What if we strip off half of the hydrogens and try to flatten ring?

Carbon atoms are not very happy as each now has only three bonds!

Leaving each carbon as (including its neighbor's bonding electrons):

What happens to that very unhappy unpaired electron (at the top)?

But it's not a B-B, it's more of a cloud

Other electrons are in plane

So leftover electron wants to get OUT of that plane
Two ways to get leftover electron out of that plane:

Alternative #1: Squeeze it upward (or downward) out of the plane

Produces unpaired electron pointing outward

=> FREE RADICAL => Oxidizer => Disorganizer

Possible on all "graphitic" surfaces (graphene, nanotubes, Buckyballs)

Alternative #2) Squeeze electron cloud both upward and downward

Like squeezing a water balloon in the middle:

DOES get leftover electron out of the crowded plane

But STILL leaves electron unpaired – how is this any better?
Because this configuration **DOES** allow for pairing/bonding:

Because those six electrons can now link up (bond) above and below plane:

**OR:**

Pairing #1  

OR:  

Pairing #2
But which pairing is right?

**BOTH!** They both do the same thing and save the same amount of energy!

So "nature" USES both - switching rapidly between them giving:

It's called a "resonance bond"

It "resonates" rapidly back and forth between the two linkages!

Significance? "Resonant" electrons are no longer locked into a single position.

They can move around (for instance under the influence of an electric field!)

This "**Benzene**" molecule can conduct electricity (where cyclohexane cannot!)
Connect the rings and get "Graphene"

Simple "ball and stick" representation

Accounting for all the valence electrons

Or showing resonant bonding that gives graphene its electrical conductivity:
But mobile electrons can slosh around forming pockets of +/- charge:

What then happens if one sheet of graphene is positioned above another?

If top graphene sheet randomly assumes charge configuration left/above

Then complementary charging pattern will be **INDUCED** on bottom sheet

And sheets will then be attracted to one another:

OR:
It's called Van der Waals bonding

Very different than the covalent bonding we've been talking about

Van der Waals bonding is weaker: Not based on tight electron magnetic coupling

Van der Waals bonding is also not localized: It occurs over regions

What happens if molecule gets larger?

More room for electrons to slosh →

Bigger sloshes (larger deviations from neutrality):

So Van der Waals "bonding" gets stronger in larger molecules!
Proof? Boiling points of similarly structured molecules:

<table>
<thead>
<tr>
<th>Alkanes</th>
<th>Alcohols</th>
<th>Amines</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃CH₂CH₃</td>
<td>CH₃CH₂OH</td>
<td>CH₃CH₂NH₂</td>
</tr>
<tr>
<td>-42.1 C</td>
<td>78 C</td>
<td>16.6 C</td>
</tr>
<tr>
<td>CH₃CH₂CH₂CH₃</td>
<td>CH₃CH₂CH₂OH</td>
<td>CH₃CH₂CH₂NH₂</td>
</tr>
<tr>
<td>0.5 C</td>
<td>97.4 C</td>
<td>47.8 C</td>
</tr>
<tr>
<td>CH₃CH₂CH₂CH₂CH₃</td>
<td>CH₃CH₂CH₂CH₂OH</td>
<td>CH₃CH₂CH₂CH₂NH₂</td>
</tr>
<tr>
<td>36.1 C</td>
<td>117.3 C</td>
<td>77.8 C</td>
</tr>
</tbody>
</table>

Within a given family of molecules (column) longer the chain → higher the boiling point

Move between families (columns), different atoms "slosh charge" differently

→ Shifts whole family's boiling points up or down

Better name for Van der Waals bonding = "INDUCED-DIPOLE BONDING"
Does this only occur for conductive molecules?

In preceding figures charge shifted from atom to atom

Possible in conductive, semiconductive, or molecules with “conjugated” bonds

But can also get Van der Waal / induced-dipole effects via simpler polarization:

Or for longer molecules:

So polarization of insulating molecules also yields VDW, growing stronger with length
Van der Waals bonding helps hold cell membranes together:

Remember "lipid bilayers" in water where hydrophobic tails gathered together?

