We love the idea that words pronounced, little more than pure information, can evoke actions in the physical world.

Sorcerer's Apprentice

Great (but lazy) hackers
Linus Torvalds

And of course, given programmable computers and robots, they can.
I only have "execute" permissions for such spell-programs on your brain-computers for the duration of my talk.

Leader/Politicians are much better. They are good at getting arbitrary programs run almost all of the time: "Build a pyramid" or "Go to war!" or, sometimes, "Drop the price of AIDS drugs."
1110110110001001100011010010011000001010011011
110100111110000100110100011110000111010101110
111001100100100100001101000010001000100001010
0000011110000010111011011011110100011111000...

"pronounced" with a computer
Hello TED!

"pronounced" with a computer

111011011000100110001101001001001100001010011011
1101001111100001001101000111100000111010101110
11100110010010010001101000010010001000100001010
000001111000001011101101101110100011111000...
Hello TED!
Hello TED!

"pronounced" with a computer
Hello TED!
Hello TED!
Hello TED!

"pronounced" with a computer

1110110110001001100011010010011000001010011011
110100111110000100110100011110000111010101110
1110011001001001000011010000100010001000001010
0000011110000010111011011011110100011111000...
Hello TED!
Hello TED!
Hello TED!
Hello TED!

#include <stdio.h>
#include <stdlib.h>

int main(void)
{
    int i;
    for (i = 1; i < 4; i++) {
        printf("Hello TED!\n");
    }
}
So computer programs are spells, and verbal or written directions to humans are spells, but this is unsatisfying.
So computer programs are spells, and verbal or written directions to humans are spells, but this is unsatisfying.

The wonderful fact is that there are spells that work without a computer (or human robot).
So computer programs are spells, and verbal or written directions to humans are spells, but this is unsatisfying.

The wonderful fact is that there are spells that work without a computer (or human robot).

The fact is, that at the molecular level, when spells are pronounced as molecules, physics can directly interpret information and run programs.
The fact is, that at the molecular level, when spells are pronounced as molecules, physics can directly interpret information and run programs.
The fact is, that at the molecular level, when spells are pronounced as molecules, physics can directly interpret information and run programs.

Strings of sequence information pronounced as amino acid chains fold into 3D protein nanomachines.

(Roughly, different combinations of letters stick to other combinations of letters in complex, context-dependent ways.)

The fact is, that at the molecular level, when spells are pronounced as molecules, physics can directly interpret information and run programs.
The fact is, that at the molecular level, when spells are pronounced as molecules, physics can directly interpret information and run programs.

PLPVYKPAASRMQIEKAVEMLIQAERPVIVAGGGVINADAAALL QQFAELTSIPVIPTLMGWGCIPDDHELMAGMVMLQTAHRYGNA TLLASDMVFIGNRF...

Strings of sequence information pronounced as amino acid chains fold into 3D protein nanomachines.

A green and purple enzyme that attacks a poor little DNA, and cuts it.

The fact is, that at the molecular level, when spells are pronounced as molecules, physics can directly interpret information and run programs.
The fact is, that at the molecular level, when spells are pronounced as molecules, physics can directly interpret information and run programs.

Changing the sequence...
The fact is, that at the molecular level, when spells are pronounced as molecules, physics can directly interpret information and run programs.

Changing the sequence...
changes the spell
and the 3D folding.

ANRHTGSVEKYTEGRKIVHIDIEPTQIGRLCPDLGIVSDAOAAL
TLLVEVAQEMQKAGRLPCRKEWVADCQQRK...
The fact is, that at the molecular level, when spells are pronounced as molecules, physics can directly interpret information and run programs.

Changing the sequence... changes the spell and the 3D folding.

The resulting nanomachine is now a ligase that connects two DNA strands together like a DNA stapler.

ANRHTGSVEKYTEGRKIVHIDIEPTQIGRVLCPDLGIVSDAKAAL TLLVEVAQEMQKAGRLPCKKEWVADCQQRK...
In the end the total action of all of these molecule programs and the nano-machines they create is to build a person like you, with its buggy and insecure neural computer.

ANRHTGSVEKYTEGRKIVHIDIEPTQIGRVLCPLGIVALVSDAKAAL
TLLVEVAQEMQKAGRLPCRKEWVADCCQRK...

Changing the sequence... changes the spell and the 3D folding.

