

# Managing Expectations for Emerging Technologies

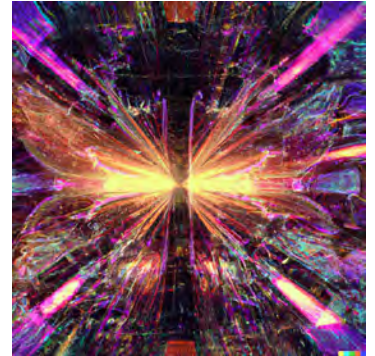
SSAB – Opening Remarks



David A. Shaywitz, MD, PhD

25 August, 2023

(All artwork via DALL-E)



# Disclosures/Affiliations



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**Note:** the views expressed in this talk reflect my own, personal perspectives, and may not reflect (and should not be assumed to represent) the views of any of the above organizations.

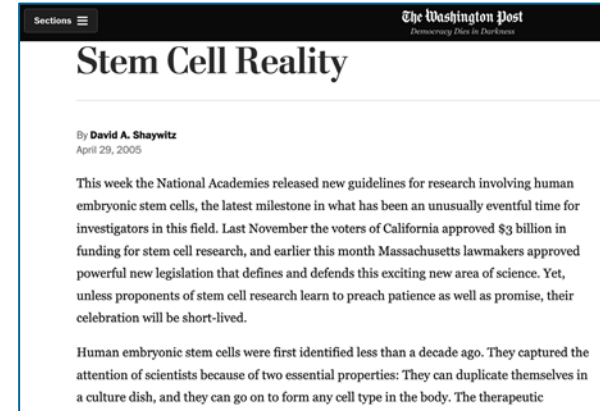
# Focus: emerging technologies in medicine



Genetics



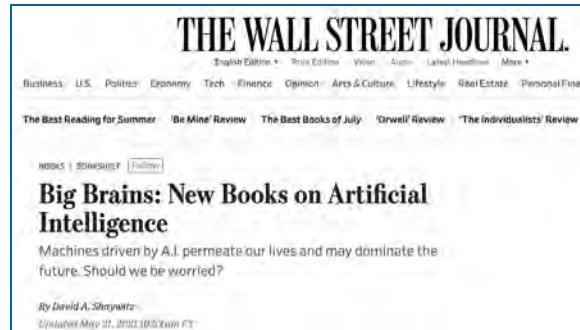
Gene Therapy



Stem Cell Biology



Digital Health



AI



Synthetic Biology

# Today

- Brief vignette: the arc of molecular medicine
- Discussion of the challenge of calibrating expectations for emerging technologies; process typically includes:
  - Initial extravagant expectations
  - Hype, hope, disappointment, disillusionment
  - Eventual realization of tangible, often profound, impact
- Takeaway: emerging tech powerful but impact rarely immediate

# Vignette: Molecular Medicine



Sydney Brenner

**1982:** With complete DNA sequence and a big enough computer, you can “compute the organism”



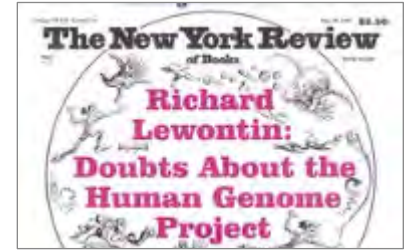
Walter Gilbert

**1991:** With complete human genome, “We’ll know what it is to be human”



Richard Lewontin

(1992)



“FETISH...An inanimate object worshipped by savages on account of its supposed inherent magical powers, or as being animated by a spirit. (OED)”