Electrons in tails polarize ("slosh") producing Van der Waals bonding

So cell wall self-assembly has **two** components:

1) Hydrophillic heads orient out toward water

2) Hydrophobic tails drawn together by VdW
Everyday application: "Saturated Fats"

Here “saturated” means saturated with hydrogens: Saturated carbon chain (fat):

Straight saturated chains pack closely => Strong VdW bonding => High melting T

So they can SOLIDIFY within your arteries => Heart Attacks / Strokes
Change to "unsaturated" by removing pair of hydrogens:

Carbons that lost hydrogens form double bond. But 2 configurations are possible:

- "TRANS"
- "CIS"

Producing these alternative full fat chain structures:

**TRANS FATS** are straight, like saturated fats
Which do pack closely
So they too solidify in our arteries

**CIS FATS** are kinky
But which don't pack closely
So they stay liquid in our arteries
Getting back to graphene

Van der Waals bonding between graphene sheets forms GRAPHITE:

Although not shown, there are also "resonant bonds" → electrical conductivity

Weak Van der Waals interplanar bonds → Sheets slip or separate easily

Giving Graphite it’s well known lubricating properties

And providing the tape trick we use to obtain fresh "HOPG" layers for STM in lab
What about other deliberately *man-made* molecules?

Field is called "Synthetic Chemistry". It is incredibly powerful!

But kept secret from those of us who never got beyond Chem 101

To describe its richness, we must first learn Organic Chemist's shorthand:

1) Carbon is EVERYWHERE, so get lazy and don’t draw it

   If no atom identified at intersection of bonds, ASSUME it is C:

2) In water, hydrogen is ALWAYS available to fill in any bonds left over, so get even lazier

   Don't show hydrogen atoms OR their bonds, just infer their presence

   (Can work out number because KNOW carbon must have 4 electrons in bonds)
Which produces shorthand diagrams like the following:

"Fully saturated" alkane:

"Conjugated" alternation of single / multiple bonds:

Rings of Cyclohexane:

Or Benzene:

Or propyl alcohol (with extra OH group at end represented explicitly):
Chemists build smaller molecules by addition and subtraction:

Step by step they add reagents (black) to remove or add pieces to the starting molecule.

Gradually transform it into final product shown at bottom.

Can actually pinpoint atoms such as which F is removed from benzene ring (? vs. ??).

How? Depending on ring position, F's bond slightly more strongly or weakly.

Courtesy of Professor Jim Tour, Rice University (from our DARPA MOLEapps collaboration)
Followed by purification:

Because steps like those on previous slide are only 30-80% successful

That is, 30-80% of molecules do what was drawn, others do something else

So you must sort out intended from unintended products using:

1) **Distillation:** Different molecules = Different boiling points

   Condense different components in progressively cooler regions

   Exploits Van der Waals bonding!

2) **Crystallization:** Like molecules try to fit into single crystals, excluding unlike

   Remember trying to freeze juice into popsicles? Sugar on outside - ice inside

3) **Chromatography:** Diffuse the mixture through paper, gel . . .

   Same thermal energy per molecule = $1/2 \, mv^2$, smaller molecules $\rightarrow$ higher $v$!
But to self-assemble larger structures, need other tricks

One useful trick employs an amine (left) and a carboxylic acid (right):

Where the following reaction can occur, linking the two sub-molecules:

Stripped off as water molecule

After a little rearrangement
Two every day applications of (just this one!) trick:

Double up reactive groups, one at each end of subunits:

Mix subunits together to produce a self-assembled polymer:

\[
\begin{align*}
R_1, R_2 &= \text{C}_6 \text{ alkane} \Rightarrow \text{ NYLON } \\
R_1, R_2 &= \text{ benzene} \Rightarrow \text{ KEVLAR }
\end{align*}
\]
That gives you a glimpse of organic chemistry's power

And, via standing waves, finally explains chemists' mysterious "orbitals"

The remaining challenge is to cope with all of the field's crazy names

And to do that, I offer: John's Organic Chemistry Cheat Sheet

(Derived from my own close collaboration with an organic chemist)

But for the penultimate form of nanoscale self-assembly,

we have got to follow this path all the way into biology

Which will bring us in the next hour to:

Nature's ultimate tool for self-assembly - DNA
Credits / Acknowledgements

Funding for this class was obtained from the National Science Foundation (under their Nanoscience Undergraduate Education program).

This set of notes was authored by John C. Bean who also created all figures not explicitly credited above.

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