

The top of the page features a decorative background with a large, stylized SFI logo on the left, composed of concentric circles and a central geometric pattern. To the right of the logo are several curved, parallel lines in a light yellow color. Scattered across these lines are small, white icons representing various scientific fields: a DNA double helix, a chemical structure, a network diagram, a microscope, and a hand holding a test tube. The main title 'SFI TRANSMISSION' is centered in a large, bold, black sans-serif font. Below it, the subtitle 'COMPLEXITY SCIENCE FOR COVID-19' is centered in a smaller, bold, black sans-serif font.

# SFI TRANSMISSION

## COMPLEXITY SCIENCE FOR COVID-19

**STRATEGIC INSIGHT:** The COVID-19 pandemic offers an opportunity to out-evolve the virus by evolving our own scientific ingenuity and social practices.

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If there is one thing that the coronavirus pandemic has exposed, it is that there is much that we still don't know about the world around us. Forget about the trillions — okay, more than trillions — of galaxies in the universe that we'll never explore. Just at our feet or in the air around us are cohabitants of our own world — viruses — that occupy an odd liminal space, pushing our understanding of the meaning of *life*. They exist in what is effectively a hidden world, almost a “first Earth” that is both just offstage and right in front of us, and even inside of us. It's a world teeming with activity, full of blooming, buzzing confusion, competition, and evolution. Sometimes we explore this world intentionally, but at other times we run into it by accident, most noticeably when the alarms on one of the megafauna bio-detectors — people and animals — go off. It's when these encounters happen that we remember that the space of things we don't know is truly unfathomable.

Puttering around on the edge of the known and the unknown is the standard work of science and scientists. While the twinkling of the night sky may often be an inspiration for meditations on how little we understand, it's actually what we can't see in the cosmos that is the best reminder of our limited vision. In 1933 Fritz Zwicky observed a huge discrepancy in the amount of gravitational force needed to account for the rotational movement of galaxies and the amount that could be attributed to the visible matter in the galaxy. Naturally, he called this “dark matter.” In 1980 Vera Rubin and Kent Ford used spectrographic data — its own form of making visible the invisible — to show definitively that galaxies contain at least six times as much dark mass as visible mass. As it turns out, Aristotle was wrong: nature *loves* a vacuum — that's where it stores most of its gravitational potential.

Countless studies and observations point to the conclusion that nearly 30 percent of the universe is made of dark matter. Dark matter is a big part of what holds the universe

together — more stuff for creating attractive forces between things. But, as you may know, ever since the Big Bang, the universe is actually expanding. The cause of this is a different force of darkness, or, rather, something that goes by the name “dark energy.”

Our understanding of the biological world has also been a story of the discovery of dark matter and dark energy, and our collision with the coronavirus is just the most recent reminder of that theme. Early censuses dramatically underestimated the amount of living matter, a darkness of understanding largely borne of poor optics. Our inability to see at the scale of microorganisms was a source of a good deal of pseudoscience bordering on mythology, especially when it came to disease. “Vapors” and humors were the first dark matter. It was only in the 1880s, twenty years or so after the publication of Darwin’s *The Origin of Species*, that Robert Koch discovered bacteria and, in so doing, revealed a material cause for infection. Among Koch’s great advances was his use of staining and culturing to make visible the agent of infection. We now know that bacteria and other microorganisms account for most of the world’s genetic diversity, not only in the environment at large, but also within our own bodies, where our inner microbial ecosystem of the microbiome turns out to be crucial to human health. Some forms of “infection” are deadly, but some are necessary.

Viruses like the coronavirus are even smaller than bacteria, and so were also dark for some time. They were brought to light in the late nineteenth century, discovered by the Dutch microbiologist Martinus Beijerinck in the course of investigating the etiology of mosaic disease in tobacco plants. Repeated efforts to culture the source of the disease failed, so it wasn’t bacterial in nature — biologists were the first to understand that you need culture to live — but whatever was causing the disease was able to replicate. It was alive in some ways, but dead in others. Beijerinck called this “infectious agent” a virus.