# A DNA Sequence Is Not A Drug (after Brown & Goldstein, JCI)



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CGGGAAGGA AGCAGGCTCT CTGAAGAAAT ACTTCAGGAG TAGAAAGAGG ARGCTAGAGG
GAGTTAGTAT ATGTCTAGAG GTGTAGTAAJ CTAMACAGG TCTTGARTTG CATACCGGCA
AGGGAAATTC GACGCTCTGT ATTACTAGAG AGCTTCTATC AACCGGCTCA AACCGGCTCA
AACTTGTCTT GCATCCGATG GPCATGAGGC TCCAGTCTGA CBAITCTGAAG CATGGGCAAG
TGGCTCTTTA TGCGAAGTAC CTGGTCTTTC CATCTCTGT TTAAGCTAGG GCTTCTCTTG
TCATTCTAT AGATTAAJAA AAAAGAAATC AATGGAAGGC ARGTBATTAA GCTTCTCTTA
BAGCGGATTA ACCYACAGAG AAGGTCCAGG GAATAGGCTT ATTTCTTATG CTATTTCTTA
TCTCCATCCA CTCTCTCTAG CTCTGGCTTG AAGCTATCTT TAAAGGTAGC CTGTACAGGC
TCTTCATTA GGACACATCT CATTCGCAGA TAAACAGGCA AGTTATATA TGTATGAAGC
GTCTTAAGAC TATAGTAATJ TCTTCAGCTC AAAAGGCCCT CTATTATCTC TATCTGAGAT
TAATCCGACC TGGCTCTACJ AAGCTAGGCT GGACAGACTT TTAAGCAATC ATCTCTTAC
AAAAACCAAJ GTGAGCATCC CATCTCTCTC CATCTCAATG ACCTAGAGCA AAGGACTAGG
CAATGAAATC TCTTTCTAT ATAGTGNCA GGAACACTCT TTTATCTTAC AACTTGGCTG
AAGGTTTACG TGGACTTAA AGGTGAGGAG GAANACAAJ GGTTAAGAGC TGTGTCTCTG
CTATATCTT CTAGAGCAT CTCTCTCTCT GCTTCTCTG TATGTCTGAG TCTGAAAGAG
TGGACAGTCT ATACTCTAGG TCTCTTACTC AGAGCATATG CCTTCTCTCT TCTCCCATTA
GGACAGATCT CATACCTCAA ATAGCTAATA CTCTGATAGC TATGATCTCT AAGGCTCAAJ
TATATTTTAC GCTTCTCTCT TGGCAAGGAT GTTCTGCTAG GGTCTGCTAA AAATAATGCT
CTCCAGAAAG TGGTAGAGG CTCCAGGAGC CAATCTCTCT TGGAGCTCA GACTAGCTAC
CTGACCTTAA TTAGCTTACT GAGCTGAGAG AAGCTCTTCT TCCCTCCACT ACACCTAAGC
TTCGAATTCG TTAACAAAT ATCTTCACT CTAACTATA ATACCACTAT GAGACAGCTC
AGCCAGACAC ATGCTCTTAT GAGCTGGCTA CTACCCAGG GCTTCTCTCT GAGACAGCTC
    
