

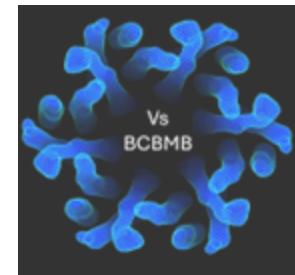


**Kia Ora, Hello and Welcome
VsBCBMB**

Cell Biology

A Not So Typical Introduction

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Setting the Stage

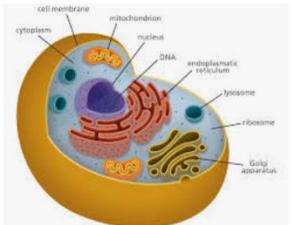


Google: “Cell Images”
scroll through the search results and
try to sum up in you own words what you see

This is what it showed to me....



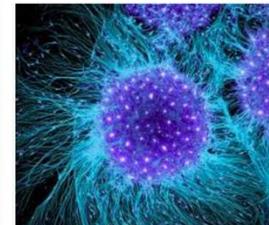
Cell Images, Stock Photos & Vectors ...
shutterstock.com



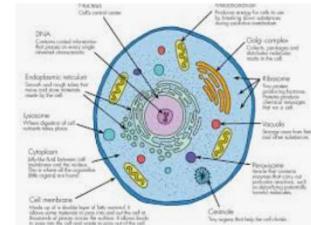
What is a cell? | Facts | yourgenome.org
yourgenome.org



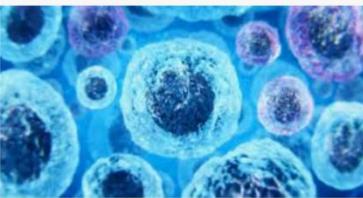
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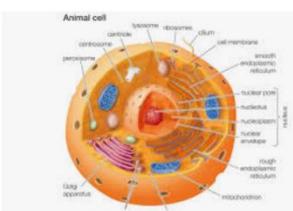
How human embryonic stem cells spa...
nature.com



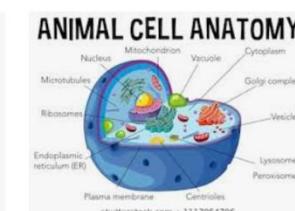
Cells - Haleo
haleo.co.uk



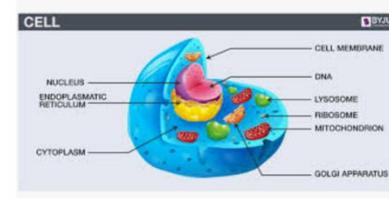
cell biology | Quanta Magazine
quantamagazine.org



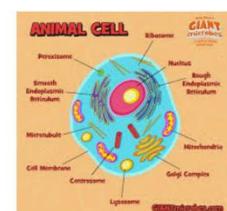
Animal Cells and the Membrane-Bound Nuc...
thoughtco.com



ANIMAL CELL ANATOMY
shutterstock.com • 1117954796



Cells: Definition, Types of Cells ...
byjus.com



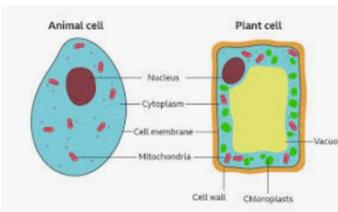
Animal Cell
giantmicrobes.com



Animal Cell
giantmicrobes.com



Stem Cell Toxicology | Asymmetrex
asymmetrex.com



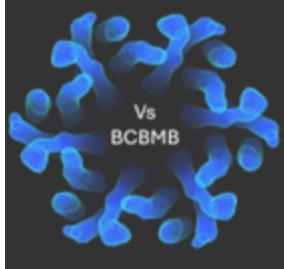
What are cells? - BBC Bitesize
bbc.co.uk



Human stem cell combination could help ...
drugtargetreview.com



Mitochondria behind blood cell formation
phys.org

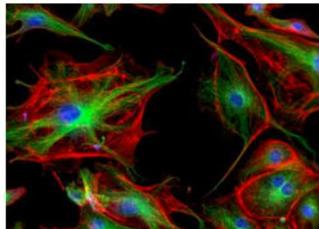


Setting the Stage

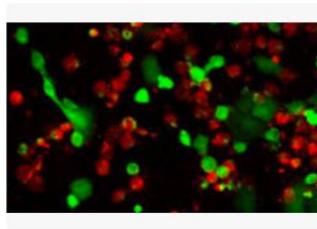
Google: “Cell Fluorescence Images” – scroll through the results and write down observations of what you see. Explicitly identify features you may recognize.



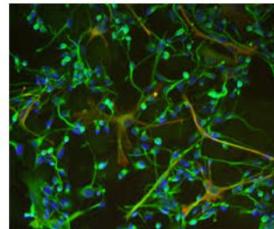
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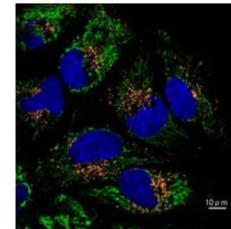
shows promise for fluorescent cell imaging
europeanpharmaceuticalreview.com



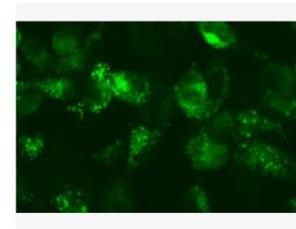
Live Cell Imaging Reagents | Sigma-Aldrich
sigmaaldrich.com



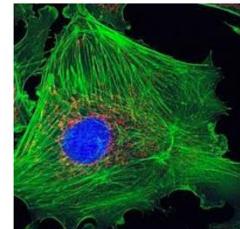
Innopro
innoprot.com



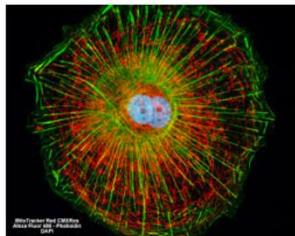
Live Cell Imaging – Monitor ...
tebu-bio.com



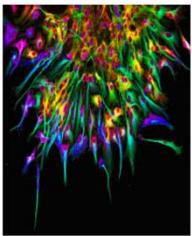
Live Cell Imaging Reagents | Sigma-...
sigmaaldrich.com



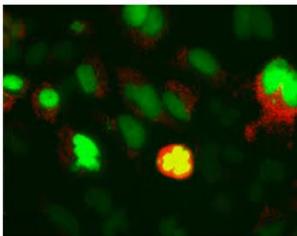
micrograph. Fluorescent dye...
pinterest.com



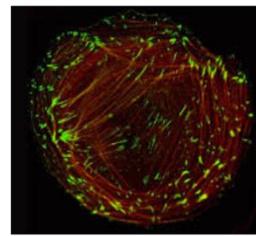
ZEISS Microscopy Online Campus ...
zeiss-campus.magnet.fsu.edu



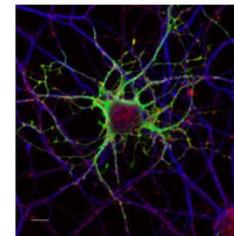
“cell-sight” with Deep L...
towardsdatascience.com



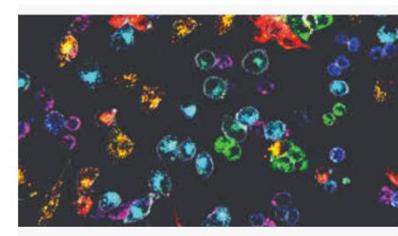
Preparing for Live-Cell Imaging ...
thermofisher.com



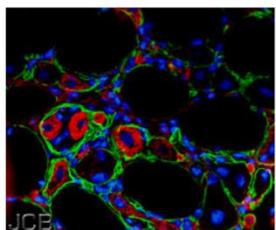
CellLight Fluorescent Protein La...
thermofisher.com



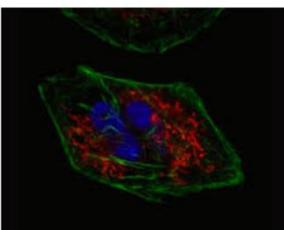
Fluorescent microscopy - LN...
Inf-wiki.eecs.umich.edu



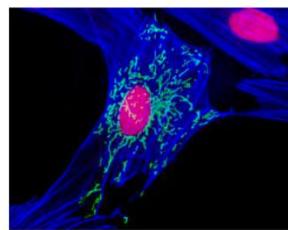
Rainbow Cell Barcoding: Fluorescent ...
advancedsciencenews.com



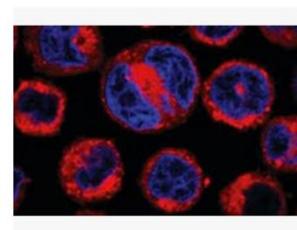
Fluorescent Nanodiamonds – the ...
sustainable-nano.com