The resulting nanomachine is now a ligase that connects two DNA strands together like a DNA stapler.
DNA nanotechnologists cast molecular spells with DNA.

Erik Winfree
Algorithmic self-assembly

Len Adleman
First DNA computer

Bernie Yurke
DNA tweezers and motors

Ned Seeman
Father of DNA nanotech.
DNA nanotechnologists cast molecular spells with DNA.

DNA is cheaper, easier to handle, and easier to understand than proteins.

Erik Winfree
Algorithmic self-assembly

Len Adleman
First DNA computer

Bernie Yurke
DNA tweezers and motors

Ned Seeman
Father of DNA nanotech.
DNA nanotechnologists cast molecular spells with DNA.

DNA is cheaper, easier to handle, and easier to understand than proteins.

We want to build stuff.
Smaller faster computers.
Black boxes in cells.
DNA analogs of protein motors.

Erik Winfree
Algorithmic self-assembly

Bernie Yurke
DNA tweezers and motors

Len Adleman
First DNA computer

Ned Seeman
Father of DNA nanotech.
DNA nanotechnologists cast molecular spells with DNA.

DNA may be handicapped; perhaps less functional than protein. But we have a head start. And we have a hope of writing compilers...

We want to build stuff. Smaller faster computers. Black boxes in cells. DNA analogs of protein motors.

Erik Winfree
Algorithmic self-assembly

Bernie Yurke
DNA tweezers and motors

Len Adleman
First DNA computer

Ned Seeman
Father of DNA nanotech.
How can one make any arbitrary shape or pattern out of DNA strands?
How can one make any arbitrary shape or pattern out of DNA strands?

Perform a type of "DNA origami":
Fold a single long strand of DNA (the paper) into the desired shape.
Given a shape:

100 nanometers
Given a shape: 100 nanometers

A computer program designs a set of 250 short DNA sequences, on average each is about 32 letters:

1. s10t15f, A1, AAAGACAAAGCAAGGCCGGAAACGT
2. s10t17f, B1, AGAGAGAACCACAAGAATTGAGTTCCAGCGCC
3. s11t14e, C1, AGCACCATTACCATTAAAGGGCGA
...
250. s11t16e, D1, CATTCAACATATCAGAGAATACTAACATAA

Their job will be to fold the long strand.
Given a shape:

100 nanometers

A computer program designs a set of 250 short DNA sequences, on average each is about 32 letters:

1. s10t15f, A1, AAAGACAAGCAAGGCCGGAAACGT
2. s10t17f, B1, AGAGAGAACCACAAGAATTGAGTTCCAGCGCC
3. s11t14e, C1, AGCACCATTACCATTAAAGGGCGA
...
250. s11t16e, D1, CATTCAACATATCAGAGAGATAACTAACATAA

Their job will be to fold the long strand.

Sequences are "pronounced" using a DNA synthesizer

(The "opposite" of a sequencer.)
Given a shape:

100 nanometers

Sequences are "pronounced" using a DNA synthesizer

(The "opposite" of a sequencer.)

A computer program designs a set of 250 short DNA sequences, on average each is about 32 letters:

1. s10t15f, A1, AAAGACAAGCAAGGCGGAAACGT
2. s10t17f, B1, AGAGAGAACACAAGAGATTGAGTTCCAGCGCC
3. s11t14e, C1, AGCACCATTACCATTAAAGGGCGA
   ...
250. s11t16e, D1, CATTCAACCATATCAGAGAGATAACTAATCTAA

Their job will be to fold the long strand.

Each letter is replaced by a 30-atom cluster, a different one for each DNA base A, C, G, or T.
All 250 different DNA strands are mixed together.
Add a little magnesium salt.
M13mp18 viral genome 7249 bases

Mg$^{2+}$
100 nanometers
100 nanometers
Atomic force micrograph (AFM) image.

Gray is DNA, black is the mineral mica on which it sits.
Change the sequence of staples and one can make a shape with precise holes.
Change the sequences of staples and one can make a shape with precise holes. Who likes to stick to friends.

72% are well-formed

100 nm
The technique is not limited to raster-filled shapes. Rigid domains can be combined at defined angles.

88% are well-formed
With still different staple sequences, arbitrary patterns of dots (DNA bumps) can be made on top of rectangles ---200 pixels with a resolution of 6 nanometers.
How can we combine pattern covered shapes into larger objects?