```

*Ceci n'est pas un médicament.*

2010 Goldstein and Brown

Figure 6. Top: *La trahison des images* (*The Betrayal of Images*), René Magritte, 1929. Text reads "This is not a pipe." Bottom: A contemporary version of Magritte's painting adapted to the biotechnology industry. Text reads "This is not a drug." © 1997 C. Herscovici, Brussels/Artists Rights Society (ARS), New York.

# 2001 Cancer Hope: Genome + Gleevec



(2001)

# 2008 Cancer Despair



## **We Fought Cancer...And Cancer Won.**

After billions spent in research and decades of hit-or-miss Treatments, it's time to rethink the war on cancer.

## **The New York Times**

Advances Elusive in the Drive to Cure Cancer

# But then... A New Hope



(2013)

## The Nobel Prize in Physiology or Medicine 2018



© Nobel Media AB. Photo: A. Mahmoud

**James P. Allison**

Prize share: 1/2



© Nobel Media AB. Photo: A. Mahmoud

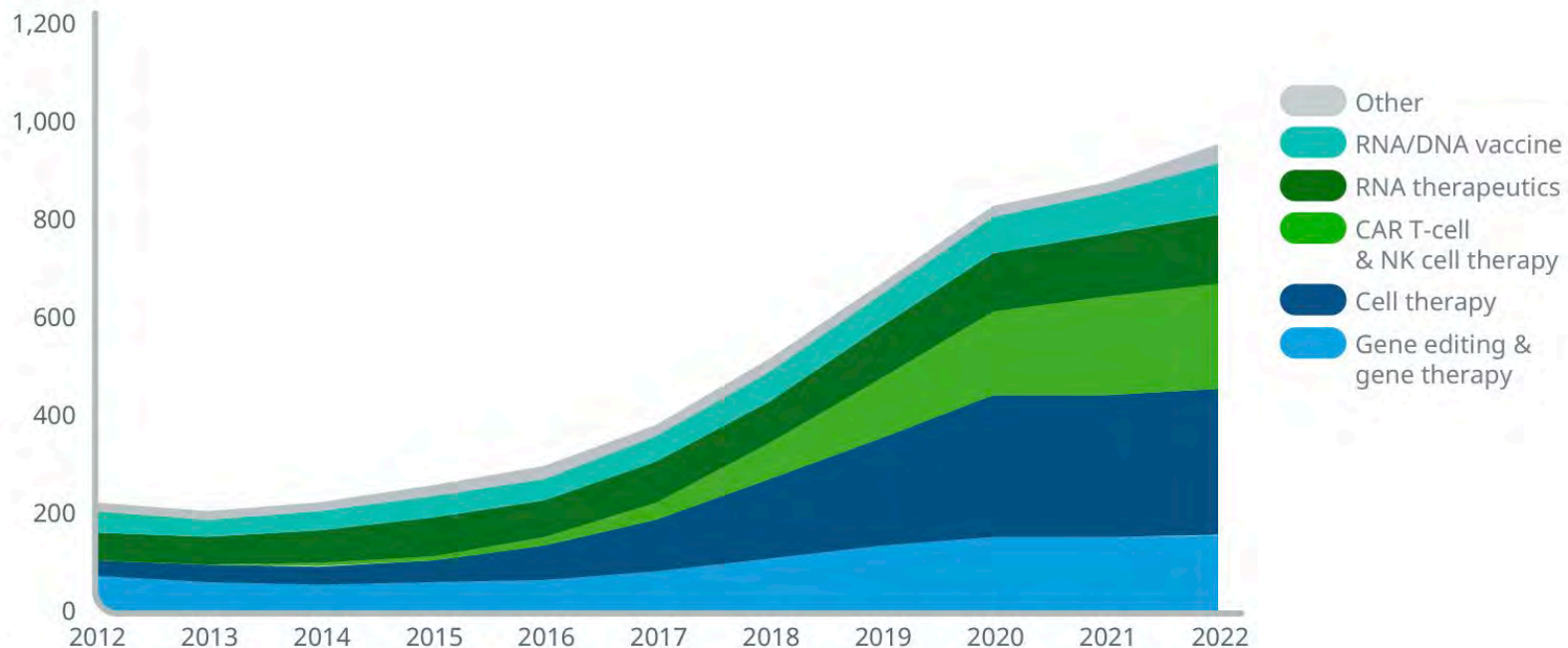
**Tasuku Honjo**

Prize share: 1/2

The Nobel Prize in Physiology or Medicine 2018 was awarded jointly to James P. Allison and Tasuku Honjo "for their discovery of cancer therapy by inhibition of negative immune regulation."

# The next-generation biotherapeutic pipeline is focused on gene editing, CAR T-cell and other cell therapies

Exhibit 13: Next-generation biotherapeutics Phase I to regulatory submission pipeline by mechanism, 2012–2022



# Abundant opportunities in biology

Tremendous biomedical and investor excitement around