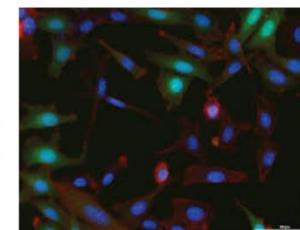
CellLight Fluorescent Protein Labelin...
thermofisher.com



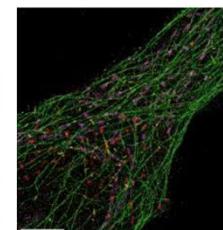
Molecular Expressions Microscopy Pr...
micro.magnet.fsu.edu



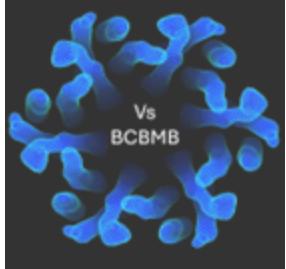
Live Cell Imaging Reagents | Sigma-Al...
sigmaaldrich.com



Fluorescence Microscopy ...
biotek.com



Ultra-Sharp Images of Cel...
wired.com

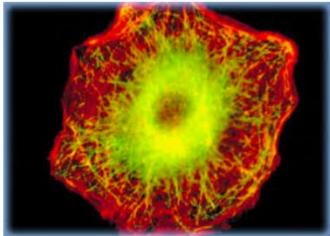


Setting the Stage

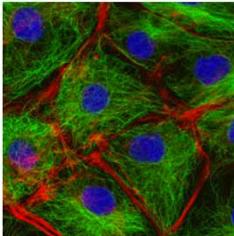
Google: “Cytoskeleton Fluorescence Images”



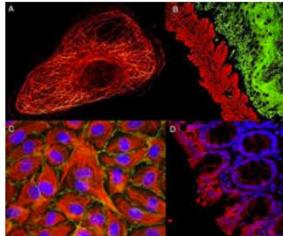
Things it showed to me....



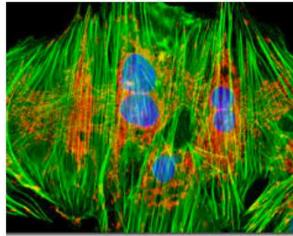
Cellular Cytoskeleton | Olympus Life ...
olympus-lifescience.com



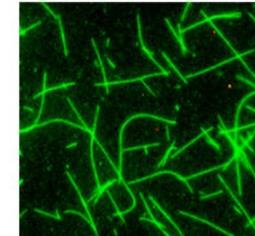
Cytoskeleton – the movers a...
bscb.org



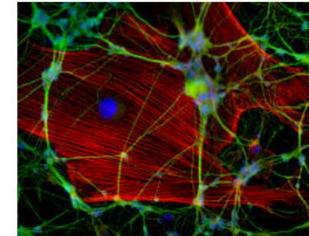
actin assays for cytoskeleton dyna...
tebu-bio.com



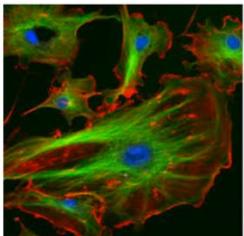
Molecular Expressions Microscopy Pri...
micro.magnet.fsu.edu



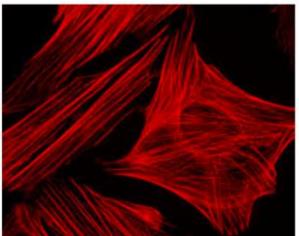
Fluorescent Tubulin Proteins
cytoskeleton.com



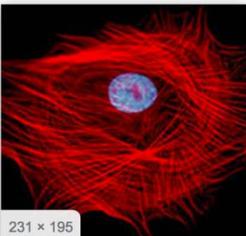
CIL:41649, glial cell, neuron. CIL. Dat...
cellimagelibrary.org



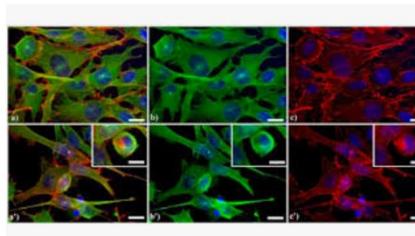
Snapshots of the Cytoskeleto...
sustainable-nano.com



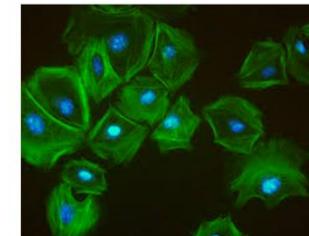
Indian Muntjac Actin Cytoskele ...
microscopyu.com



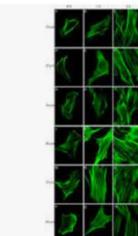
Cytoskeleton Structure | Ther...
thermofisher.com



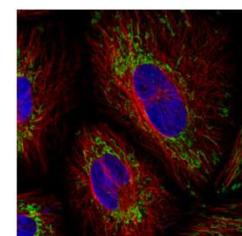
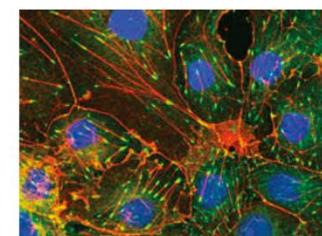
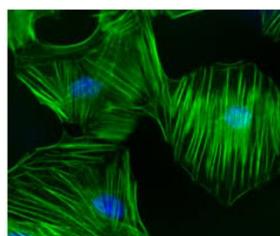
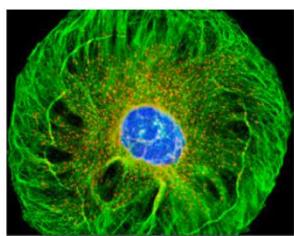
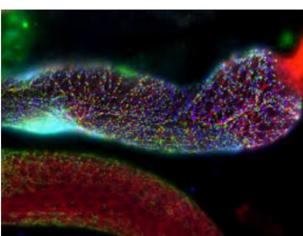
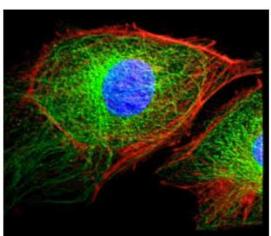
Fluorescence microscopy after double ...
researchgate.net

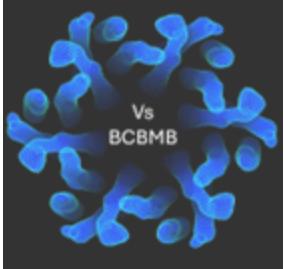


micrograph showing cell nuclei ...
pinterest.com



actin cytoskeleton of t...
researchgate.net



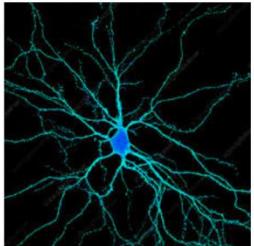


Setting the Stage

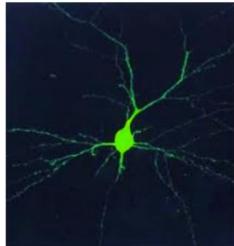
Google: “Neuron Fluorescence Images”.....



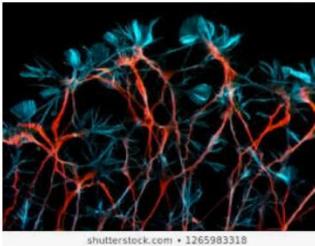
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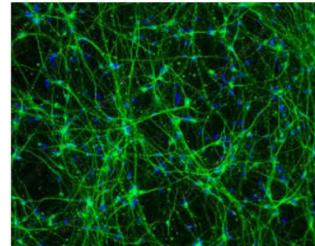
Neuron, fluorescence microgra...
sciencephoto.com



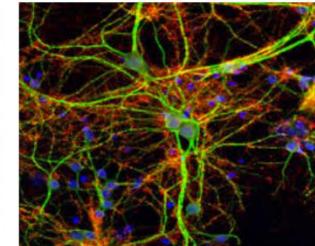
A morphology of a single ne...
researchgate.net



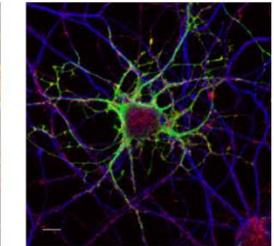
Neurons Fluorescence Images, Stock ...
shutterstock.com



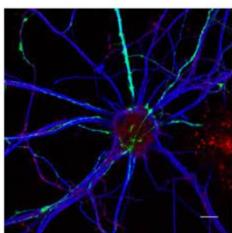
Neurons from stem cells, fluorescence ...
sciencephoto.com



