Several Nanotechnology Trends, including in Nanomedicine

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National Science Foundation and National Nanotechnology Initiative

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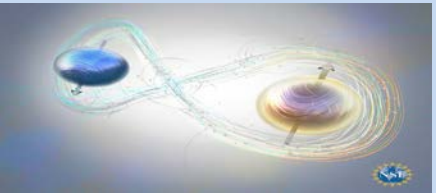
Convergence is a core opportunity for progress
Nanotechnology is an earlier illustration in S&T

Contents

- Three essential stages of science and technology convergence
  - *Nanotechnology - global S&T challenge since 2000*
  - *Foundational emerging technologies (NBICA)*
  - *Global society oriented initiatives*
- Several trends for the next decade (USA), with illustration to nanomedicine

Nanotechnology development



integration of disciplines

2000 ⟶ 2030

- Nanotechnology is a foundational, general-purpose technology

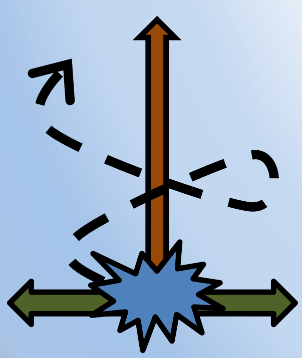
- Nanotechnology in 2019 continues quasi-exponential growth penetration in: (i) disciplinary platforms, (ii) vertical science-to-technology transition, (iii) horizontal expansion to areas such as agriculture/ textiles/ cement/ plastics, and (iv) spin-off areas (> 20) as nanophotonics, metamaterials, spintronics, nano -medicine, -neuro, -agriculture, and -env.

- Nanotechnology promises to become a primary S&T platform for investments and venture funds once efficient design & manufacturing methods are established

A general trend:

Convergence of nano with other emerging fields

- NS&E discoveries on accelerated path, with horizontal integration of disciplines and new spin-off fields *("push")*
- Setting visionary goals and new application areas, via: S&E initiatives, Grand Challenges, Big Ideas, societal goals; need for vertical integration *("pull"),*
- Integration of knowledge & innovation across turbulent, hierarchical and emerging fields *("spiral integration")*



<u>Convergence is:</u> a problem solving strategy to holistically understand and change an ecosystem for reaching a common goal

(Refs 1, 5)

Convergence of knowledge, technology and society

<u>*is* guided by seven principles</u>

A. **Holistic view** – Interdependence-coherence in nature and society *(find 'unity in diversity', 'essential interactions' for deep integration)*

B. **Common goal** - Vision-inspired basic research for long-term challenges

C. **Dynamic pattern** - Processes of spiral convergence and divergence

D. **Unifying actions**- Ecosystem-logic deduction in decisions & problem solving

E. **Cross-domain** - Higher-level languages

F. **Multi-tasking**- Multiple cause-effect pathways

G. **Added-value** - Confluence of resources leading to ecosystem changes *('S curve')*

PRINCIPLES FOR CONVERGENCE

(to a neural network system)

Ref 7: "Science and technology convergence..", JNR, 2016, 18:211

Nanotechnology development

also is guided by the convergence principles

A. Holistic view – *Unity of matter in disciplines; 'essential interactions' for deep integration*

B. Common goal – *Systematic control at nanoscale for properties/functions/devices/sys.*

C. Dynamic pattern - *Spiral convergence to unified methods & divergence in applications*

D. Unifying actions - *Nanosystem-logic deduction in decisions & problem solving*

E. Cross-domain – *languages, concepts, methods*

F. Multi-tasking - *Concurrent nanoscale phenomena and processes*

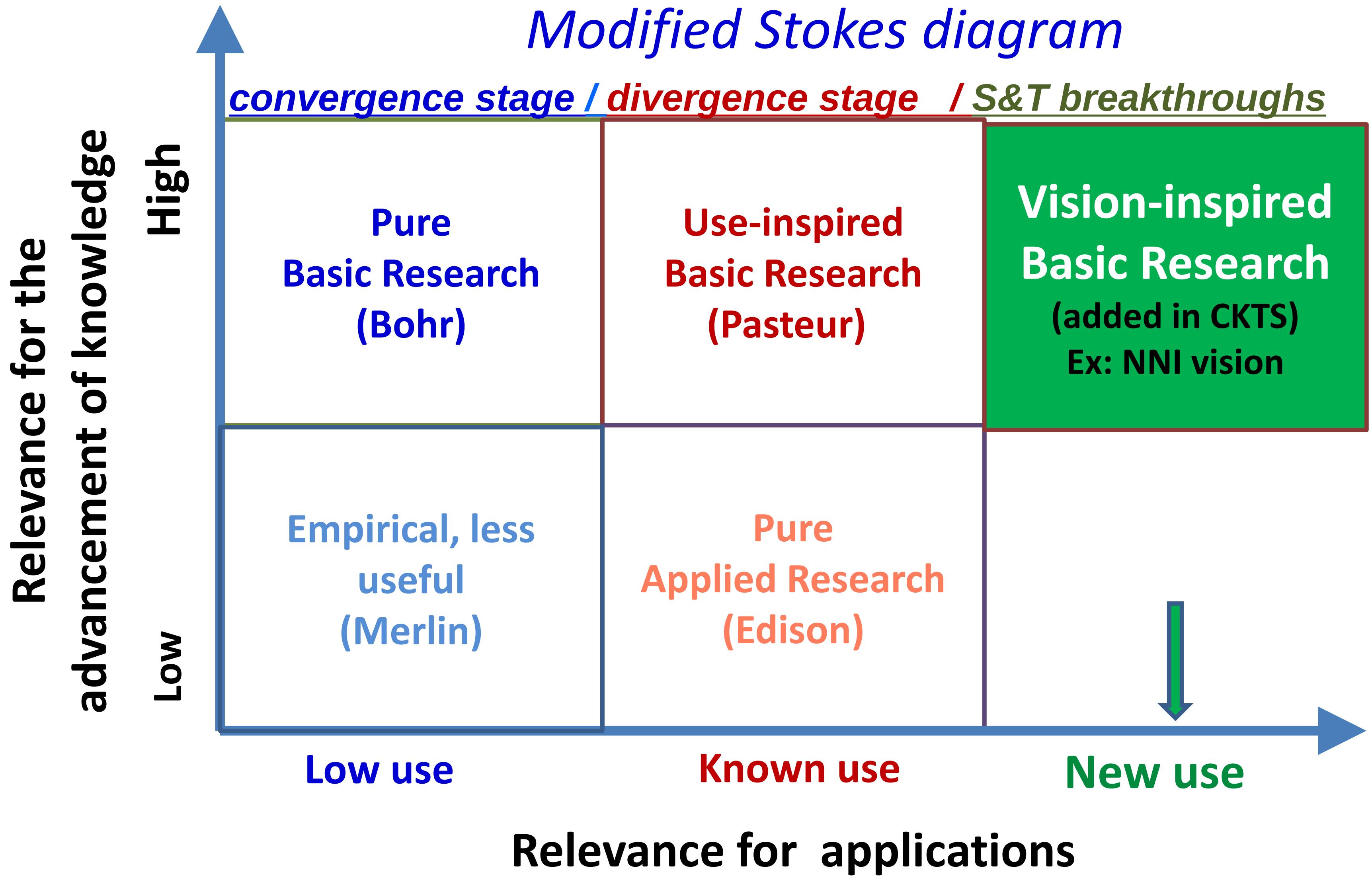
G. Added-value - Confluence of effects leading to novel phenomena and processes

PRINCIPLES FOR CONVERGENCE

(to a neural network system)

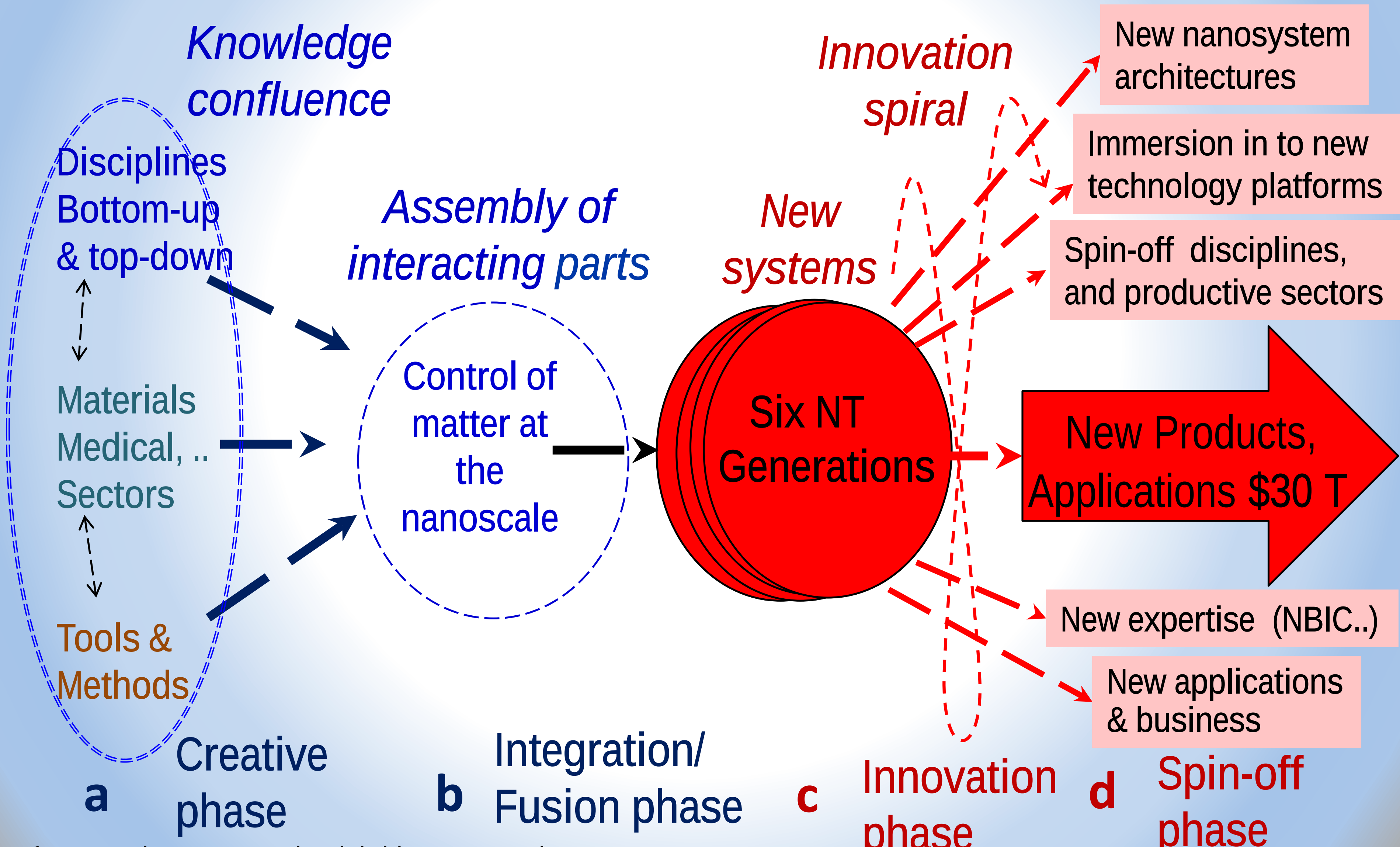
Ref 7: "Science and technology convergence..", JNR, 2016, 18:211

