Abstract

Why are we building two new species: *Homo chippus*, a milliHuman, and *Homo chippiens*, a microHuman? Microfabricated humans-on-a-chip! Why? Because it’s fun and a REAL challenge. Using the tools of physics, chemistry, engineering, physiology and molecular biology, we are exploring the unfathomable complexity that affects our development and growth and individual responses to disease, drugs, and aging. Multidimensional phase space illustrates the variables that affect *H. chippus, H. chippiens* and the scientists doing the work.
Homunculus, *noun*  
[hō-ˈməŋ-kə-ləs]  
*plural* ho·mun·cu·li  
A miniature representation of a human.
Why are we building homunculi?

- Human biology is complex
- Homunculi can simplify:
  - Drug development
  - Environmental toxicology
  - Physiology
Raise your hand if you or a friend have had an adverse drug reaction.

Do household cleaners, garden chemicals, fragrances, or air pollution bother you?
Multidimensional phase space illustrates the variables that affect homunculi and the physicians, scientists and engineers building them.
Phase space
[fāz spās], noun
A geometrical space in which each possible state of a system is represented by a single point.
One axis in phase space can represent the range of one variable.
There are as many axes as variables.
Swing Phase Space

Front and back

Left and Right

Orbit

Twist

Front-Back Angle

Twist

Right-Left Angle

Right-Left Velocity

Twist Velocity

Front-Back Velocity

Six-Dimensional Phase Space is fun!
You can do lots of things at one time!
Part of the problem is that human biology is COMPLEX. Organs talk to each other, but we seldom hear what they are saying.
Silo -- A place to store stuff without mixing.

Silo Mentality -- Thinking without mixing.
How is a new drug tested?

Petri dishes → Mice → Humans
Organs from a Silo Mentality

- Brain
- Lungs
- Kidney
- Heart
- Liver
Organs from a Silo Mentality
Organs from a Petri Dish
Mentality

Brain Cells
Lung Cells
Kidney Cells
Liver Cells
Heart Cells
Testing drugs in Petri Dishes

Brain Cells

Lung Cells

Kidney Cells

Liver Cells

Heart Cells
Testing drugs in Petri Dishes

- Lung Cells
- Kidney Cells
- Liver Cells
- Heart Cells
- Brain Cells
Testing drugs in Petri Dishes

- Lung Cells
- Kidney Cells
- Liver Cells
- Heart Cells
- Brain Cells
How is a new drug tested?

Petri dishes

Mice

Humans

If each individual “organ” is OK, start testing that drug on mice.
Test drug in mice...
Test drug in mice...
Test drug in mice...
How is a new drug tested?

- Petri dishes
- Mice
- Humans

If the mice are OK, then the drug is tested on humans.
Test drug in humans...
Test drug in humans...
Test drug in humans...
Test drug in humans...

What went wrong?

• Human genes ≠ mouse genes?
• Organ-organ interactions?
How is a new drug tested?

- Petri dishes ✓
- Mice ✓
- Homunculi
- Humans ×
Our homunculi will be alive, built with human cells!
Test drugs in homunculi!
Test drugs in homunculi!

Unexpected human organ-organ interaction.
No human dies.
We’ve just seen why we are building homunculi

• Human biology is complex
• Homunculi can simplify:
  – Drug development
  – Environmental toxicology
  – Physiology
How do you build homunculi?

• Use human cells to make microfluidic organ chips that work like the real organs.

• Connect organs together.

• Do lots of things at the same time. (phase space)
Lung on a chip

Don Ingber, Harvard
Mammary gland on a chip

Lisa McCawley and Dmitry Markov, Vanderbilt
Kidney on a chip

Shuvo Roy, UCSF and Bill Fissell, Vanderbilt
T cells in a lymph node on a chip

Kevin Seale, Jake Brady and Shannon Faley, Vanderbilt
Brain on a chip

Simpler than a human but has the key functions of the blood-brain barrier!