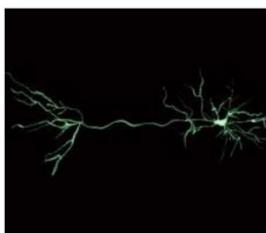
Fluorescent Probes | Thermo Fisher ...
thermofisher.com



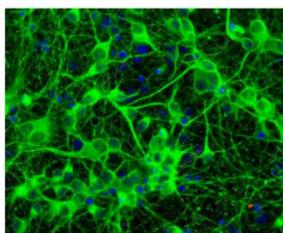
confocal fluorescence microsc...
flickr.com



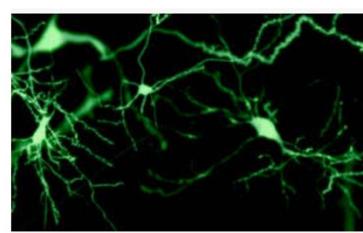
Neurons, confocal fluoresce...
flickr.com



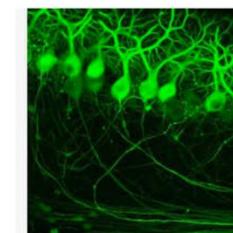
Pyramidal Neuron, Fluorescence...
123rf.com



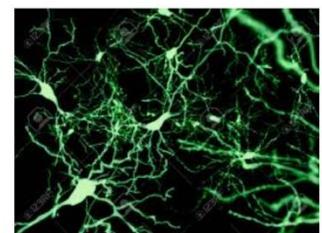
Brain hippocampus neurons, fluores...
sciencephoto.com



Fluorescence Stock Footage ...
shutterstock.com



Fluorescence microscopy im...
pinterest.com



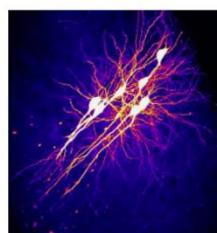
Marked By Fluorescence Stock Photo ...
123rf.com



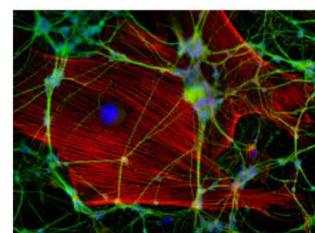
science biology microscopy neuron ...
rebloggy.com



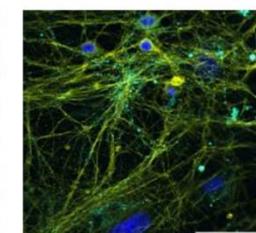
Seeing the brain's electrical activity ...
news.mit.edu



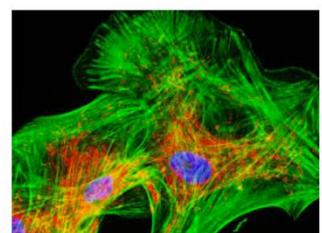
science biology neuroscie...
rebloggy.com



CIL:41649, glial cell, neuron. CIL. Dataset
cellimagelibrary.org



Confusion at the neuronal leve...
fau.eu



Human Cortical Neuronal Cells (HCN-1...
microscopyu.com

Test Your Knowledge

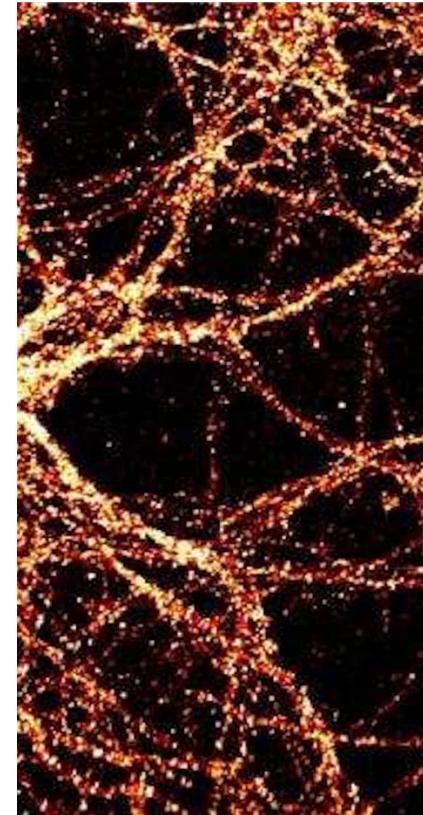
Based on what you looked at so far and using what you know/remember from previous encounters with biology – take a guess what the following images show ...start on the right....

Dark Matter/Energy Simulation

https://www.youtube.com/watch?v=Ssxd_dvnuYo

(this video is amazing)
Illustris project

Yellow: normal matter
Purple: dark matter
Black: Dark Energy

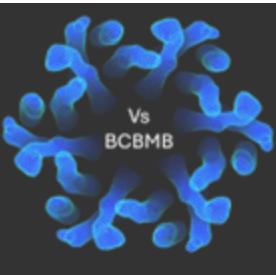


Hippocampal Neurons

© Yu, H et al (2015)
Nat Neurosci 18:836-43

©
<https://medicalxpress.com/news/2015-04-neurons-constantly-rewrite-dna.html>

The resemblance between the structure of the Universe and biological structures at the microscopic level is stunning (to me), loudly broadcasting one message: **“fundamental patterning in nature is independent of scale”** = you will find recurrent organizing principles in things that may seem completely unrelated ...let say: quantum mechanics, biology, sociology, or urban planning.



Setting the Stage

Likening the structure of the Universe to that of biological structures based on phenomenological similarity creates an interesting puzzle. **Why?**



Answer: analogy calls for equating visible matter (5%) **and** invisible dark energy/matter (95%) with macromolecules in living systems ...

....dark matter is called "dark" because we cannot directly see it = **the analogy implies that in a living system, any given molecule sees mostly "nothing/empty space".**

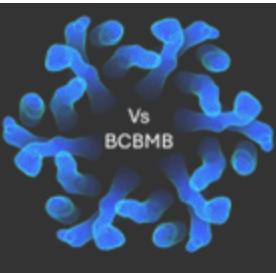
→ this not only is true, but life is even more extreme in that most molecules "see" only a tiny fraction of 1% of all other molecules (in most cases don't even see identical copies of themselves).

→ **How then can biology work if any one molecule "sees" mostly nothing/"empty" space?**



Answer: works because what may look like "empty" space to any one molecule **is not really** empty = we don't see dark energy/matter directly....but....it's still there, and it sure impacts us! → Same holds in biology: any one molecule doesn't see most of what is around it ...but...that "something" is still there and impacts all the things that can't see it (and that it cannot see either).

→**In other words:** components of a complex system neither need nor want to "see" everything (in fact, they must not "see everything") to know what to do because **operating instructions are issued AND moderated by the entire ensemble.**



Setting the Stage



The importance/role of ensembles is something you can understand through your own life experience....

- For instance: teamsports – your team cannot win if **everybody ALWAYS** wants to drive the action.
- Or: in the armed forces – a Private neither needs to know nor will they discuss the logic behind orders issued by the commander in chief ...

Another example, but at a much larger scale, is related to **“six degrees of separation”....do you know what that refers to?**

Answer: it's the idea/theory that each person is related to each other person on the planet through at most six social interactions/intermediaries.

What do “six degrees of separation” mean in terms of microscopic biology and what is the impact of this on the dynamic behavior of a biological system?

Thought Experiment: imagine you stand in a room with 100 people. Now imagine moving around as you see fit. What would you experience?