- Gene therapy
- Cell therapy
- Gene editing/CRISPR
- Imaginative combinations – engineering cells, dialing in and out features and capabilities in shockingly audacious fashion

# Golden Age?

The New York Times Magazine

## Suddenly, It Looks Like We're in a Golden Age for Medicine

We may be on the cusp of an era of astonishing innovation — the limits of which aren't even clear yet.

Give this article



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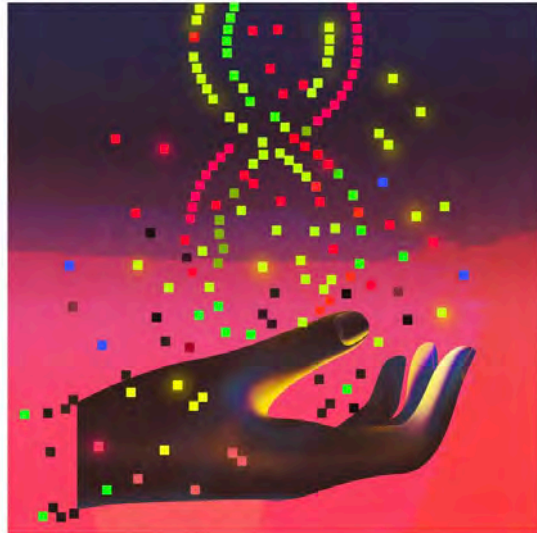


Illustration by Ibrahim Rayintakath



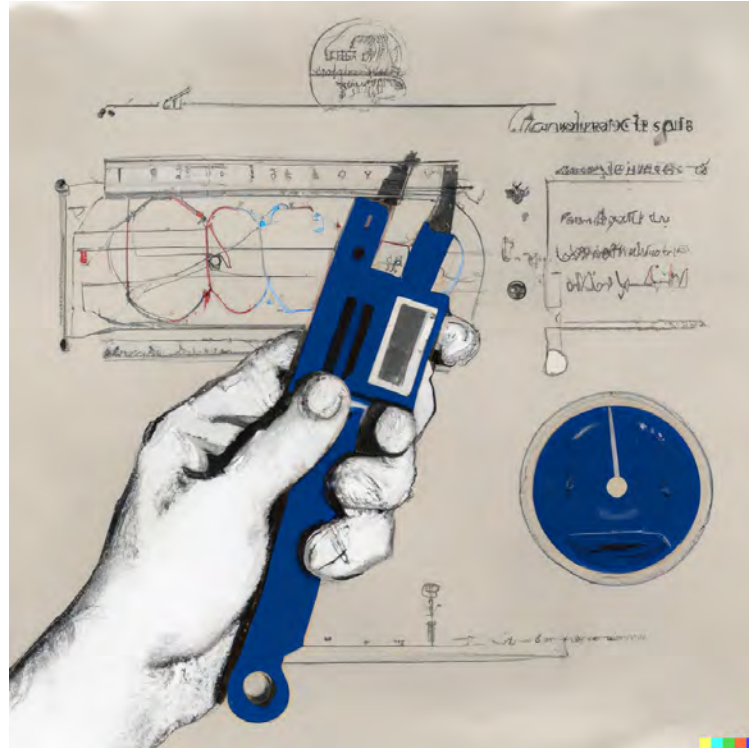
By David Wallace-Wells

June 23, 2023

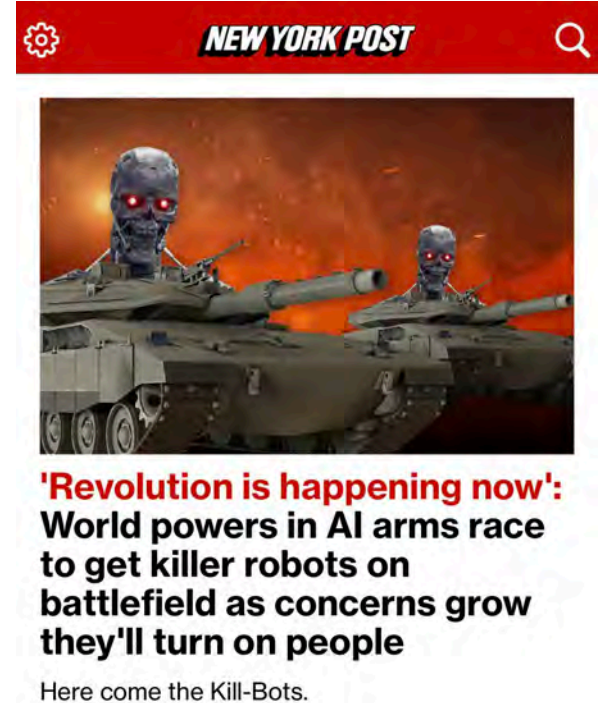
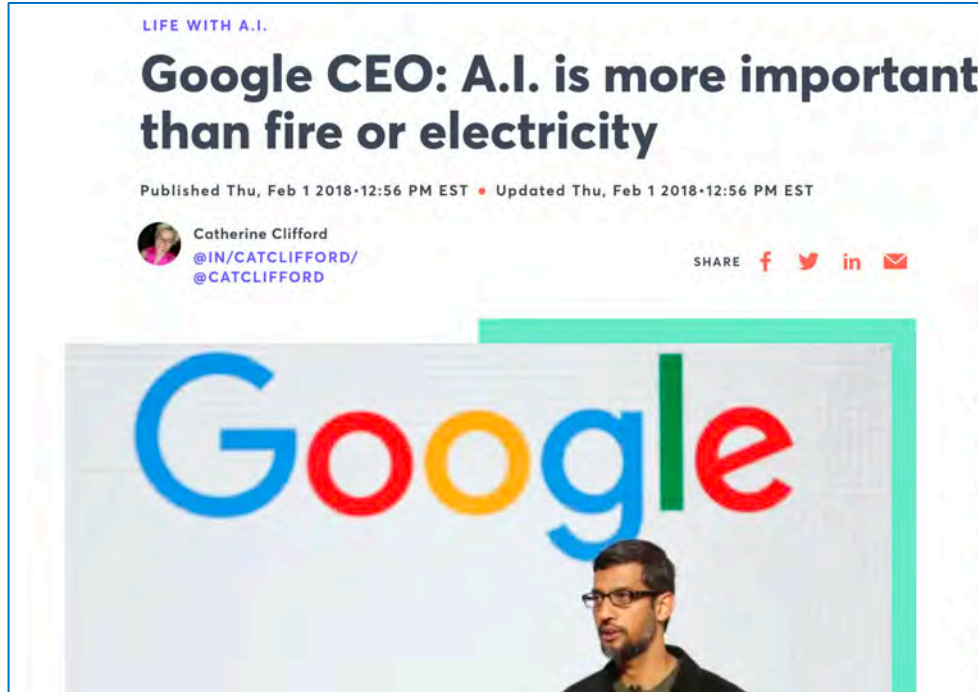
Hype springs eternal in medicine, but lately the horizon of new possibility seems almost blindingly bright. “I’ve been running my research lab for almost 30 years,” says Jennifer Doudna, a biochemist at the University of California, Berkeley. “And I can say that throughout that period of time, I’ve just never experienced what we’re seeing over just the last five years.”

NYT June 23, 2023

# Calibrating Expectations For Technology



# Emerging technology often characterized by extremes...

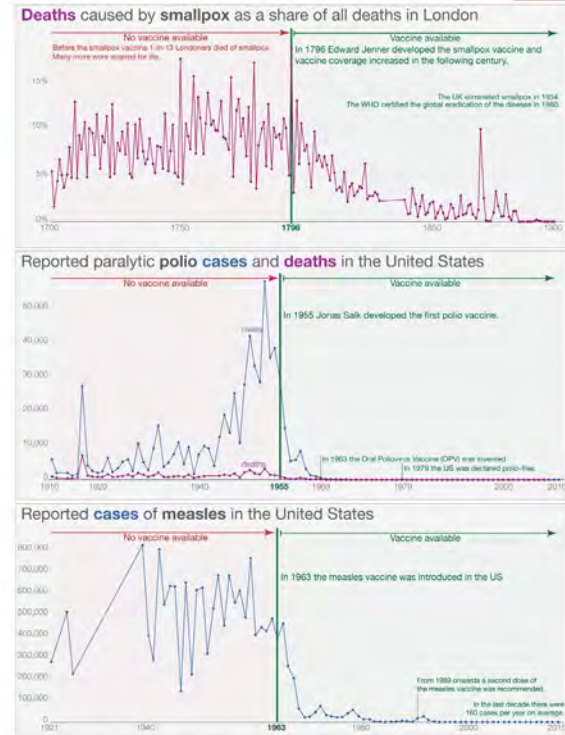


July 10, 2023

# ...Yet there is also the demonstrated possibility of life-altering progress

## Infectious diseases before and after a vaccine became available

Our World in Data

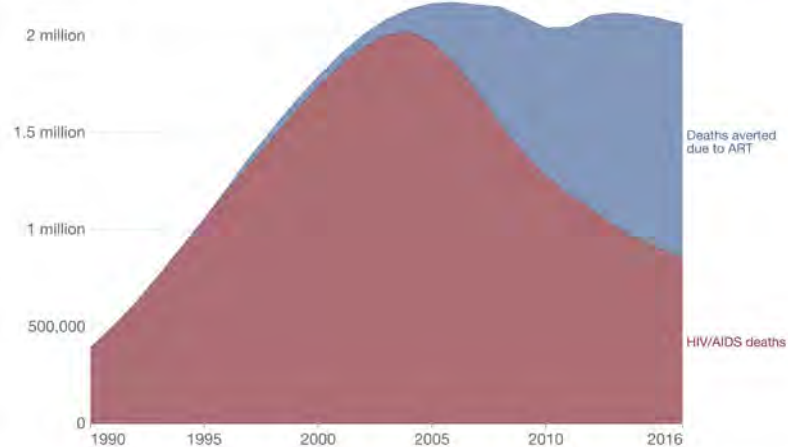