We now know that a viruses are basically nano-encapsulated genetic information. They have existed from the beginning of biological time, emergent from the proverbial primordial soup, a string of atoms, clumped into molecules, wrapped in another kind of molecular shell, a kind of biological M&M. The *raison d’être* of the virus is reproduction, which ironically leaves a fair amount of death in its wake. But really, the virus is an engine of life whose dynamics and mechanisms of existence and reproduction make it the agent of genetic expansion, a “dark life” biological force to the dark energy physical force fueling Universal expansion that is dark energy. Not quite twins separated at birth, but siblings separated by several billion years, give or take.

It is now believed that the nucleated eukaryotic cell, upon which all animal and plant life is based, would not exist were it not for simple viral genes that first copied themselves into ancient host genomes. This led to selection pressures fomenting the formation of cellular membranes and cellular inclusions. It has been hypothesized that without

the constant drive from highly mutable viruses there would have been no need for the evolution of recombinational sex — the kind that all animals and plants use, not to be confused with recreational sex!

In a kind of Nietzschean “that which does not kill us makes us stronger” way, any ability that we do have to fight off some diseases can also be at least partly attributed to viruses. Had jawed vertebrates (all vertebrates but lampreys and hagfish) not acquired genes of viral provenance some 500 million years ago, they would have no adaptive immune system and thus minimal means of fending off viruses,

If bacteria had not absconded with viral endonucleases, they would have had no restriction enzymes to protect themselves against viral infection. And without restriction enzymes, our society would have had no science of genetics which made progress based on the unique ability of these enzymes to cleave DNA. Furthermore, CRISPR, the most revolutionary genetic engineering tool in the history of biological science, is effectively the recapitulation of a bacterial anti-virus defense system that kills an infiltrating virus by slicing it into genetic pieces. Current vaccine delivery techniques and other forms of biological therapies rely on a mimicry or instigation of virus insertion mechanisms. What was once dark was eventually brought to light, and once brought to light, helped to bring light — and life.

<b>VIRAL INNOVATION</b>	<b>EXAPTED ADAPTATION</b>	<b>ENGINEERING UTILITY</b>
Mobile Genetic Element	Prokaryotic CRISPR	Genetic Engineering
RAGs	Adaptive Immunity	Immuno-therapy
Endonuclease	Restriction Enzyme System	Molecular cloning
Group II Introns	Eukaryogenesis	Targetrons
Oncolytic virus	Tumor antigens	Oncolytic virus therapy
Membrane proteins	Cellular tropism	Vaccine vectors

**Figure 1. VIRAL EDUCATION:** This table represents paths from nature to therapy. It shows viral genetics (viral innovation) that have been co-opted by other forms of life (exapted adaptation) and that have been used as a part of human genetic engineering (engineering utility).

Our all-too-human tendency to focus on what is directly or instrumentally visible, or of comparable scale to ourselves, has blinded us to both the largest and smallest scales of the universe — scales where physical forces shape the elementary structure of matter. We are also blinded to those living scales invisible to the eye that have shaped the form and

function of adaptive matter. The COVID-19 crisis has made the terrifying dark energy of evolution visible and has brought us closer than is comfortable to the engines of selection. We live in an invisible ocean of microbial diversity and menace, one that is insensitive to the transience of multicellular life. Maybe now is the moment for us as a culture to learn from our microbial allies in the universe of dark matter — the bacteria — from whom we acquire our symbiotic microbiome — that the best way to defeat the dark energy of the virus is to turn its entropic ingenuity against itself and out-evolve the virus by evolving our scientific ingenuity, and probably our social practices too. We'll have to adapt; what choice do we have?

*Read more posts in the Transmission series, dedicated to sharing SFI insights on the coronavirus pandemic: [santafe.edu/covid19](https://santafe.edu/covid19)*