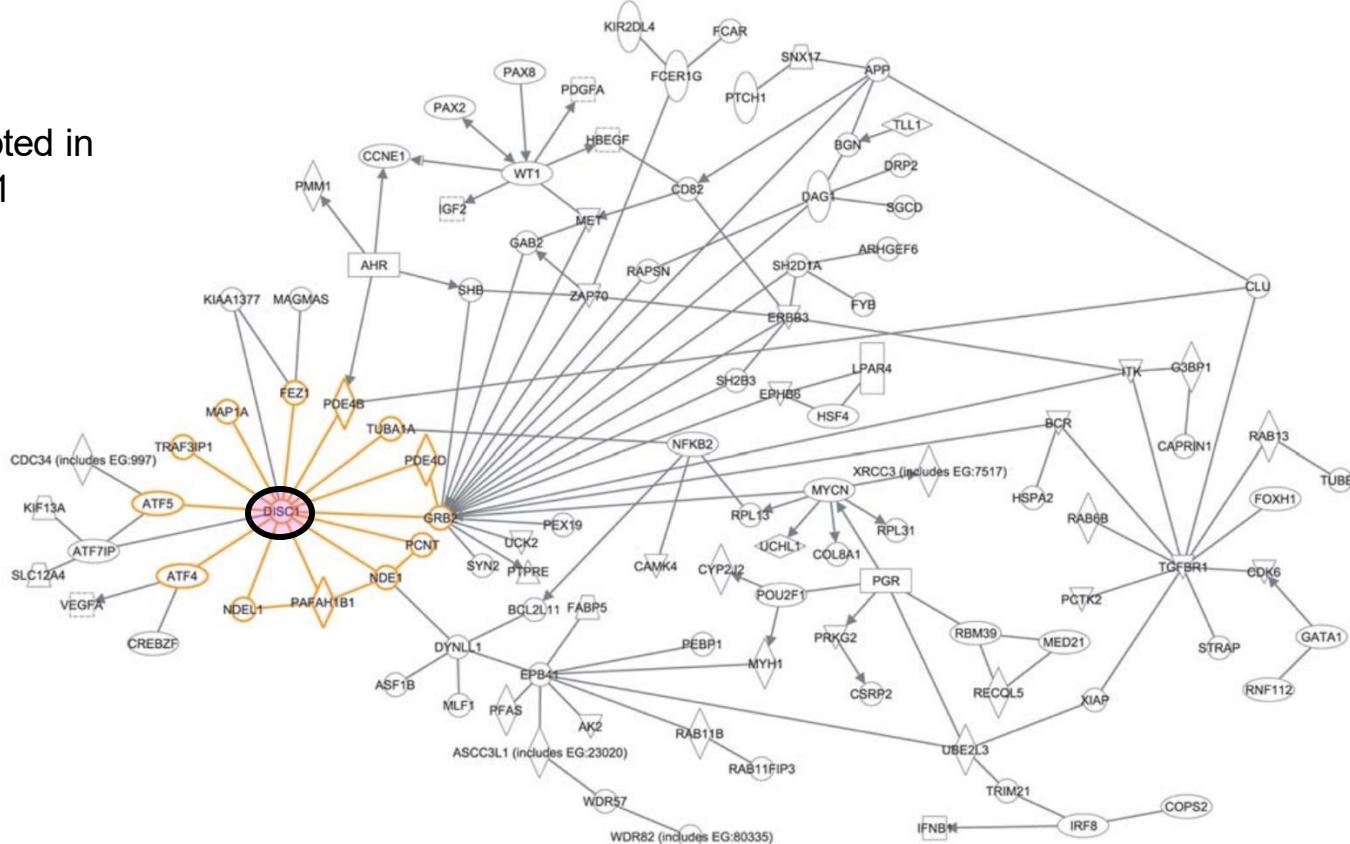
Thought Experiment – Step 2: at some point, randomly gab the hands of two people close to you – if you are first or last person in the chain...put your free hand on the shoulder of anyone in the chain that you can reach within a few steps. Now, close your eyes and try again to move exactly like **YOU** want.

What do you experience?

Setting the Stage

How does this thought exercise look in terms of molecules?
instead of people?

DISC1 – Disrupted in
Schizophrenia 1



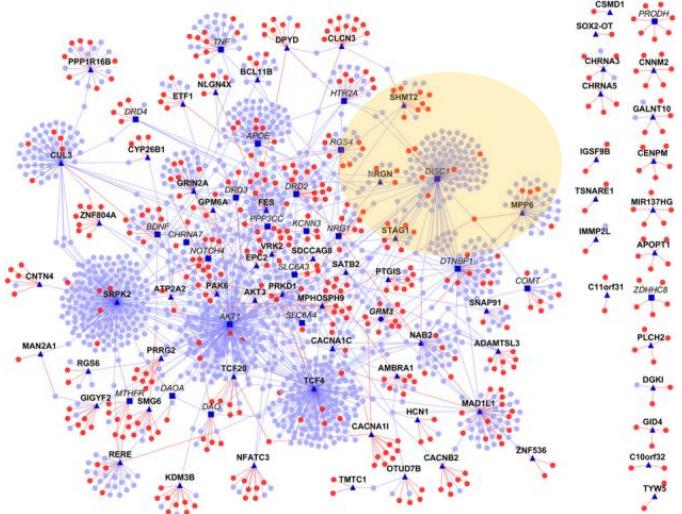
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Figure 2. Network of how 100 of the 528 genes identified with significant differential expression relate to DISC1 and its core interactors. Network generated through the use of Ingenuity Pathway Analysis (Ingenuity Systems®, www.ingenuity.com), using the build function and connecting the identified genes to the core DISC1 interactome, only allowing for direct interaction. Relationships are supported by at least 1 reference from the literature, from a textbook, or from canonical information stored in the Ingenuity knowledge base.
doi:10.1371/journal.pone.0004906.g002

Citation: Hennah W, Porteous D (2009) The DISC1 Pathway Modulates Expression of Neurodevelopmental, Synaptogenic and Sensory Perception Genes. PLoS ONE 4(3): e4906

Setting the Stage

InteractomsZooming “Out”



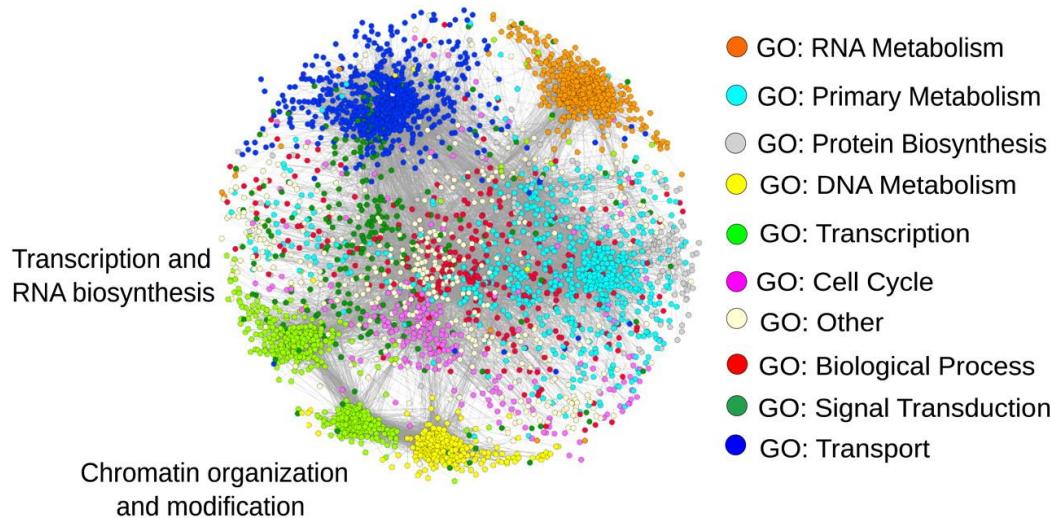
© 2016 Schizophrenia International Research Society/Nature Publishing Group

Ganapathiraju, MK et al (2016)

NPJ Schizophr 2:16012

“Schizophrenia Protein:Protein Interactome”