B. Common goal - Vision inspired discovery and inventions are essential for the future of innovation



Ref 6: "Convergence of Knowledge, Technology and Society:" (Springer,2013)

C. 2000-2030 Convergence-Divergence cycle for global nanotechnology development



Ref 7: Based on Roco and Bainbridge, 2013 , Fig. 8

C. Example convergence-divergence opportunities: the cellular phone

Phases to achieve convergence:

- Creative phase: Confluence of fields
  CMOS 90 nm (2000) to 7 nm (2019)
- Integration phase: Data storage to cognition
- Innovation phase: Smart phone and its platform
- Outcomes, spin-off phase: Social networks, controlling swarms, healthcare, aspects in society

High "innovation index" in a convergence process

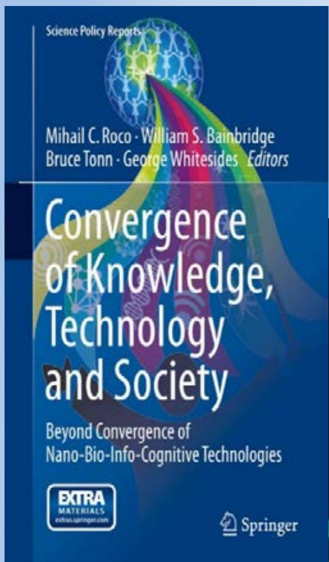
$$I \sim k(S,E)\ S^2\ O\ /\ T^3$$

(Ref 6: CKTS Report 2013)

Approach to improve convergence:

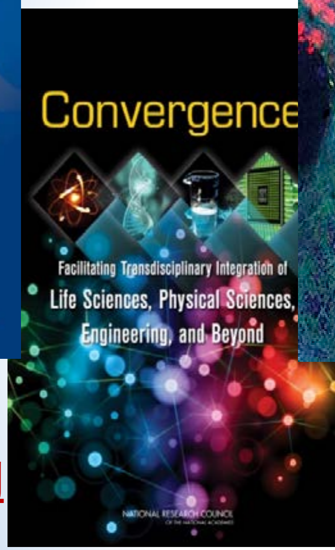
- Enlarge the working domains S↑
- Convergence accelerators T↓

Key convergence reports since 2013



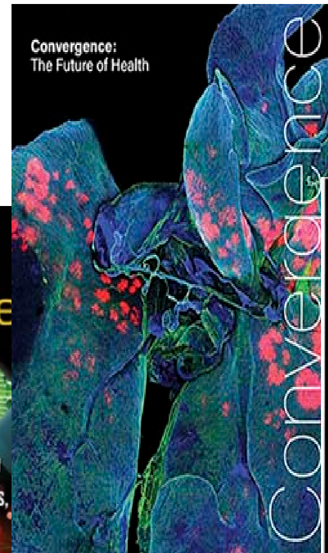
International benchmarking

2013



Life, physical & engng. sciences convergence

2014



Convergence of health

2016

Convergence principles and methods

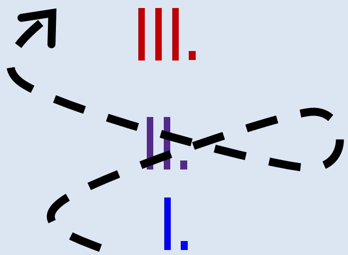
2016

Convergence engineering centers

2017

Culture of Convergence

2019



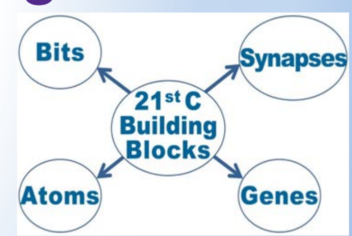
Three stages of convergence

(Ref 6: CKTS, Springer, 2013)

III. Conv. Knowledge, Technology and Society “CKTS”

Integrates NBICA & other essential platforms of human activity using seven convergence principles

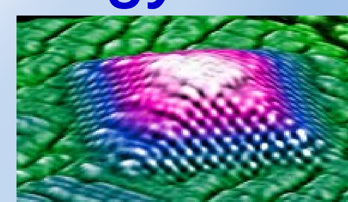
II. Converging Technologies Nano-Bio-Info-Cognitive-AI “NBICA”



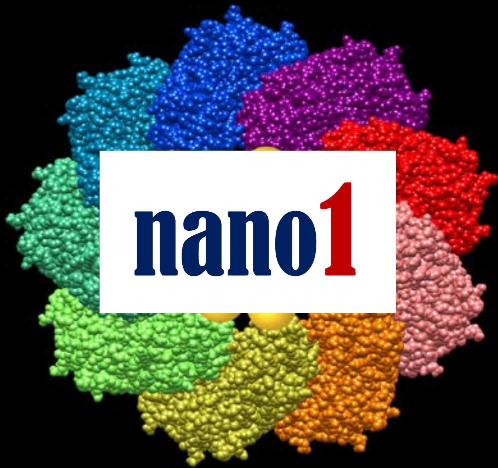
Integrates foundational and emerging technologies from unifying - basic elements using similar system architectures and dynamic networking (neural networks)

I. Nanoscale Science, Engineering and Technology “Nanotechnology”

Integrates disciplines and knowledge of matter from unifying concepts at the nanoscale



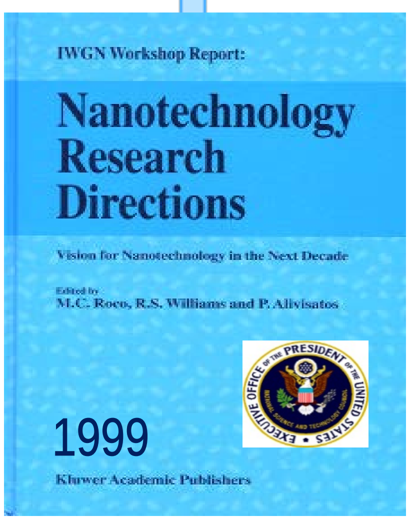
2000

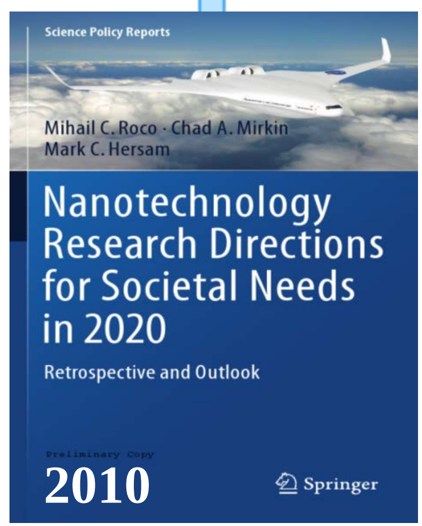


2010

2020

2030





30 year vision to develop nanotechnology in three stages changing focus and priorities

Reports available on: www.wtec.org/nano2/ and www.wtec.org/NBIC2-report/ (Refs. 3-6)

CREATING A GENERAL PURPOSE NANOTECHNOLOGY IN 3 STAGES

Based on NANO 2020, Fig. 5 (Ref. 4)

2030

DIVERGENCE

New socio-economic capabilities, architect

nano3 Technology divergence

2020-2030

To general purpose technology, moduls

nano2 System integration

2010-2020

CONVERGENCE

Create library of nanocomponents, function

nano1 Component basics

2000-2010

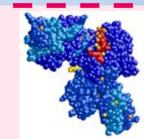
2000

GENERATIONS OF NANOPRODUCTS

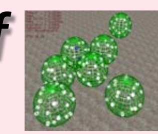
6. Nanosystem Conv. Networks

5. NBICA Technology Platforms

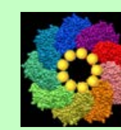
4. Molecular Nanosystems



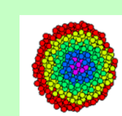
3. Systems of Nanosystems



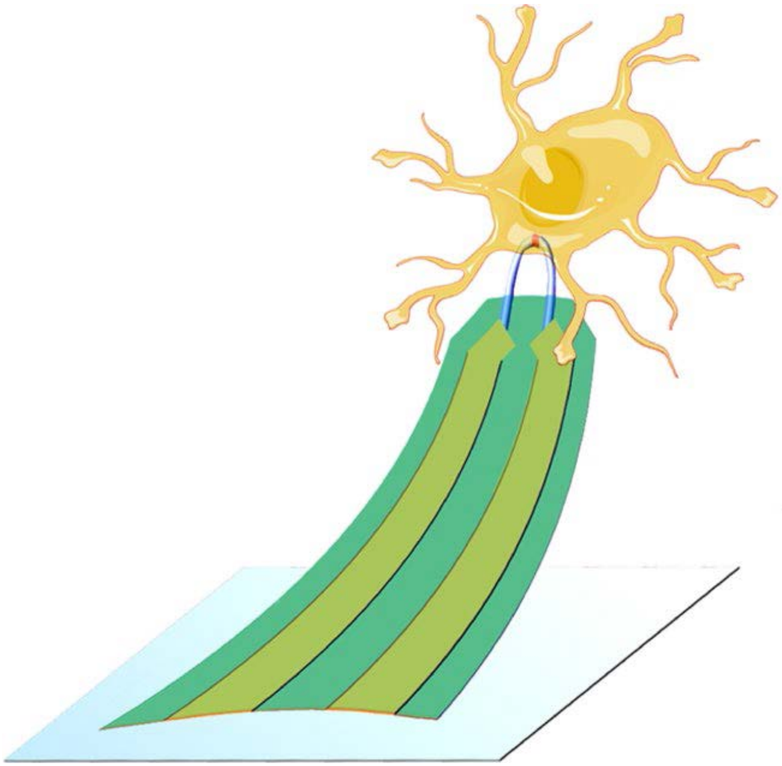
2. Active Nanostructures

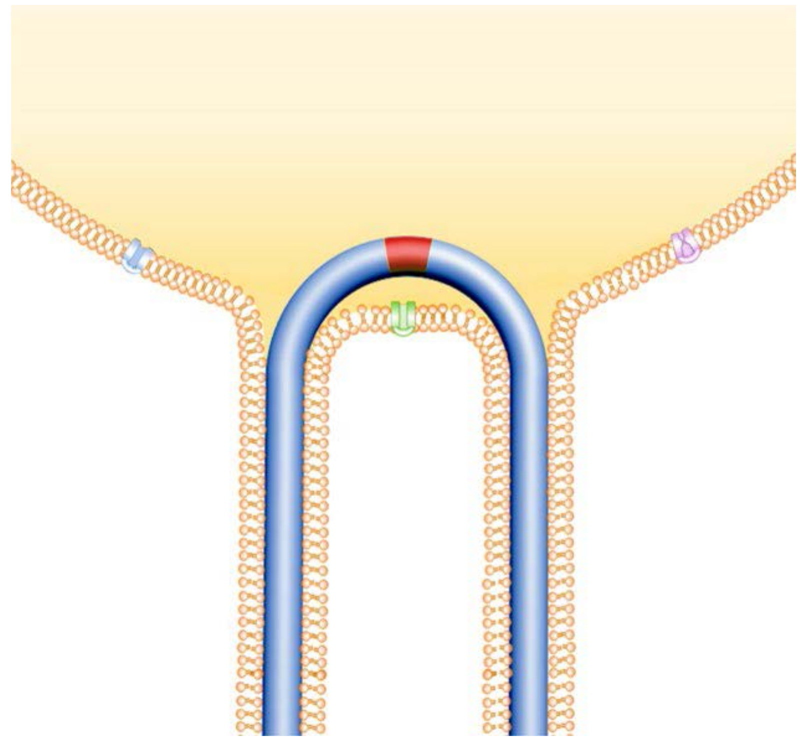


1. Passive Nanostructures



Nanowire transistor probes for intracellular recording





Credit: Charles Lieber group (Y. Zhao et al, Nature Nanotech 2019)