A small change to the sequences does the trick.
Better, higher yield ways must be found (2%)
An atomic force microscope "feels" the height of DNA structures with a microscopic finger. Thus these false color 3D topographic images are appropriate.

Many scientists are working to turn this DNA artwork into functioning devices and circuits.
Why attempt to make self-assembly an exercise in programming? Eventually we want to learn how to self-assemble anything...

Solar farm

A desalination plant

Bizarro Erik

(I don't really pretend to know what the real applications will be; what will we want to make?)
Erik Winfree

Inventor of algorithmic self-assembly

This is the very coolest approach, is truly programming DNA, (in the computer science sense) but I don't have time to talk about it!!!

Paul Rothemund
pwkr@dna.caltech.edu
626-390-0438
www.dna.caltech.edu/~pwkr

A 2nd year grad student in China has reproduced this work and made China--Lulu Qian.

Real soon now (as soon as I get a job) I will release my crappy MATLAB code for DNA origami. 6-12 months from now, a company will release 3D WSIWYG free, open source python for DNA origami. Yay! Send me email to join the release list.

I work in this guy's lab.

This is the very coolest approach, is truly programming DNA, (in the computer science sense) but I don't have time to talk about it!!!
GACTTTGGTGCGCAAGAGGAGCTGGCGGAGCCAGCCAGTGGGCAGGGCCAGGGGAGGGCGGGCAGGTAGGTGCAGCCACTCCTGGGAGGACCCTGCGTGGCCAGACGGTGCTGGTGACTCG...

TAGAGGCCAGCCTTGGACACTTGCTGCCCCTTTCCAGCCCGGATTCTGGGATCCTTCCCTC

TGAGCCAAACATCTGGGTCTGCTGCCTTCGACACCCACCCCCACGGCTTCTACCCTTGCGTGC...
Written using ~30 atoms per A, C, T or G base. The writing is "molecular".

http://www.web-books.com/Mobio/Free/Ch3B.htm
"pronounced" in a fertilized egg cell, through the processes of RNA transcription, protein translation, and biological development
"pronounced" in a fertilized egg cell, through the processes of RNA transcription, protein translation, and biological development.
"pronounced" in a fertilized egg cell, through the processes of RNA transcription, protein translation, and biological development
"pronounced" in a fertilized egg cell, through the processes of RNA transcription, protein translation, and biological development
pronounced through biological development

evolved code, we don't know biology's high level language very well.

55
Clearly, molecular information can direct the spontaneous self-organization of amazing artifacts.

How can we write such programs?
Homo Sapiens

GACTTTGGTGGAAGAGGAGCTGGCGGAGCCAGCCAAGCAGTGGGGGCGGGCCAGGGGAAGGGCGGGCAGGTAAGGTGCAGCCACTCCTGGGAGGACCCTGCGTGGCCAGACGGTGCTGGTGACTCG...
TAGAGGCCAGCCTTGGACACTTGCTGCCCCTTTCCAGCCCGGATTCTGGGATCCTTCCCTGAGCCAACATCTGGGTCCTGCCTTCGACACCACCCCAAGGCTTCCCTACCTTGCAGTGC...
E. Coli Homo Sapiens

Homo Sapiens

E. Coli

2 microns
AATGCTACTACTATTTAGTAGAATTTGATGCCACCTTTTCAGCTCGCCCCCACATGAAAATATAGCTAATAACAGGTTATTGACCATTTGCGAAATGTATCTAATGGTCAAACTAAATCTACTCGTTGCGCAGAATTGGGAATCAAATGTTATATGGAATGAAAACTTTCCAGACACCGGTACTTTAGTGGCATATTATTTAAAACATGTTGAGCTACAGCATATATTGAGCAATTAAGCTCTAAGCCA TCCGCAAAAATGACCTCTCTTATCAAAGGAGCAATTAAAGGTACCTCTCTTAATCCTGACCTGTTGAGGTGGCTTCTCTGCTGTTGCTGGTTCGCTTTGAAGCTCGAATTAAAACGCGATATTTGGAAGTCTTTCGGGCTTCTCTTAATCTTTTTTGGATG...

Homo Sapiens

E. Coli

M13 bacteriophage

2 microns

0.2 microns

59