pale orange shade: DISC1

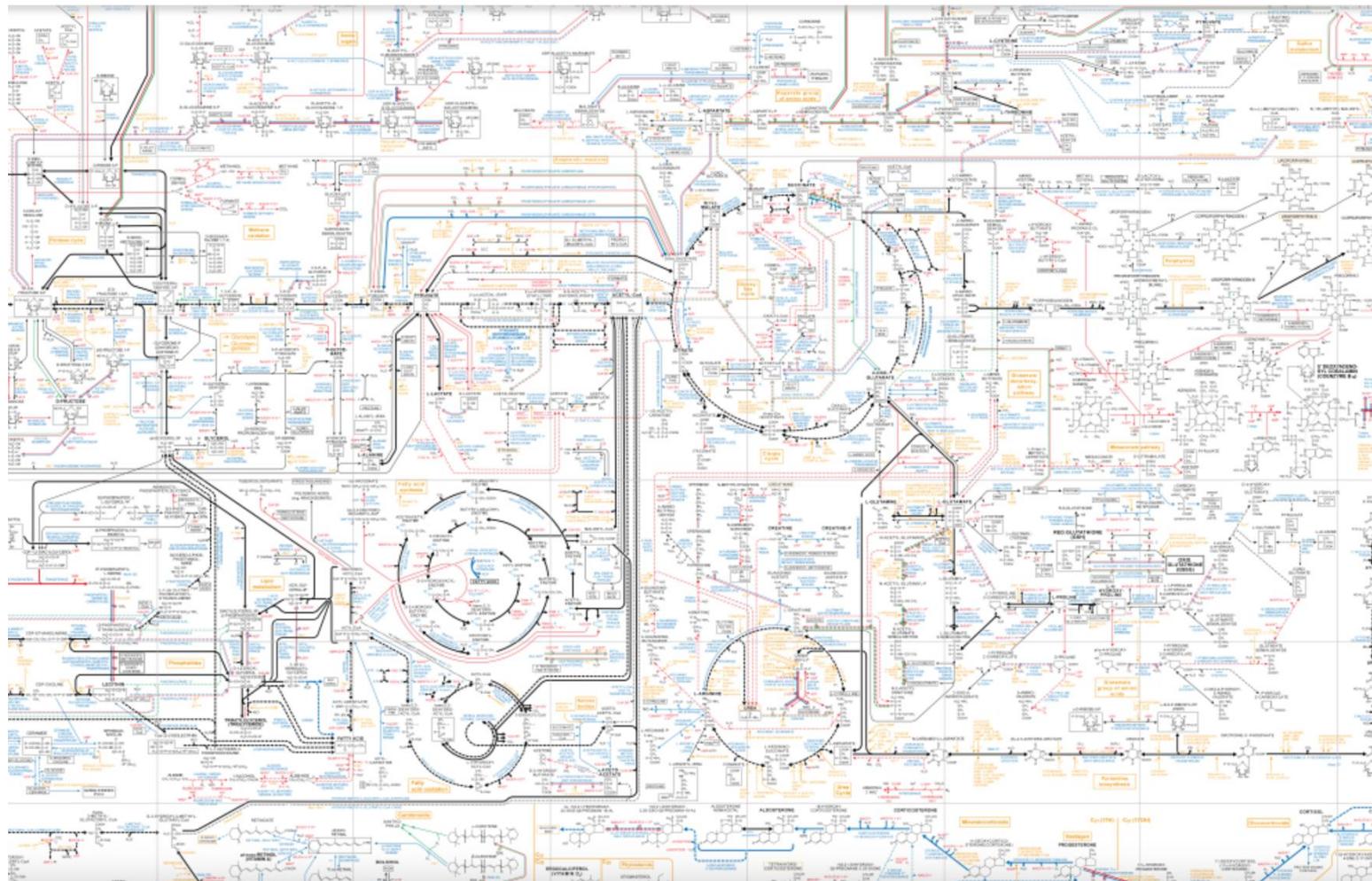


© Pancaldi V et al (2012),
Genes, Genomes, Genetics 2(4):453-67

GO means: Gene Ontology (a bioinformatics initiative to annotate genes and functions of gene products in a consistent way and with a uniform vocabulary)

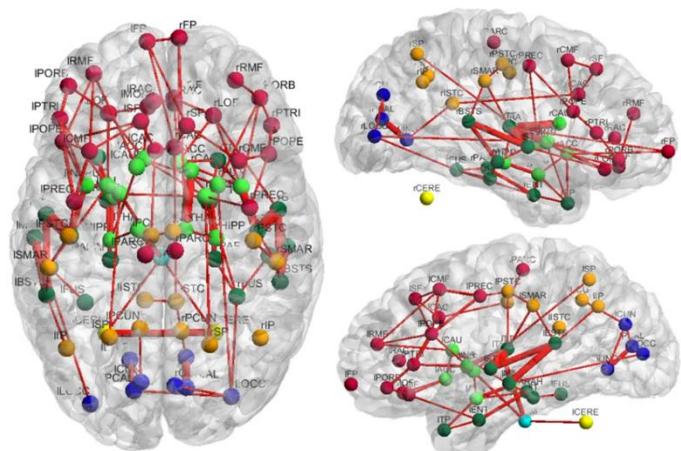
Setting the Stage

Similarlythe chemical engine inside biology is highly integrated and interconnected because many of the individual chemicals act as regulators in loops that control the activity of the biological catalysts (= the “interactome and metabolome” are extensively interconnected)



Setting the Stage

....and making our way back towards the “Universe” by zooming out.....



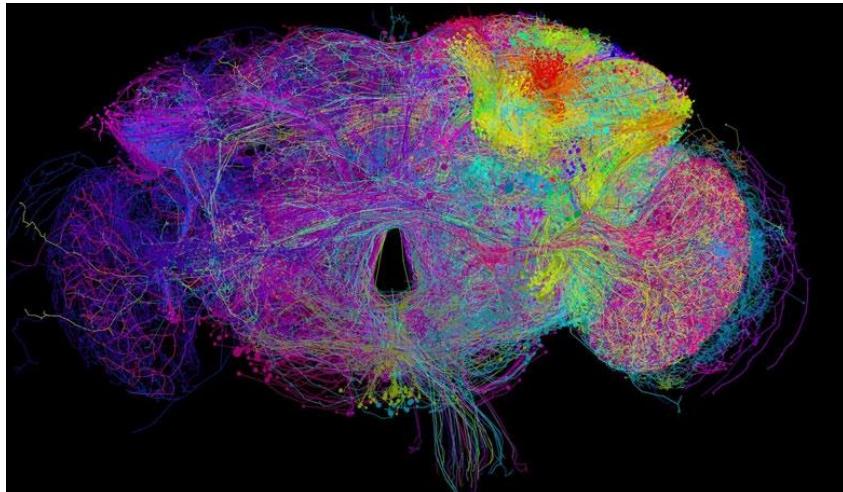
Structural-Functional- Connectivity Map Language Processing Human Brain

Showing Top 20 connectivities observed in test subjects; line thickness represents consistency between different subjects

© Chu SH, Parhi KK, Lenglet C.
Sci Rep. 2018 Mar 16;8(1):4741

Circuit Map of Whole *Drosophila melanogaster* (fruitfly) brain

Colorized to distinguish neural paths originating in different brain regions



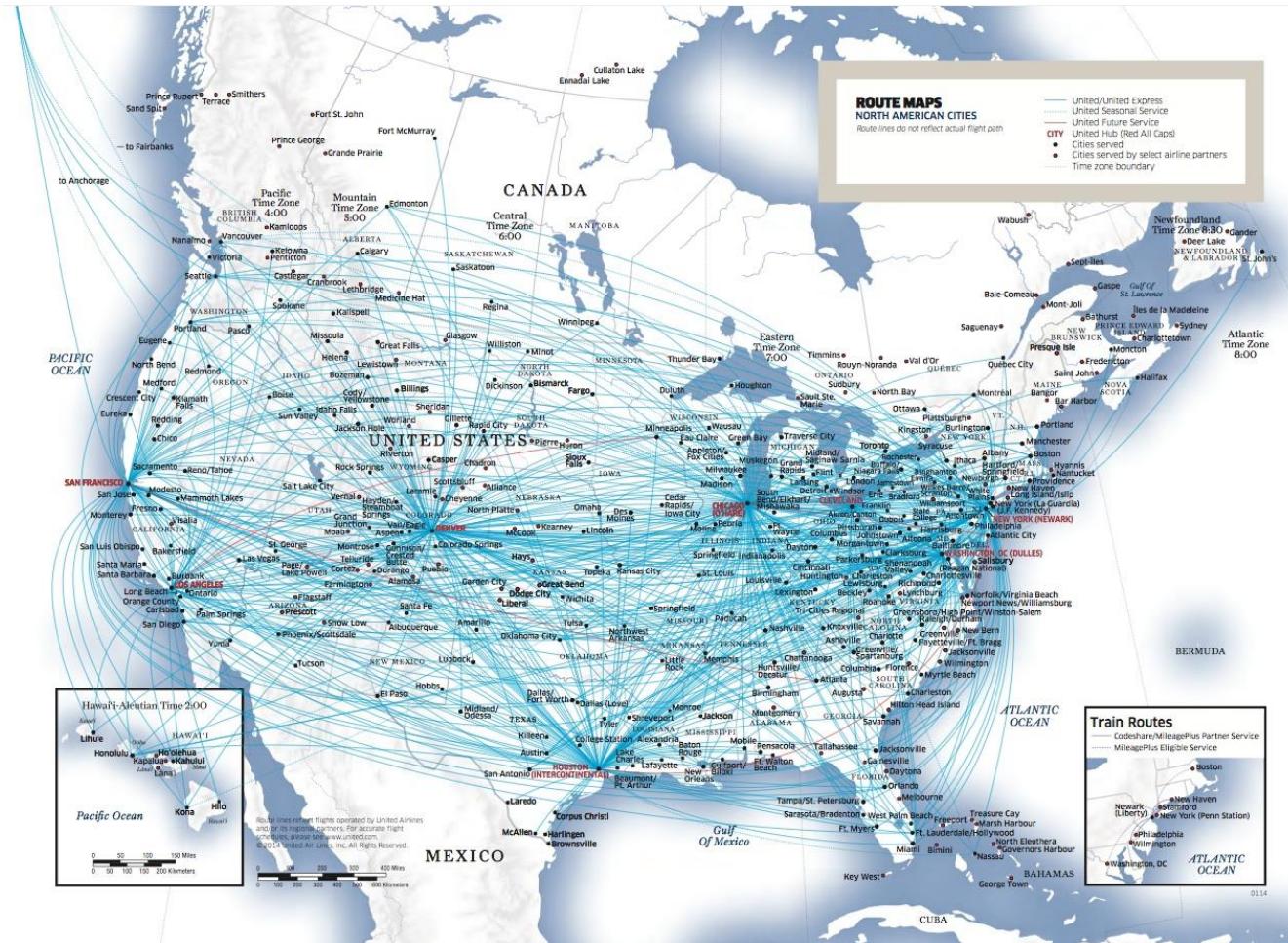
©

<https://www.sciencenews.org/article/most-complete-look-yet-fruit-fly-brain-cells>

Univ Cambridge/UK

Setting the Stage

....and zooming some more.....