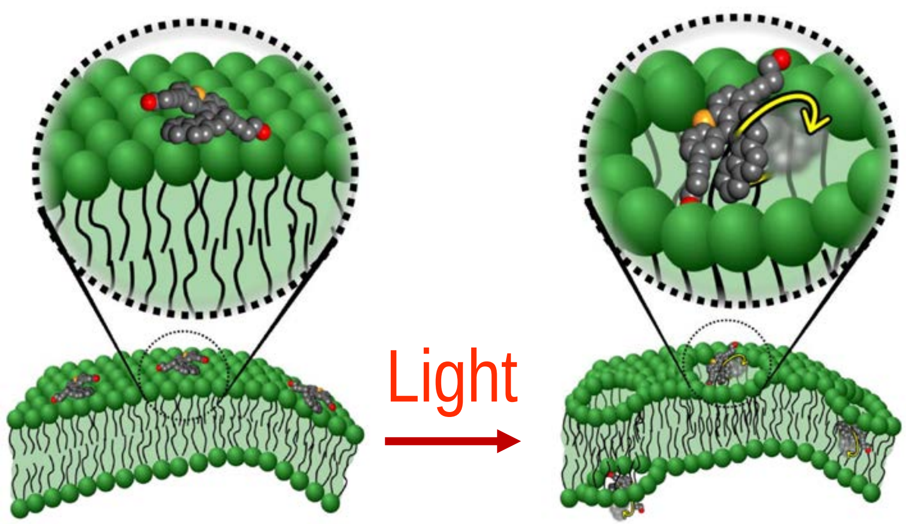
Example discovery in nanobio-medicine

Motorized molecules drill through cells

Motorized molecules driven by light can drill holes in the membranes of individual cells, promising to bring therapeutic agents into the cells or directly inducing the cells to die

Rotors in single-molecule nanomachines activated by ultraviolet light - spin at 2 to 3 million rotations per second

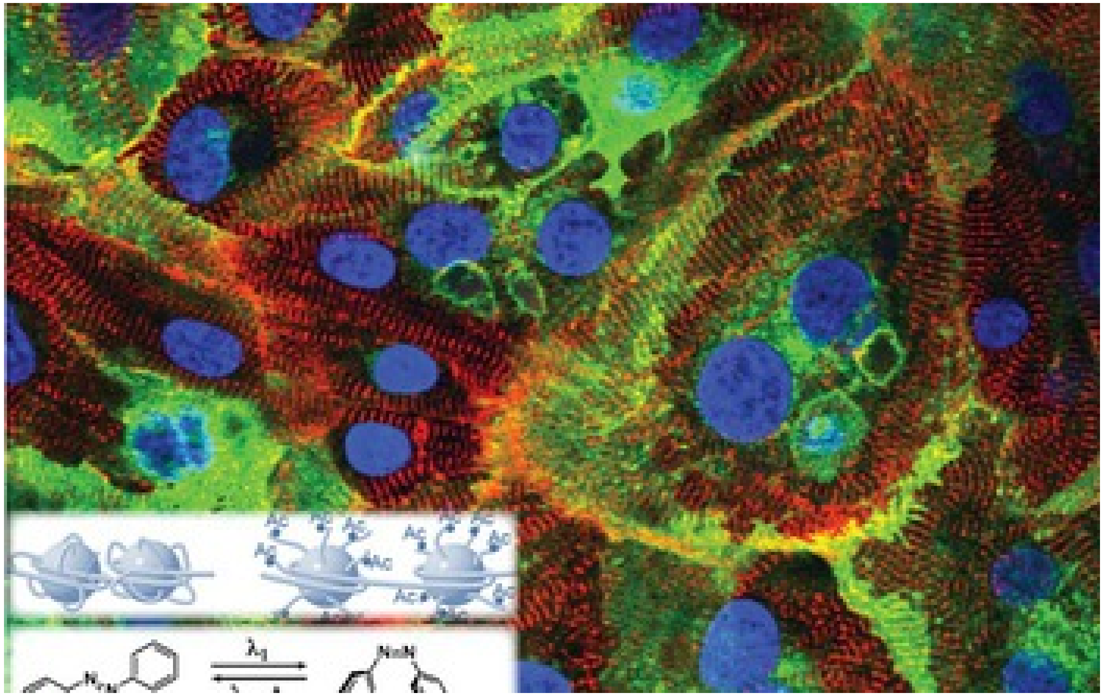
Credit: James Tour group, et al., Nature Aug 2017, Rice U., Durham (U.K.) and NCSU



Example discovery in nanobiology

Engineering biology through DNAs environment

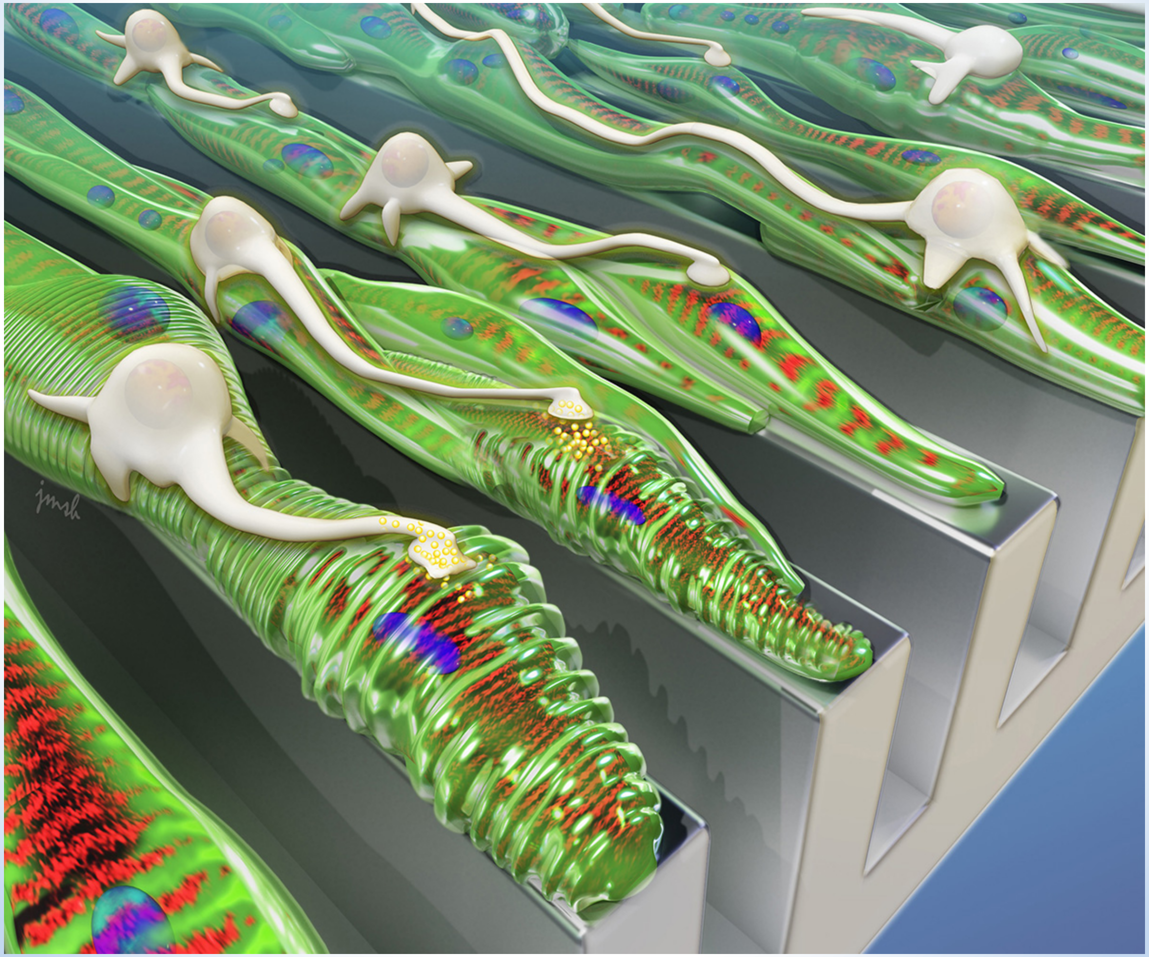
Chromatin and Epigenetic Engineering (NSF 17-578 & 18-077)



Light-mediated epigenetic control at the nanoscale in human induced pluripotent stem-cell-derived cardiac muscle cells

Credit: R. Mazitschek, Mass General Hospital/Harvard U.; E. Entcheva and A. Villagra, GWU

Integrate the muscle grow with neurons at the nanoscale on grooved platforms



H. Kong, R. Bashir et al., U. of Illinois (2019)

National Nanotechnology Initiative, 2019

Nanotechnology Signature Initiatives

(https://www.nano.gov/signatureinitiatives)

Sustainable Nanomanufacturing

Water Sustainability through Nanotechnology

Nanoelectronics for 2020 and Beyond

Nanotechnology Knowledge Infrastructure

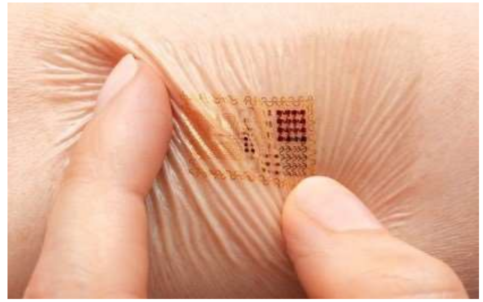
Nanotechnology for Sensors

Nanotechnology for Solar Energy (2011-2015)