Smallpox: [Smallpox: Vaccination Cases and Deaths \(1900-1980\)](#) and [Smallpox: Deaths Between 1949 and 1969](#) (WHO).  
 Polio: [Polio: Paralytic Cases and Deaths \(1916-1979\)](#) and [Polio: Paralytic Cases and Deaths \(1916-1979\)](#) (WHO).  
 Measles: [Measles: Reported Cases and Deaths \(1916-1979\)](#) and [Measles: Reported Cases and Deaths \(1916-1979\)](#) (WHO).  
 OurWorldInData.org. Research and data to help progress against the world's largest problems. Licensed under CC BY by the author Max Roser.

## HIV/AIDS deaths averted due to antiretroviral therapy, World

The annual number of deaths from HIV/AIDS<sup>1</sup>. This is shown with the estimated number of deaths averted due to antiretroviral therapy<sup>2</sup>.

Our World in Data



Source: UNAIDS

OurWorldInData.org/hiv-aids • CC BY

**1. HIV/AIDS:** The human immunodeficiency virus (HIV) is a virus that is transmitted through sex, blood transfer, or from mother to child during pregnancy, childbirth or breastfeeding. It targets immune cells that help the body respond to infection. Without effective treatment, the immune system will become weakened to the point that it can no longer fight infection and disease. Acquired immunodeficiency syndrome (AIDS) is a condition that describes the most advanced stages of HIV infection. It is defined by the occurrence of at least one of more than 20 life-threatening cancers or "opportunistic infections" that can take advantage of a weakened immune system.