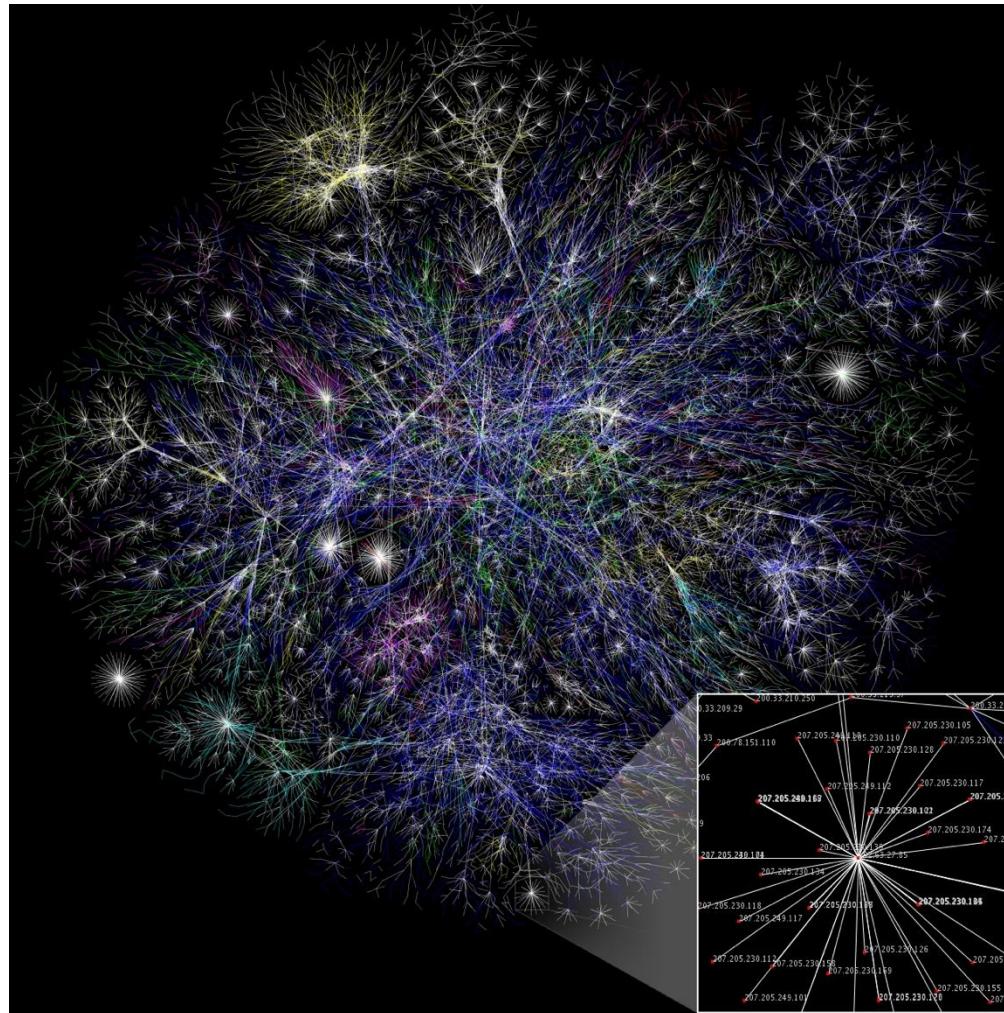


© United Airlines Domestic Route Map (not current)

Setting the Stage

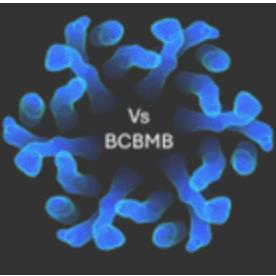
....and zooming some more.....

Partial map of the Internet by IP numbers



1

https://upload.wikimedia.org/wikipedia/commons/d/d2/Internet_map_1024.jpg



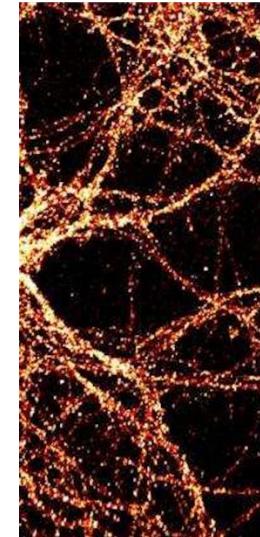
Setting the Stage

.....and look where we got.....starting by googling “cell images” we ended up in a very different place. That place teaches us what very well may be **the most important things** to take away from this entire quarter....



Insight 1: Life, the Universe and “Cell Biology” are **idiosyncratic, emergent properties of matter that is capable of non-random atomic/molecular interactions.** The non-random interactions drive self assembly processes that create remarkably similar patterns and ensemble dynamics, independent of scale.

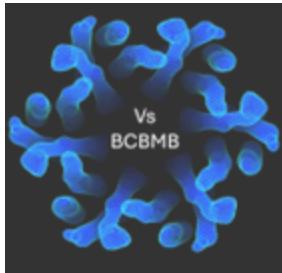
Insight 2: “emergent property” implies many, equally valid trajectories and solutions. That is: **the observable status quo of the entire ensemble is a local minimum that reflects boundary conditions past and present**



Meaning for Life: despite its mindboggling complexity, **Life is NOT overdesigned.**

While one can simplify processes in isolation, any significant (mechanistic) change causes ripples within the entire system that, overall, reduce fitness of the lifeform because the observed complexity of the status quo is Nature's strongest safeguard to allow survival and adaptation.

→**bottomline:** as of today, synthetic biologists can build minimal bacterial cells, but even their biology contains unresolved mysteries

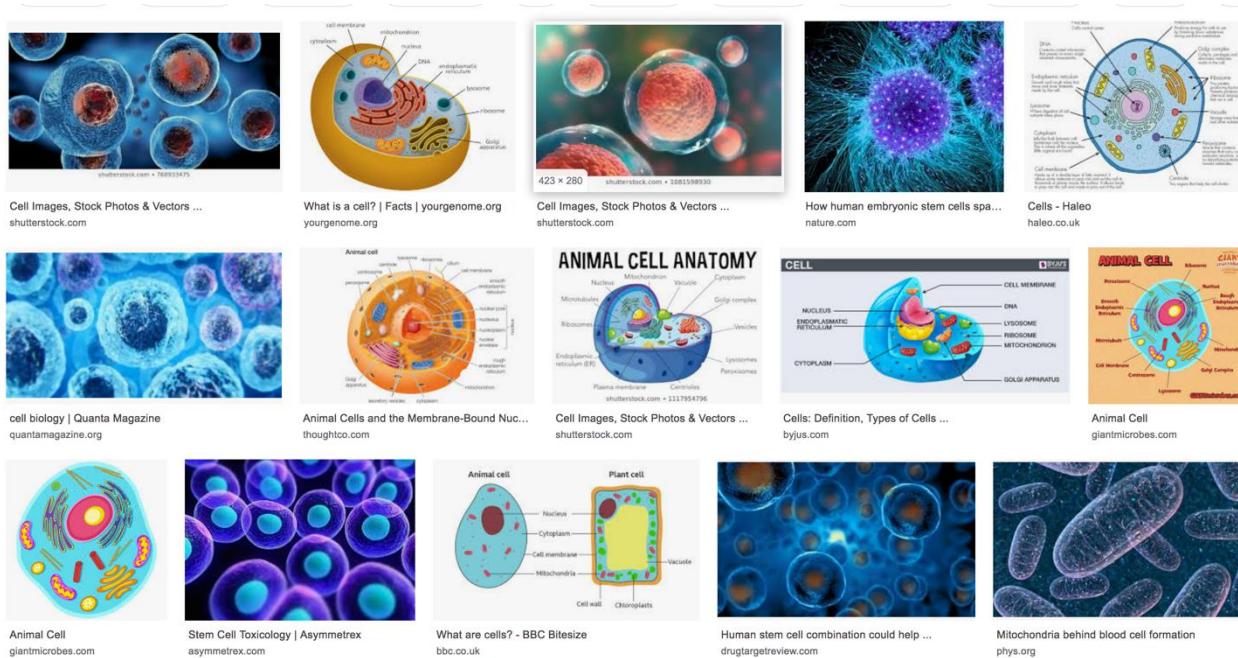


Setting the Stage

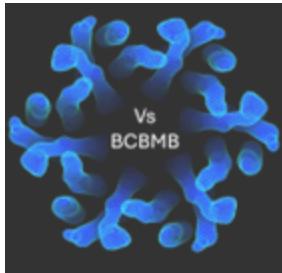


Realizing that the macroscopic structure of the Universe is eerily similar to seemingly different things like biological structures or airline route maps clarifies why the result from a Google Search on “Cell Images” is ...frankly...puzzlesome and scary **How so?**

Answer:.... asked “what is a cell?” is, Google **ONLY shows you**



- exceptionally biased and narrow, with seemingly just one answer!
- Scary!! And untrue..... – open your mind and ask....**what contexts other than biology use the term “cell”?**thank you!