Nanoplastics in the Environment (under consideration) nano2

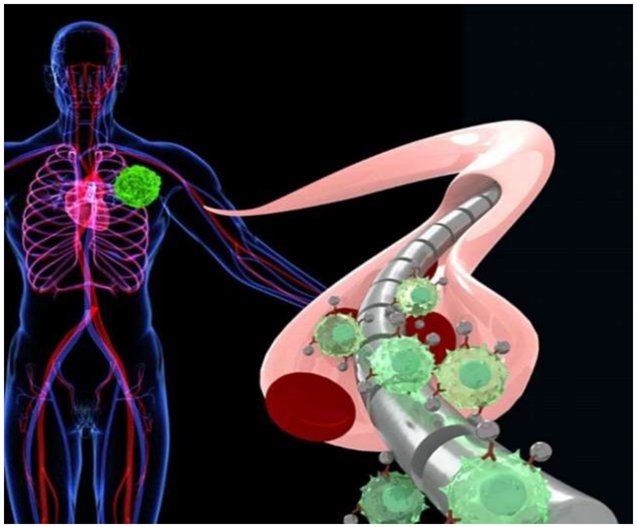
Nano for Sensors & Sensors for Nano

Improving and Protecting Health, Safety, and the Environment



For Diagnostics
John Rogers, NU

For plants. Liang Dong, Iowa State University



For visualization using magnetic sifter
Sam Gambhir, Stanford University Medical School

Vaporsens chemical sensor:
https://www.vaporsens.com/

Daniel Heller, Memorial Sloan Kettering Cancer Center

nano2 Twelve global nano trends to 2020

10 year perspective, www.wtec.org/nano2/ (Ref. 4)

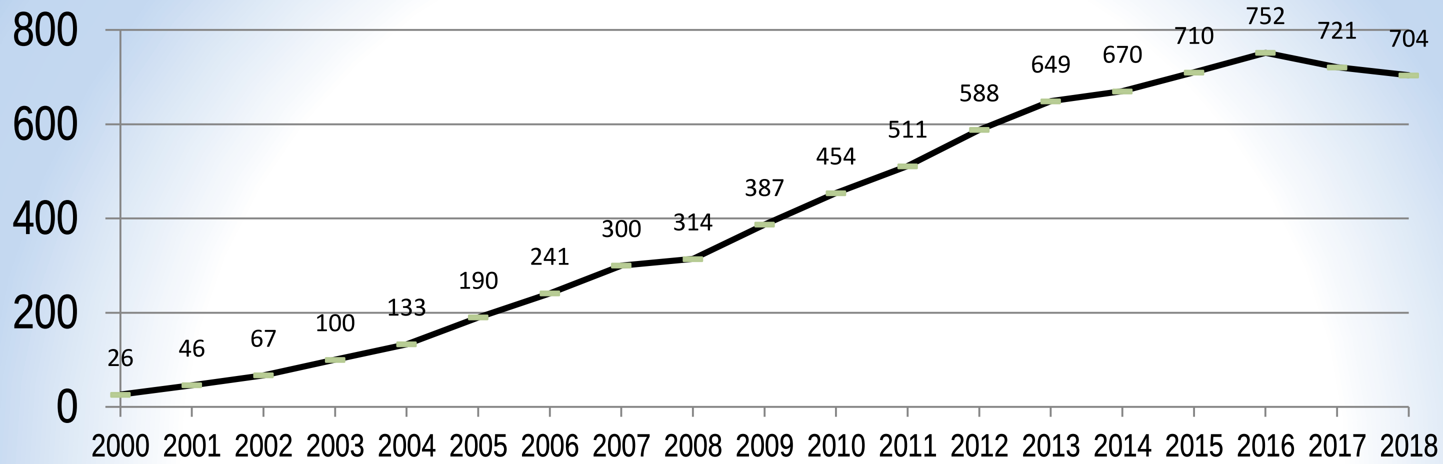
- Theory, modeling & simulation: x1000 **faster**, essential design
- "Direct" measurements – x6000 **brighter**, accelerate R&D&use
- A shift from "passive" to **"active"** nanostructures/nanosystems
- **Nanosystems**- some self powered,self repairing, dynamic, APM
- **Penetration** of nanotechnology in industry - toward mass use; catalysts, electronics; innovation– platforms, consortia
- Nano-EHS – more predictive, integrated with nanobio & env.
- **Personalized nanomedicine** - from monitoring to treatment
- Photonics, electronics, magnetics – new **integrated** capabilities
- **Energy** photosynthesis, storage use – solar economic
- Enabling and **integrating with new areas** – bio, info, cognition
- **Earlier** preparing nanotechnology workers – system integration
- Governance of nano for societal benefit - **institutionalization**

Topics in NSF nanomedicine supported nanotechnology S&E research portfolio

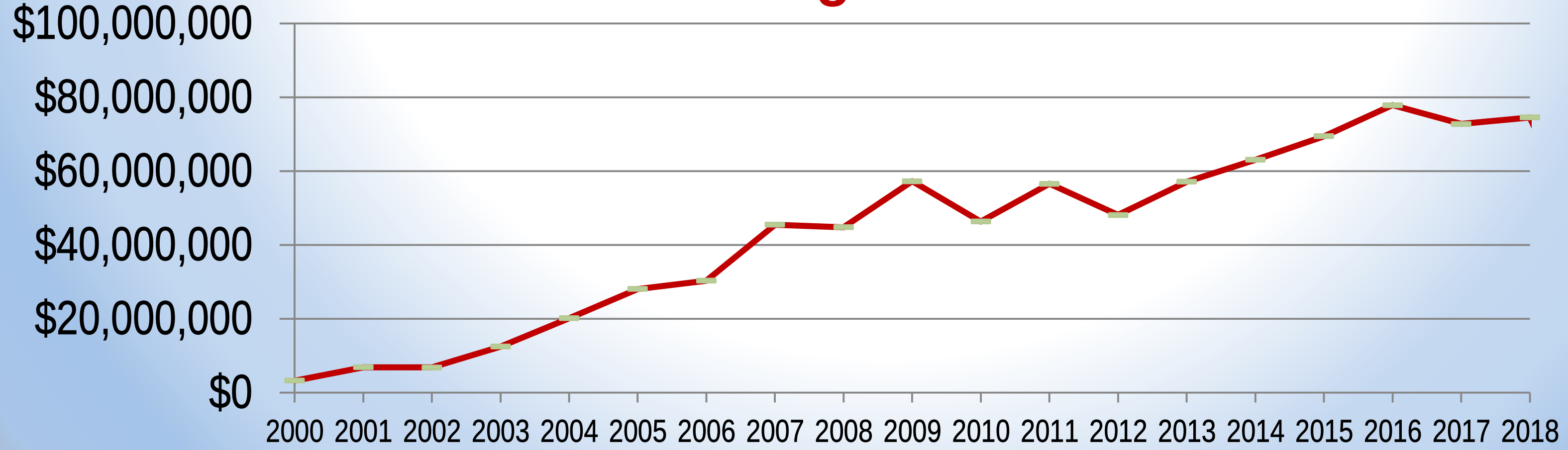
- **Diagnostics:** imaging diagnostics, blood analysis, saliva analysis
- **Therapeutics**: targeting drug delivery, targeted cancer detection and therapy
- **Nanostructured implantable materials**: bones, scaffolds
- **Regenerative medicine**: tissue engineering, gene therapy for health care, stem cells
- **Single cell conditioning**
- **Vaccines**
- **Neuro-cognitive**: neuro*, cognition, cogniti* sensors

Other topics in “Nanomedicine”

Number of active nanomedicine awards in all categories: FY 2000-2018



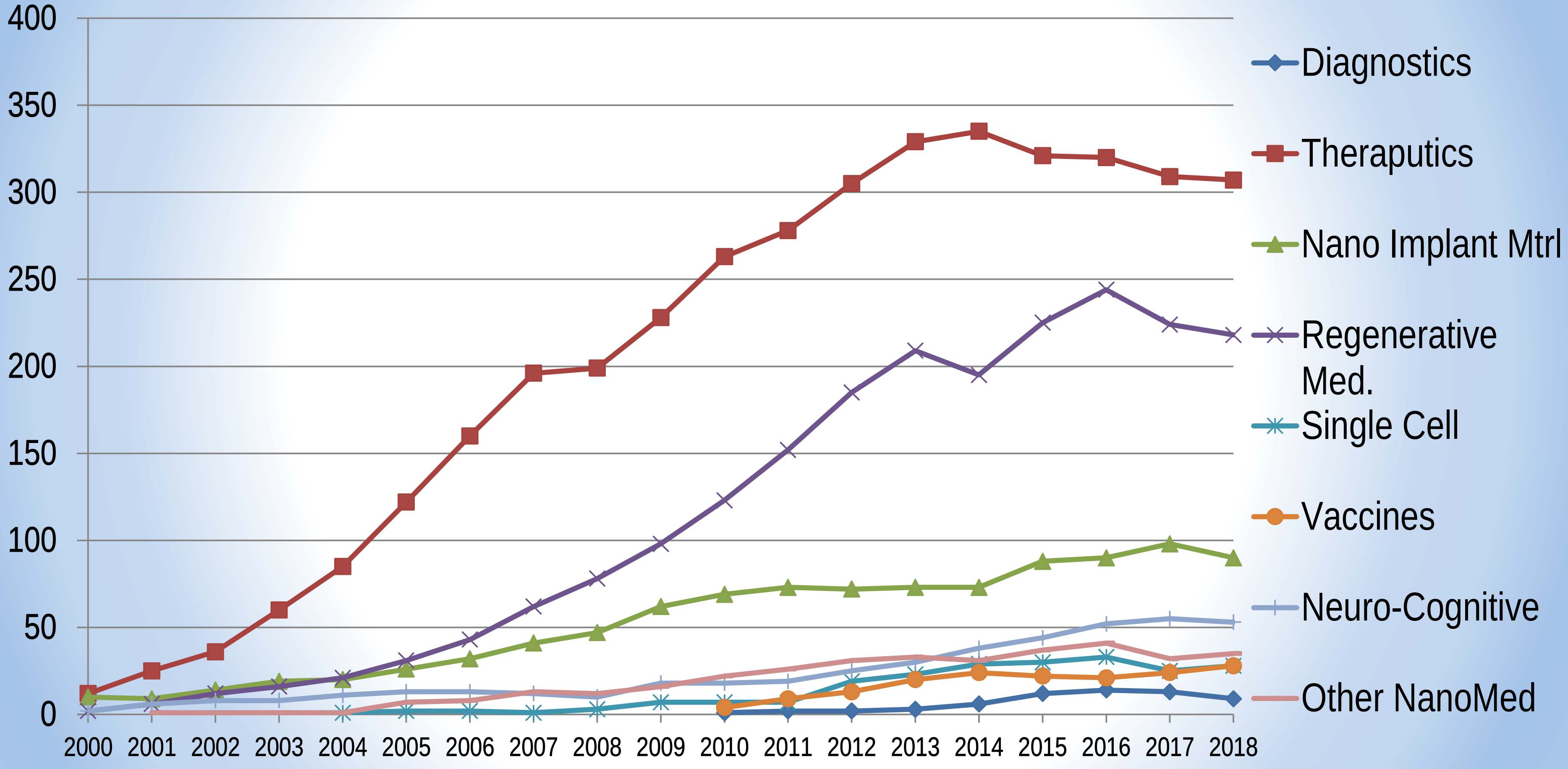
Nano amounts for active nanomedicine awards in all categories: FY 2000 - 2018