**2. Antiretroviral therapy:** Antiretroviral therapy (ART) is a long-term medical treatment for HIV/AIDS. It works by suppressing the virus from multiplying in the body. This keeps the infection under control and helps to prevent the disease from progressing.

# Why Technology (Should) Matter

- Powerful new technologies can radically change science
- Impact of: the microscope, the telescope, the calculus, the computer (see *Phase Change* [2003], Douglas Robertson)
- New technologies enable us to ask different questions, improve understanding of nature
- “Progress in science depends upon new techniques, new discoveries, and new ideas – probably in that order.” – Sydney Brenner
- Point: good reason for health scientists to be interested, not just the “neomania” Taleb critiques (*Antifragile*, 2012)

# Technology Does Not Arrive Ready To Go

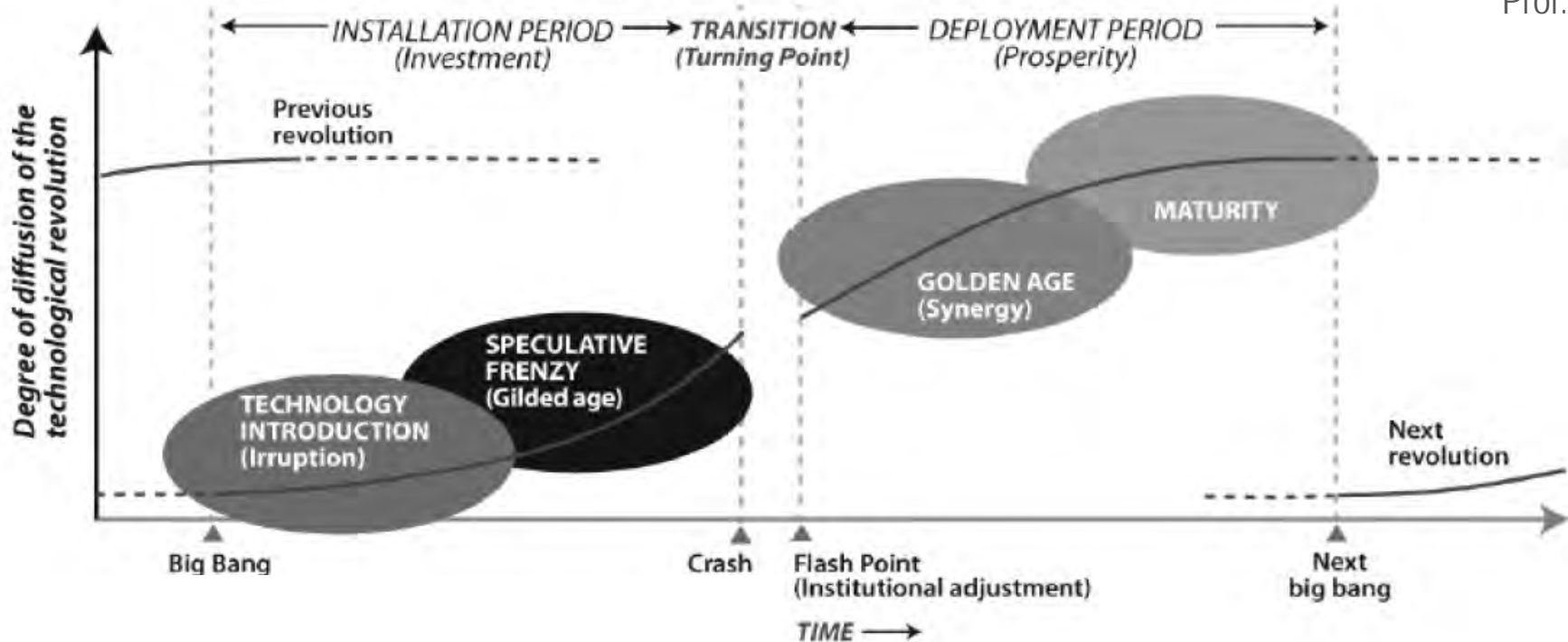




Prof. Perez

# The Life and Times of a Technology Revolution

## Recurring Phases of Each Revolution



Source: *Technological Revolutions and Financial Capital* by Carlota Perez (Edward Elgar, 2002)

# Example of steam to electricity transition

- Steam-powered factories built single source of power, in 3D
- Swapping electricity into same design -> minimal impact
- Reconfiguring design of factory -> huge impact
  - Took years to figure out
  - Done mostly by new/emerging industries & new leaders
  - Very tough for legacy companies w/sunk costs to adjust