Vanderbilt University, Meharry Medical College, Cleveland Clinic Foundation
Advanced Tissue-engineered Human Ectypal Network Analyzer

We call our chip Athena

milliHuman (mHu)

Homo chippus

Los Alamos National Laboratory, Vanderbilt, Harvard, Charité Hospital Berlin, UCSF, CFD Research Corporation
Organ

Frank Block, Vanderbilt
What kinds of people are building homunculi?
Fields of Knowledge
Silos of Knowledge

Athena needs a mix of disciplines

Humanities
- Performing Arts
- Philosophy
- Languages
- Religion
- Visual Arts
- Literature

Social Sciences
- Psychology
- Geography
- Economics
- Anthropology
- Sociology

Engineering
- Mechanical Engineering
- Environmental Engineering
- Biomedical Engineering
- Civil Engineering
- Chemical Engineering
- Electrical Engineering

Professions
- Law
- Medicine
- Business
- Astronomy
- Earth Sciences
- Biology
- Mathematics
Intellectual Phase Space

- Law
- Business
- Medicine
- Mechanical Engineering
- Environmental Engineering
- Biomedical Engineering
- Civil Engineering
- Chemical Engineering
- Electrical Engineering
- Music
- Archaeology
- Visual Arts
- History
- Religion
- Philosophy
- Languages
- Literature
- Performing Arts
- Geography
- Economics
- Sociology
- Psychology
- Anthropology
- Physiology
- Astronomy
- Earth Sciences
- Chemistry
- Mathematics
- Physics
- Biology
- History
- Astronomy
- Earth Sciences
- Chemistry
- Mathematics
- Physics
- Biology
My Knowledge
You can be more than one thing at a time in phase space!
Intellectual Phase Space

Physics

Albert Einstein
1879-1955
Intellectual Phase Space

Physics

Richard Feynman
1918-1988
Intellectual Phase Space

Physics

Enrico Fermi
1901-1954
Intellectual Phase Space

Physics

George Westinghouse
1846-1914
Intellectual Phase Space

Physics

Engineering

Nikola Tesla
1856-1943
Intellectual Phase Space

Physics

Engineering
Intellectual Phase Space

Physics

Engineering
Galen of Pergamon
AD 129-216

Intellectual Phase Space

Physics

Physiology
Intellectual Phase Space

Physics

Engineering

Physiology
Intellectual Phase Space

Physics

Emmett “Doc” Brown
1885-2015?
Engineering

Intellectual Phase Space

Physics

Leonardo da Vinci
1452-1519
Intellectual Phase Space

Physics

Engineering

Physiology

Portraits by Dominic Doyle, Vanderbilt
Behavioral Phase Space

- Focused
- Creative
- Excited
- Questioning
- Calm
- Scattered
Behavioral Silos

- Willful
- Stubborn
- ADHD
- Normal
- Introverted
- Daydreamer
Swing Phase Space

Front and back

Left and Right

Orbit

Twist

Front-Back Angle

Twist Angle

Right-Left Angle

Front-Back Velocity

Right-Left Velocity

Twist Velocity

Six-Dimensional Phase Space is FUN, but often discouraged!
Don’t put people in a single silo!
Behavioral Phase Space

Athena needs a variety of builders!
What are we learning?
Genetic Phase Space
1 Gene Phase Space

ALB

Maximum expression

Actual expression level

No gene expression
2 Gene Phase Space

ALB

CFTR
12 Gene Phase Space
100 Gene Phase Space

CRH
CXCR4
DHFR
HFE
KRT14
KRT5
PGL2
PHF8
RHO
SDHB
SDHC
SDHD
SRY
TSC1
TSC2
APP
GAST
1,000 Gene Phase Space
Our 20,000 genes are expressed differently in each organ!

Organs talk to each other!
Our 20,000 genes are expressed differently in each organ!

Organs talk to each other!
What does an organ on a chip sound like?