MC Roco, Sep 23 2019

Number of active nanomedicine awards

FY 2000-2018



Therapeutics: largest component is drug delivery

Regenerative medicine: largest component is tissue engineering

Current nanotherapeutics characteristics

- Current carriers mostly are relatively simple nanoparticles and nanocomposites (**liposomes, polymers, shells**, ..). They generally deliver conventional **drugs that have previously approved**
- By 2016, dozens of nanodrugs received FDA approval in the US, and additional 77 are in the clinical trials. Hundreds of therapeutic nanoparticles are in the earlier stage of development
- Structure-activity relationships (e.g. size, charge, shape, composition, architecture, magnetization) adapted to disease requirements. Trend: increase nanoparticle complexity and functions (e.g. surface architectures, nanocomposites)

Andre Nel, NASEM 2019

Nanomaterial medicine formulations currently approved for marketing

(Frontiers in Pharmacology, Review publ. 17 July 2018; fda.gov; drug.com; ema.Europa.eu)

Type	Name	Drug	Indication
Liposomal NMs	Doxil/Caelyx	Doxorubicin	HIV-related, myeloma, breast cancer, ovarian cancer
	AmBisome	Ampheotericin B	Fungal infections
	Other 10	……	…….
Micellar NMs	Genxol PM	Paclitaxel	Metastatic breast cancer, lung cancer
	Nnaoxel M	Paclitaxel	Breast cancer, pancreatic cancer, ovarian cancer
Protein NMs	Abraxene	Paclitaxel	Breast cancer, pancreatic cancer,..

Distribution of nanomedicine market

By application type

- Oncology ~1/3 (~17% - annual rate of increase 2016-2017)
- Neurology ~1/4 (~17% - annual rate)
- Anti-infective ~ 1/9 (~17% - annual rate)
- Anti-inflammatory ~1/9 (~17% - annual rate)
- Cardiovascular ~1/17 (~15% - annual rate)

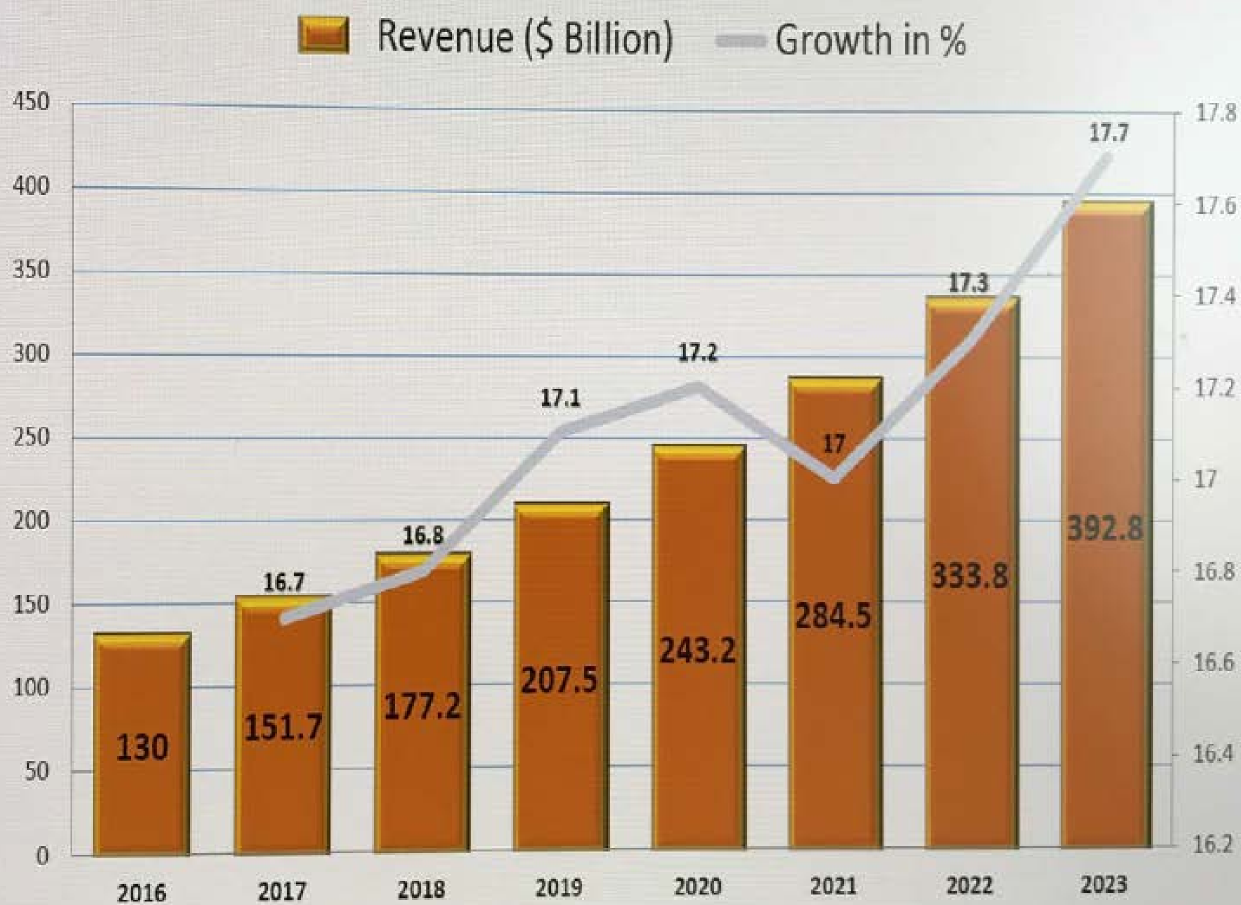
Economy	USA & Canada	Europe	Asia (incl. Japan)	Latin America	Africa	Australia & New Zealand
Market Share	42%	24%	21%	5%	4%	4%

Dr. med. h.c. Beat Löffler MA, CEO

Major players in the global nanomedicine market

- Merck
- Hoffman - La Roche
- Novartis
- Amgen
- Pfizer
- Gilead Sciences
- Eli Lilly
- BASF
- Johnson & Johnson
- Abbott Laboratories
- GlaxoSmithKline
- Bristol-Myers
- GE Healthcare
- Nanobiotics
- Safoni
- UCB SA
- Shimadzu

Predicting Global Nanotechnology Market Development related to Health



Dr. med. h.c. Beat Löffler MA, CEO

Source: Infoholic Research

NSF – discovery, innovation and education in Nanoscale Science and Engineering (NSE)

www.nsf.gov/nano , www.nano.gov

- **FY 2019 - 2021 Budgets -** various planning stages

FYs 2018 actual ~ $568 M (incl. related core programs)

– Fundamental research

> 6,000 **active projects** in all NSF directorates

(annual increases ~15% first decade, then ~ constant, with qualitative changes)

– Establishing the infrastructure

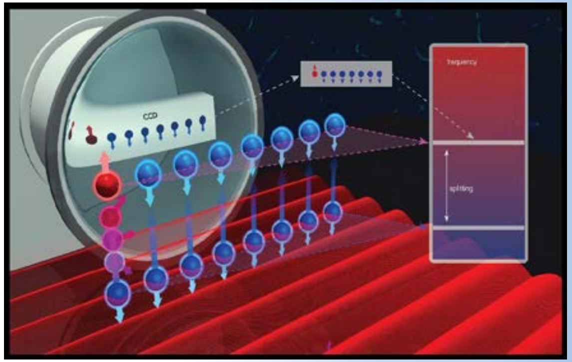
> 30 **centers & networks**, 2 general user facilities

– Training and education

> 10,000 **students and teachers/y**; ~ $50M/y

Ex II: 2016- NSF 10 Big Ideas *(4 research ideas)*

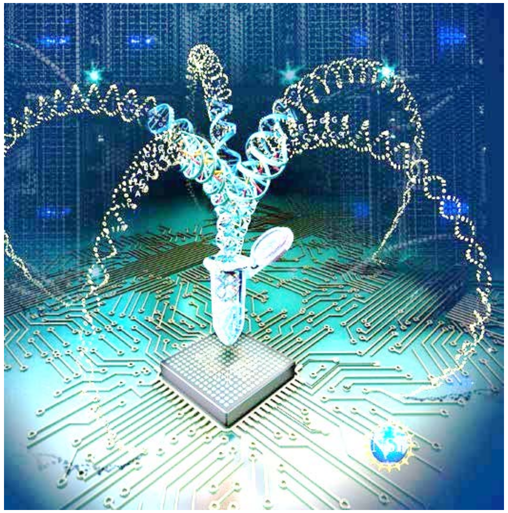
- **Understanding the Rules of Life: Predicting Phenotype**
- **Work at the Human-Technology Frontier**
- **Data Science**
- **The Quantum Leap**



Ex II-III: 2016- NSF 10 Big Ideas *(2 research ideas)*

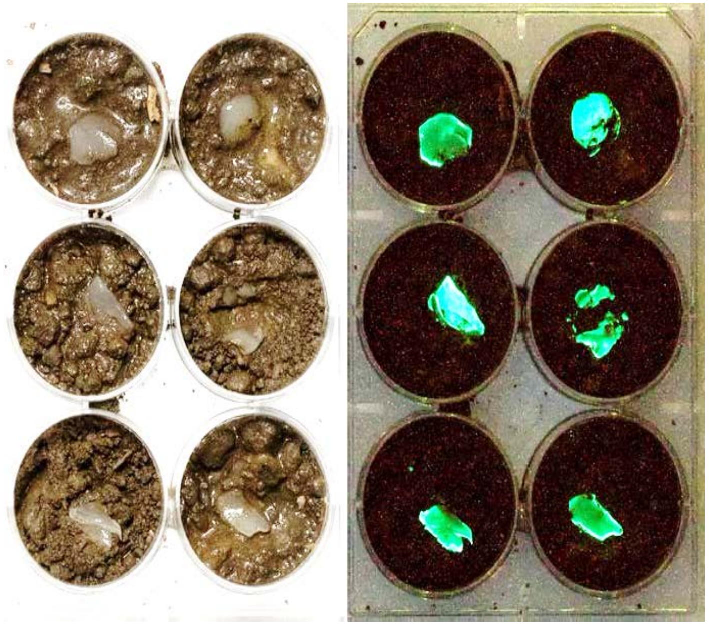
- **Windows on the Universe: Multi-messenger Astrophysics**
- **Navigating the New Arctic**