Sources: Brynjolfsson & McAfee, *Second Machine Age*, 2014; Paul A. David, "The Dynamo and the Computer," *Amer Econ Rev*, 1990.

# Invention vs Implementation



Benz Patent Motor Car, 1886



# Invention vs Implementation



German road, late 19<sup>th</sup> Century



SF Highway system today

# Implementation Not Instantaneous

“The distinction between invention and implementation is critical and too often ignored.”

“75-95% of the productivity gains from many major new technologies were realized only after decades of improvement in the implementation.”

- James Bessen, *Learning by Doing*

**Table 3.1 Time to Commercialization**

Invention	Year First Patentable	Years to First Commercialization	Years to “Shakeout”	Total Years
Ballpoint pen	1938	7	28	35
DDT	1874	68	14	80
Fluorescent lighting	1850	24	2	76
Freon refrigerator	1931	2	36	38
Gyrocompass	1852	56	59	111
Ice engine	1791	151	27	170
Magnetic recording	1898	41	24	107
Nylon and Dylon	1940	9	34	43
Penicillin	1928	16	7	28
Radio	1904	31	17	48
Radio	1900	15	51	66
Space rockets	1925	19	23	42
Streptomycin	1921	23	23	46
Television	1905	35	33	68
Transistor	1948	7	13	20
Xerography	1947	11	25	38
Zipper	1893	32	33	94
MEAN		35.4	27.4	62.7
MEDIAN		23	25	48

Sources: Jewkes, Sawers, and Stillerman, *Sources of Invention*; Kitch, “Nature and Function of the Patent System”; Gort and Klepper, “Time Paths.”

Hat-tip: Dr. Kevin Horgan



# Implementation Takes Time, Lead Users

- Bessen: “Major new technologies typically go through long periods of sequential innovation.”
- Gordon: “Most of the benefits to individuals [of transportation innovations] came not within a decade of the initial innovation, but over subsequent decades as subsidiary and complementary sub-inventions and incremental improvements became manifest.”
- Von Hippel: Key to application of many technologies are “lead users,” practitioners keen to apply a promising approach to a pressing problem with which they’re actively wrestling

# Bottom line:

- We've lived through the hope, disappointment, and rebirth of the (ongoing) revolution in biology and molecular medicine
- We're now living through the early days of the digital revolution in medicine
- No one knows how new tech will play out – Edison expected phonograph might be used to record wills and sermons
- Figuring out new technology is difficult, time-consuming, and requires iterative innovation, engaged lead users
- New technologies ultimately powerful tools for medicine

# Reminder: things are getting better

Life expectancy, 1880 to 2021

Our World  
in Data



Source: UN WPP (2022); Zijdemann et al. (2015); Riley (2005)

OurWorldInData.org/life-expectancy • CC BY

Note: Shown is the 'period life expectancy'. This is the average number of years a newborn would live if age-specific mortality rates in the current year were to stay the same throughout its life.

(Displayed for context; multifactorial)

# “The new needs friends.”

– Anton Ego, *Ratatouille* (Pixar, 2007)