Setting the Stage



.....solar, fuel, atmospheric/storm, religious, terror, prison, hospital, dormroom, tiny house/studio apartment, spreadsheet/table,.....looking at all of them at once, what is the common denominator?

Answer: "Cell" simply means: “small space/unit” ...and just from that generic fact we learn another hugely important thing about Life/Cell Biology/Universe...and what is that?

Answer: “small space/unit” implies partitioning across boundaries/barriers that enable a fundamental **asymmetry** in the distribution of matter. The correlated **compartmentalization** (regardless of its physical nature [eg object, phase boundary; scaffold induced spatial segregation, ideology ...]) is what allows emergent properties to manifest themselves.

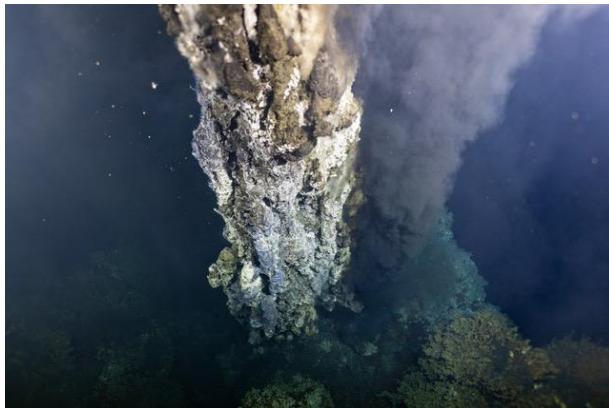
What sets biology/life apart from other emergent systems is that it learned how to deliberately manipulate and to control the properties of space over time. This brings us to a third important insight we want to add:

Insight 3: Emergent properties are more than the sum of the components, they are non-linear, and they are exceptionally damped (resilient). These characteristics allow for an enormous amount of diversification and adaptation....

...lets take a look.....

Setting the Stage

Just a small selection of conditions that Life can thrive in



© Ocean Exploration Trust

Deep vents

No light, no oxygen, 1000atm pressure, temperature near boiling



license [cc-by-sa-3.0](#) copyright Grombo

Salt Ponds

4M NaCl



© Photo by [Hans-Jurgen Mager](#) on [Unsplash](#)

Arctic

Cold/Subzero Temp

Setting the Stage

But the record holders are.....

Tardigrades (Water Bears)



©Taylor Turner/The Washington Post

https://www.washingtonpost.com/video/national/health-science/meet-the-tardigrade-the-animal-that-will-outlive-us-all/2017/07/14/4b921e54-68ae-11e7-94ab-5b1f0ff459df_video.html?noredirect=on

Typically water dwelling but **can survive**:

Temperature

A few minutes at 151 °C (304 F);
30 years at -20 °C (-4 F);
A few days at -200 °C (-328 F; 73 K);
A few minutes at -272 °C (-458 F; 1 K)

Pressure – they can withstand vacuum and also very high pressures up to 6,000 atmospheres, which is nearly six times the pressure of water in the deepest ocean trench

Dehydration – the longest that living tardigrades have been shown to survive in a dry state is nearly 10 years

Radiation – tardigrades can withstand 1,000 times more radiation than other animals, median lethal doses of 5,000 Gy (gamma rays) and 6,200 Gy (heavy ions) in hydrated animals, compared to 5-10 Gy that are fatal to a human.

Source: Wikipedia.com

Setting the Stage

.....and.....

Planarian Flatworms



©

<https://aeon.co/videos/the-blob-with-a-superpower-cut-a-flatworm-in-four-pieces-and-watch-it-regenerate-four-fold>

...you can cut them into pieces....and they regenerate complete new animals!

(...if humans had that ability, the French revolution would have had different consequences...among other things)



Setting the Stage ...Cell Biology at Last

The amazing adaptability of biological organisms is a macroscopic reflection of the underlying pliability of the basic units that make up these organisms

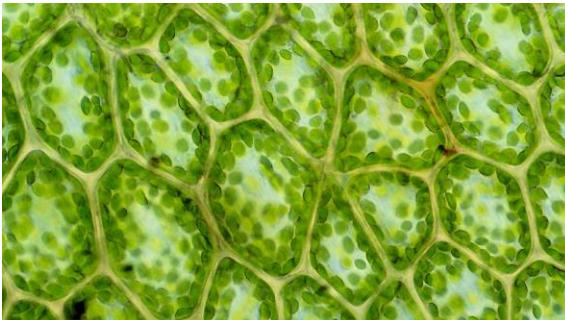
Salmonella bacteria



Image source:

<https://www.fda.gov/food/foodborne-pathogens/salmonella-salmonellosis>

Plant cells



©

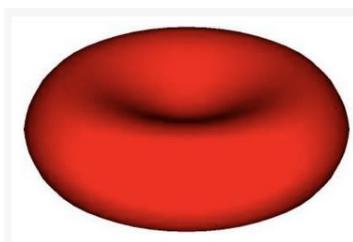
<https://www.bbc.co.uk/bitesize/topics/znyycdm/articles/z2vrr2p>

Neuron



© Image by vecstock, AI generated

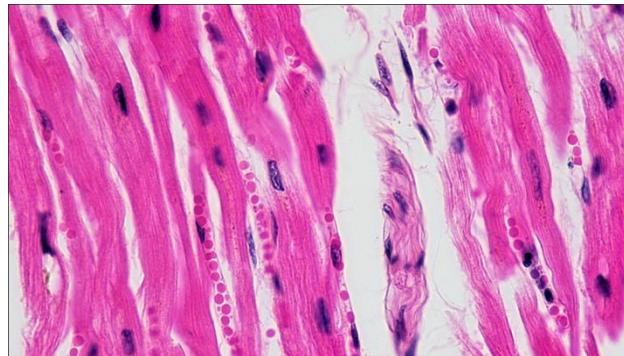
Red Blood Cell



©

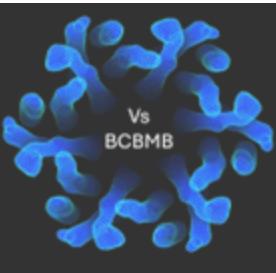
<https://doi.org/10.3390/cells11243987>

Muscle Tissue



Attribution: Berkshire Community College Bioscience Image Library, CC0, via Wikimedia Commons

Note: different cell types (e.g. red blood cells, muscle cells and neurons) in a multicellular organism ALL have the same fundamental programming, but the interpretation of that programming is **redundant** (= tweak of a given/identical template → genome of one species in this case)



Setting the Stage ...Cell Biology at Last



Curiously... **redundancy** motivates much of modern cell biology because it **triggers a vast expansion beyond the founding question that cell biologists study, which is.....**

What is a biological cell? → answering that question doesn't get you far because of the question's interrogative pronoun "what?" = will return a simple fact like "basic unit of life", or "an irregularly shaped soft object formed from various organic macromolecules and inorganic ions, capable of maintaining life".

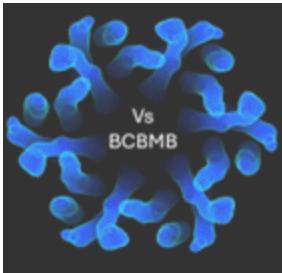
More interesting is to ask: "**How does a cell work?**". The answer to this question aims at understanding mechanism = "what molecules?"+"where?"+"when"+ "what do they do?"

→ **This "playbook" teaches you about:** How do cells/cellular components form? How do they exchange matter? How do they build (their own) components? How do they power the chemical engine? How do they store information? How do they replicate? How do they communicate with the environment? How do they move if they are motile?