Ex II. "Understanding the Rules of Life" (NSF)



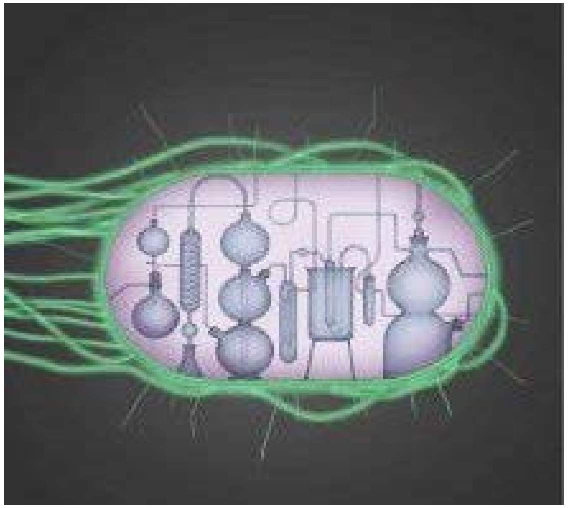
Semiconductor synthetic biology

Image credit: Nicolle Rager Fuller, NSF



Signals in the soil

Image credit: S. Daunert, S. Deo and E. Dikici, Dept. of Biochemistry and Molecular Biology and Dr. JT Macdonald Biomedical Nanotechnology Institute, U. of Miami



Synthetic cell

Image courtesy PLOS

Understanding cells & nanobiosystems from the nanoscale

Ex II. Examples of NSF programs (2019-2020)

- Understanding the Rules of Life: Building a Synthetic Cell (NSF 18-599)

  https://www.nsf.gov/pubs/2018/nsf18599/nsf18599.htm

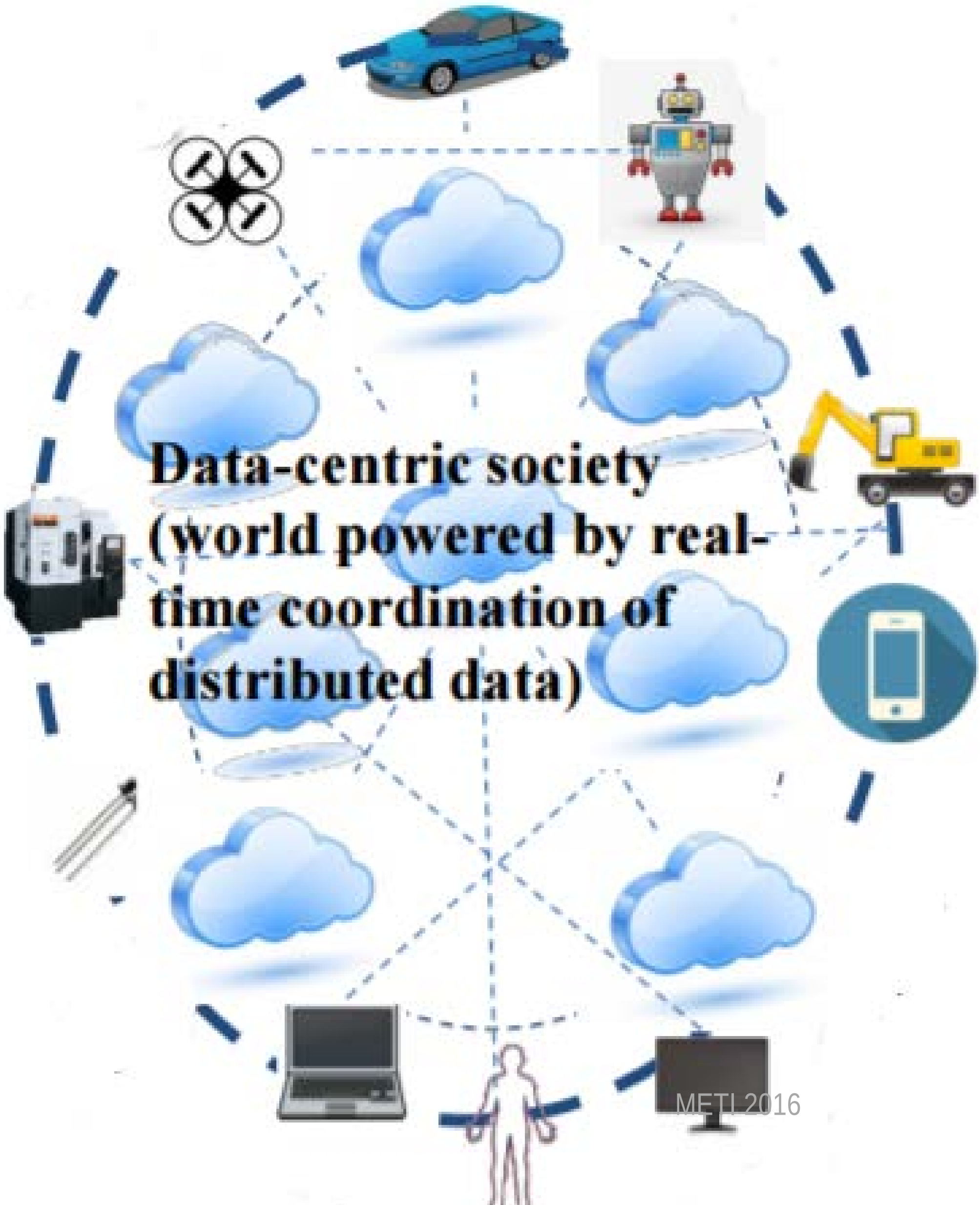
  Create synthetic cells - constructed of biological or artificial materials that mimic functions of natural, living cells. Building synthetic cells either from scratch, or start with a natural cell and remove or add components.

- Understanding the Rules of Life: Epigenetics (NSF 18-600)

  https://www.nsf.gov/pubs/2018/nsf18600/nsf18600.htm

  By altering the way genes are read and expressed -- how, when and where specific genes are turned "off" or "on" -- two cells or whole organisms with the same DNA sequence can appear or act differently.

Ex II: IoT with Nanosensors



Nanotechnology for Sensors

www.nano.gov/SensorsNSIPortal

Goals:

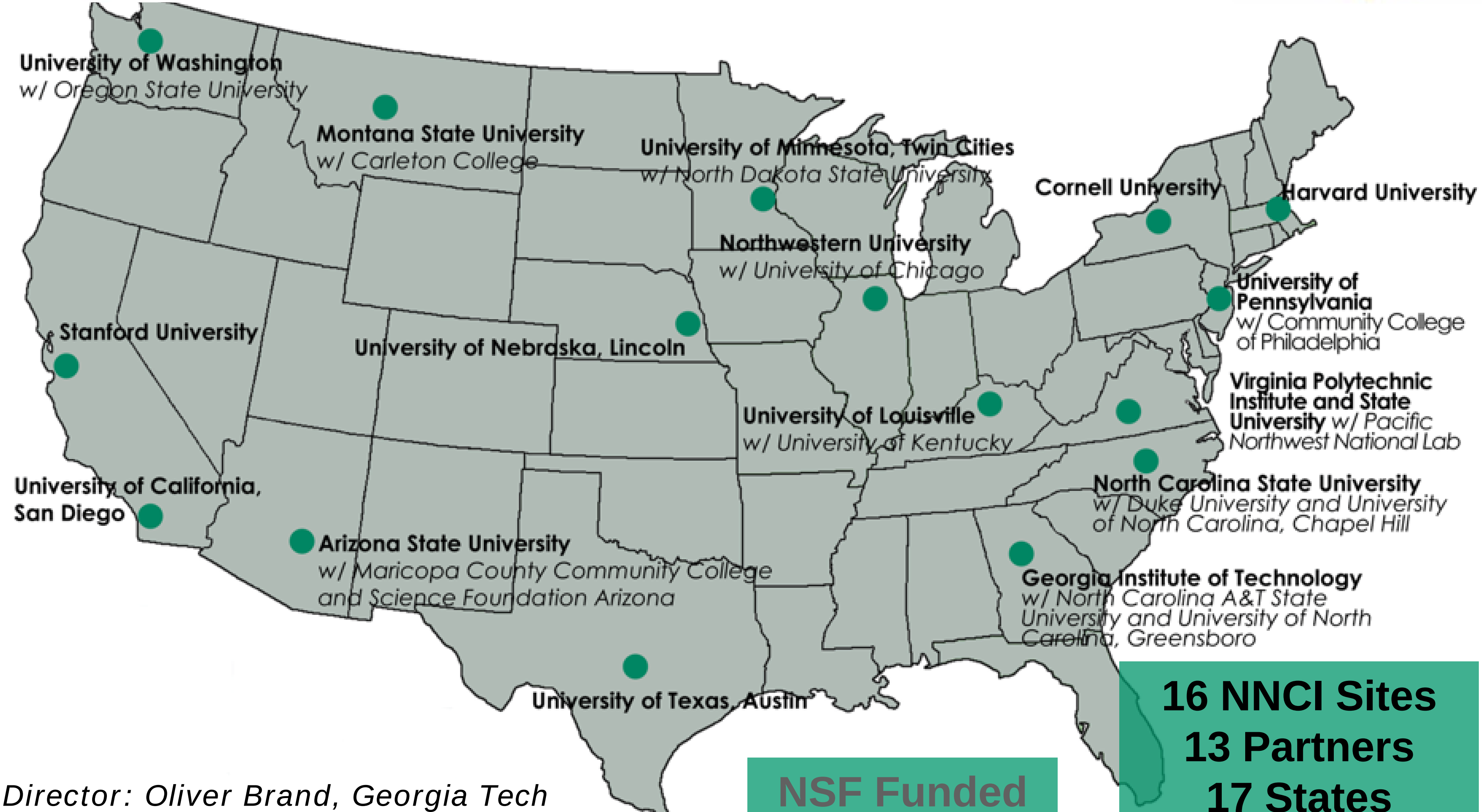
1 nm sensors self powered

Wireless networked links

Distributed network

Cyber-Physical Systems

National Nanotechnology Coordinated Infrastructure



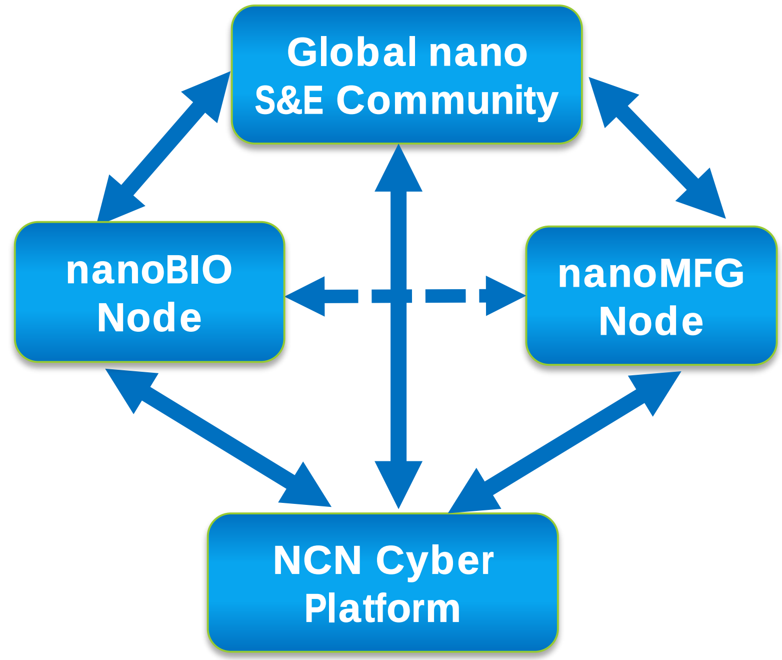
Director: Oliver Brand, Georgia Tech

NSF Funded
2015-2020
$81M total

16 NNCI Sites
13 Partners
17 States
68 Facilities
>2000 Tools

Network for Computational Nanotechnology (NCN)

nanoHUB



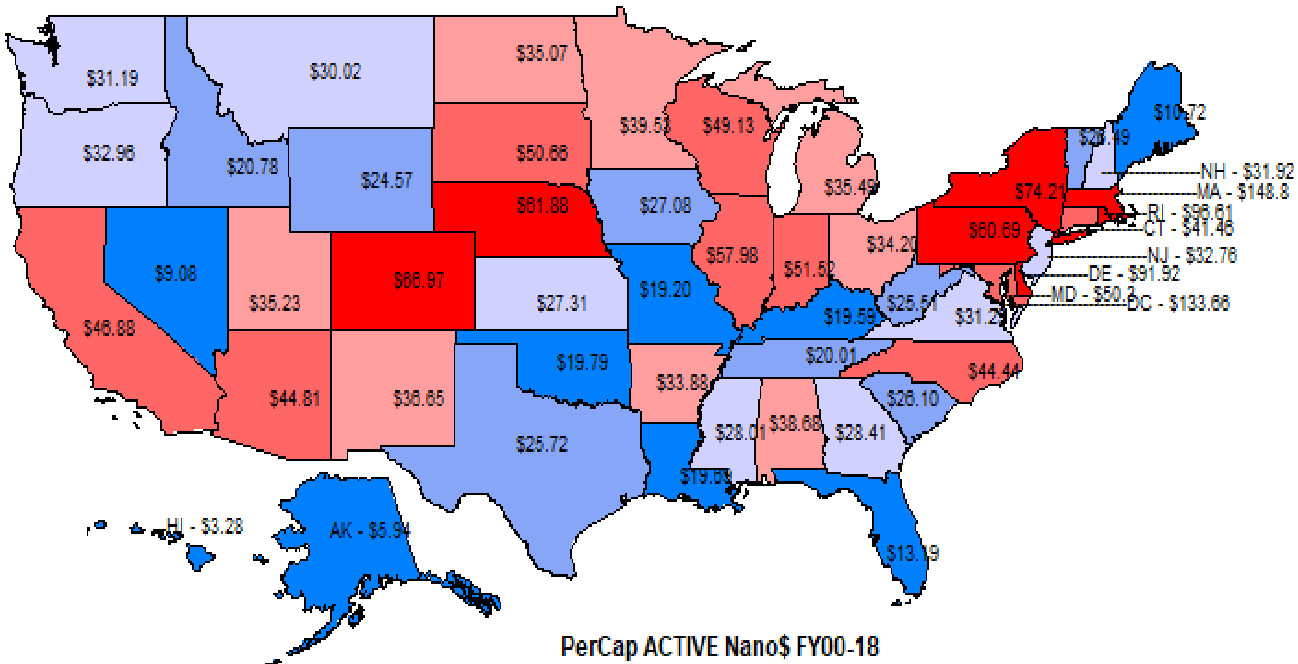
Cyberinfrastructure: 500+ nano-Apps in the cloud

5,500+ lectures and tutorials 100+ courses => MOOC 185 institutions

Director: Gerhard Klimeck, Purdue U.

NSF's NS&E amount new awards per capita

FYs 2000 - 2018: U.S. average amount ~ $41 /capita



PerCap ACTIVE Nano$ FY00-18

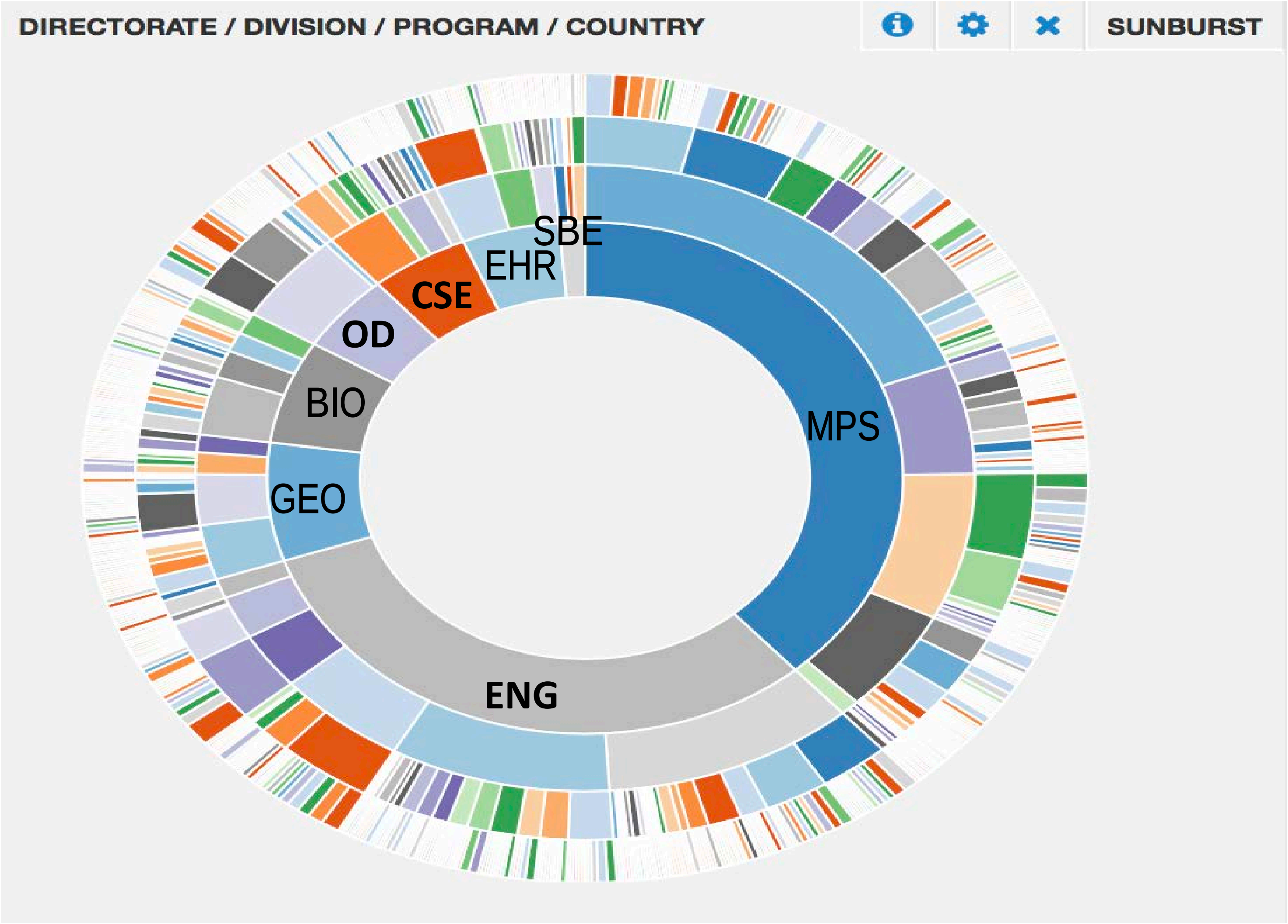
<= 19.79 | 19.79 - 27.08
27.08 - 32.96 | 32.96 - 39.53
39.53 - 57.98 | 57.98 - 148.8

2018: Over 7,000 active awards
(abstracts on www.nsf.gov/nano)

#1 MA $149 / capita (2000-2018)

AK 5.93; AL 38.68; AR 33.88; AZ 44.81; CA 46.88; **CO 66.97** ; CT 41.45; **DC 133.66** ; **DE 91.92** ; FL 13.19; GA 28.41; HI 3.27; IA 27.08; ID 20.78; IL 57.98; IN 51.52; KS 27.31; KY 19.59; LA 19.69; **MA 148.80** ; MD 50.30; ME 10.72; MI 35.49; MN 39.53; MO 19.20; MS 28.01; MT 30.02; NC 44.44; ND 35.07; **NE 61.88**; NH 31.92; NJ 32.75; NM 36.65; NV 9.08; NY 74.21; OH 34.20; OK 19.79; OR 32.96; **PA 60.69** ; PR 20.10; **RI 96.61** ; SC 26.10; SD 50.66; TN 20.01; TX 25.72; UT 35.23; VA 31.23; VT 26.49; WA 31.19; WI 49.13; WV 25.51; WY 24.57