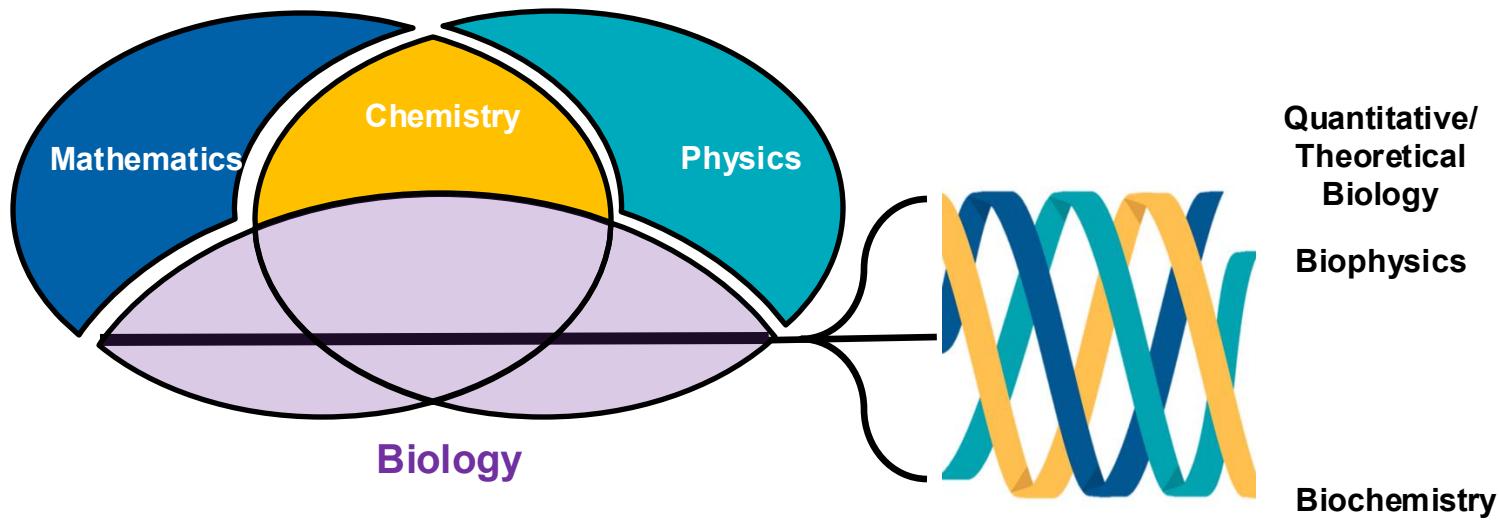
Redundancy comes in as driver in defining questions when you start to look at: how do cells specialize? → How do they form tissues? How do they form multicellular organisms?

Taken together: **Cell Biology is the Science that Studies the Structure and Functional Behavior of Life's Basic Units**

Curiously: a question that is rarely asked, answered, or taught (in biology and many other sciences) is: "why does something work the way it does?" Looking at "why?" is rare because it requires to see the bigger picture, and –ultimately/ideally- follow the trace all the way back to first principles ...



Talking about First Principles ... in the Realm of STEM: **Biology is the MOST Complex Science Because it Integrates ALL Other Basic Sciences**



➔ The high degree of integration and the fact that much of biology is still stuck at a descriptive "fact finding stage" are key reasons why studying biology can feel frustrating ... there just doesn't seem to be system in all the madness.

...until you ask "why something works the way it does?" we will try to do that whenever possible ... and while it will fall far short of going all the way to first principles, you hopefully will discover that life is amazingly organized and "logical" once you care to look closely enough.

Biology is also Evolving

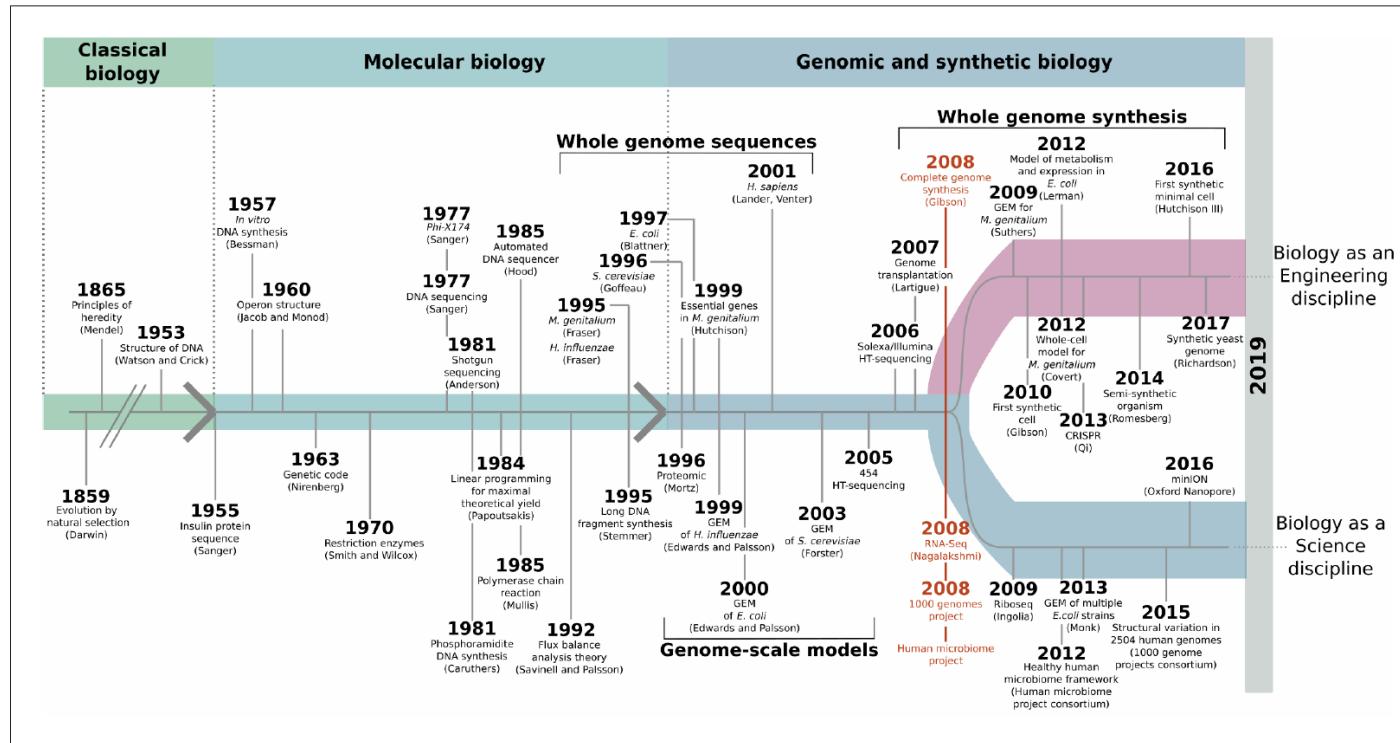
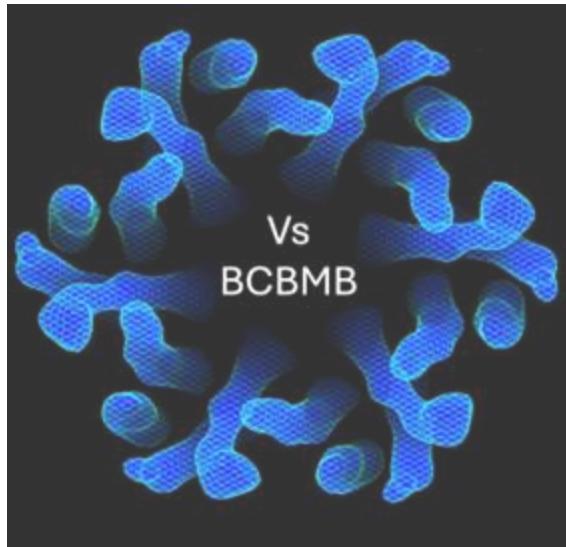


Figure 1. Synthetic biology and minimal cells: an historical perspective. Elucidating the DNA double helix marked the beginning of the molecular biology era, and it became possible to study molecular mechanisms that underpinned observable phenotypes. DNA sequencing methods improved, leading to whole-genome sequencing at the end of the 1990s. Methods for mathematical cell modeling were developed during the 1980s and 1990s, and computer simulations of metabolic networks (also known as genome-scale models of metabolism, or GEMs) could be reconstructed. A defining moment took place in 2008 (red), with the creation of the first artificial genome that mimicked the genetic information of *M. genitalium*, the free-living, non-synthetic organism with the smallest genome. Thanks to developments in next-generation sequencing methods, this was paired with the rise of large-scale genome sequencing ventures, such as the human microbiome and the 1000 genomes projects. Advances in whole-genome synthesis, assembly, and transplantation helped create the first cell living with an entirely synthetic genome shortly after. Taken together, these achievements marked the coming of age for synthetic biology.



Slides are freely available at
vsbcmbstudy.com