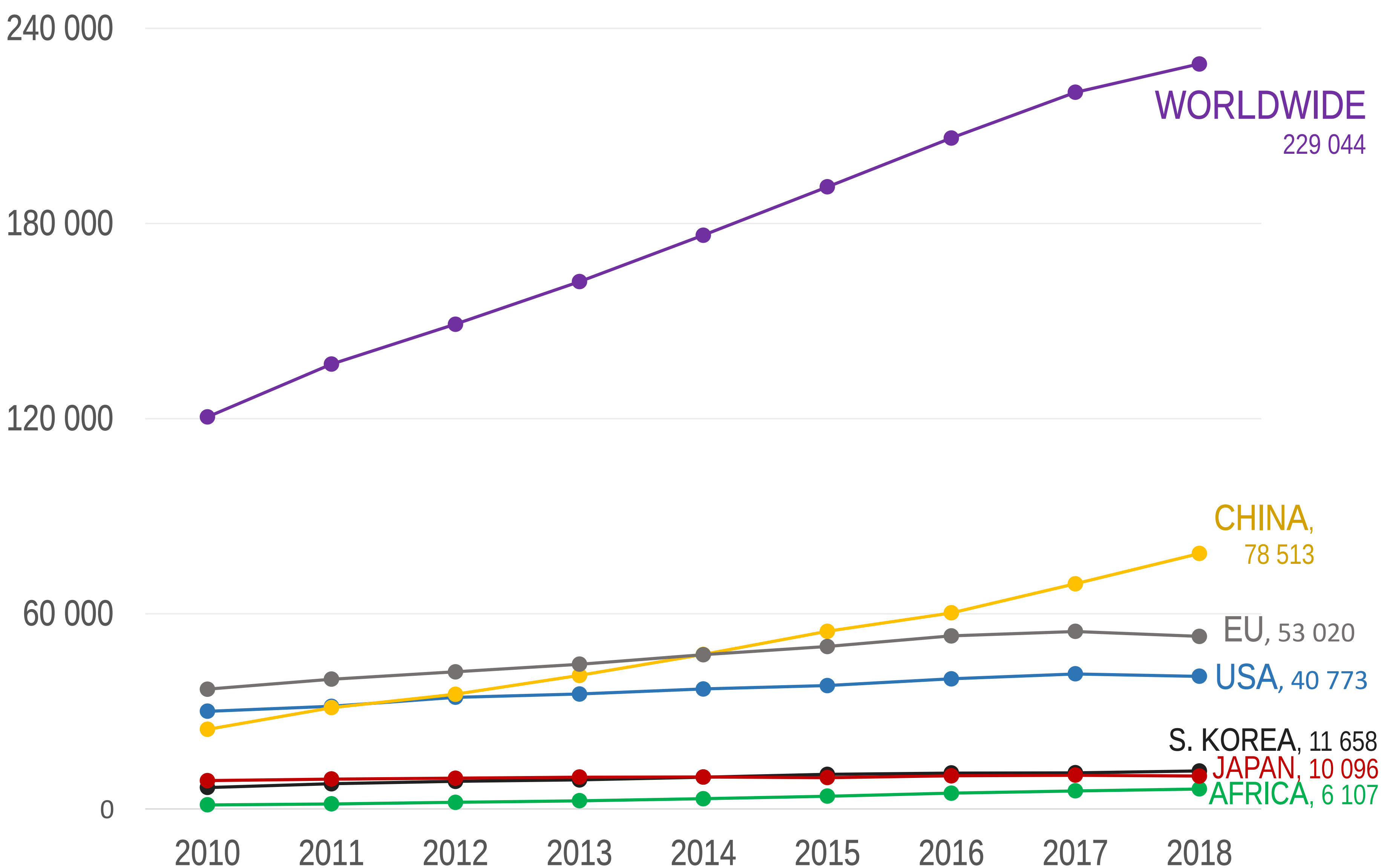
NS&E awards with international activity (21%)



Dec 4, 2018;
http://dis-checker-p02:8002/solr/banana-sankey/dist/index.html#/dashboard

Nanotechnology *publications* in the World 2010 - 2018

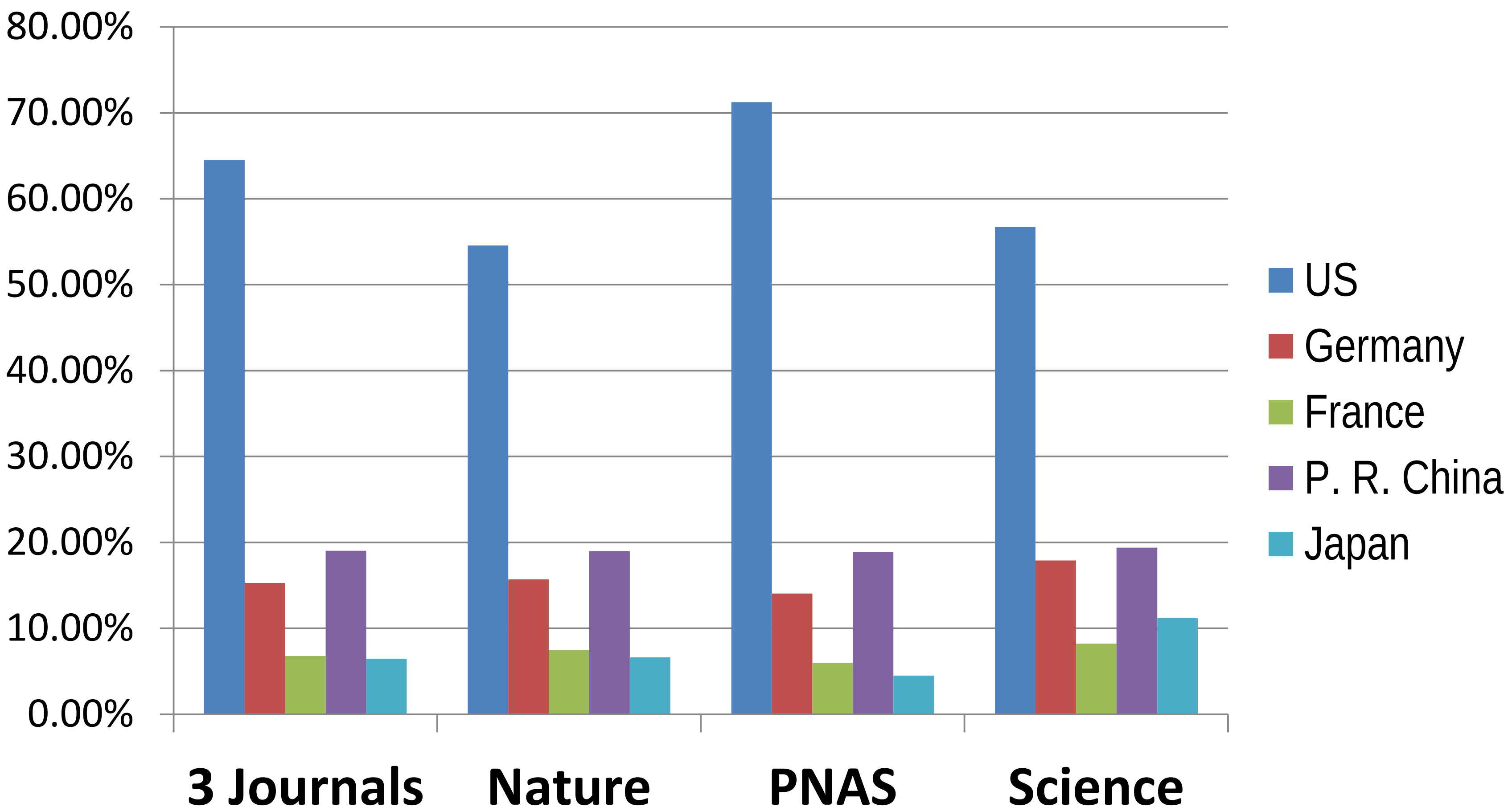
"Title-abstract" search in WoS by nano + 27 keywords (method Nano2020, Ref 3)*



MC Roco, Sep 23 2019

Five countries' contributions to Top 3 journals in 2018

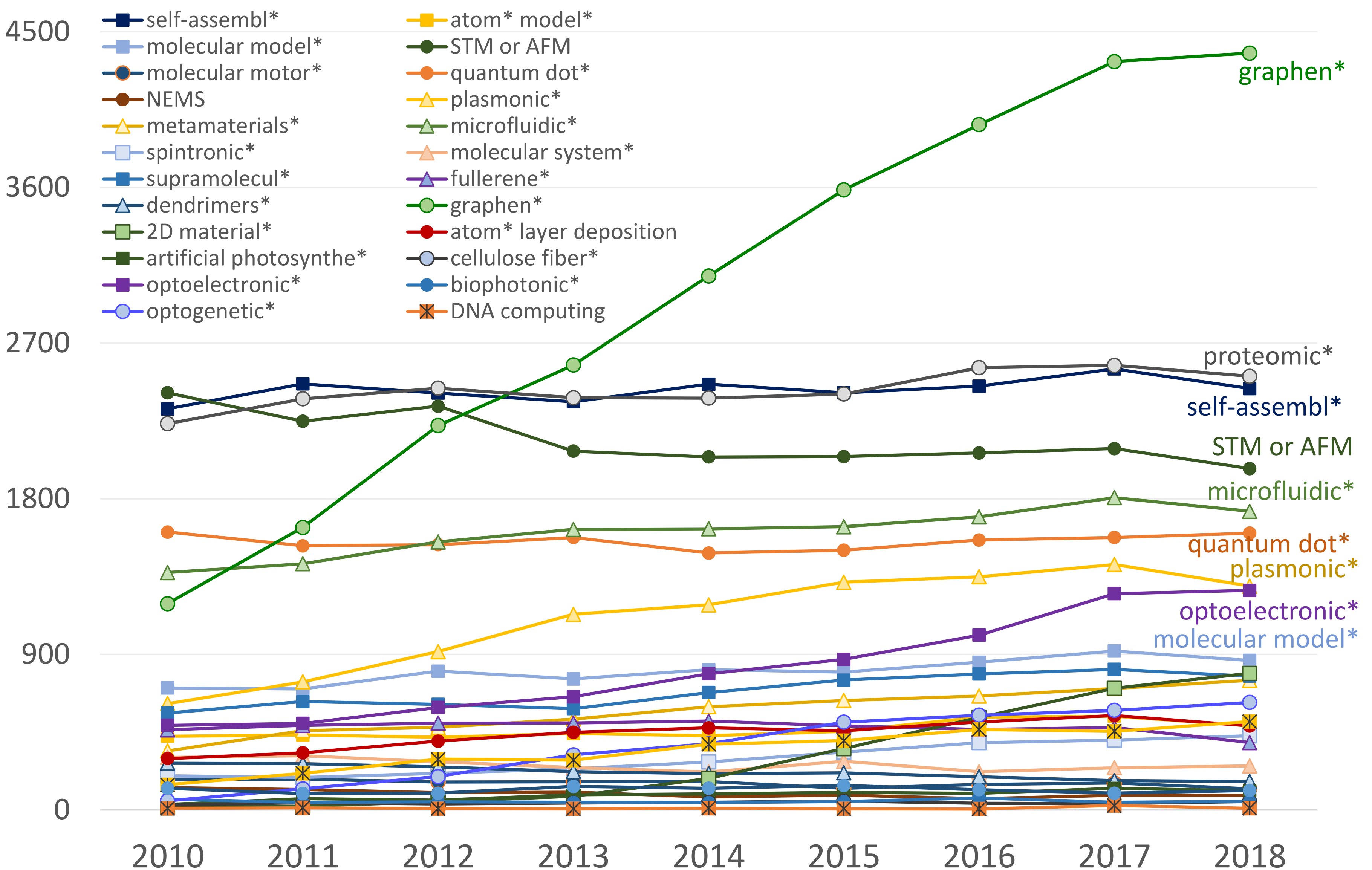
(about the average for last 5 years)



* Each article is assigned to multiple countries if its authors have different nationalities. Therefore, the sum of percentages from five countries exceeds 100%; ** Combined Keywords

Nanotechnology publications in United States 2010 - 2018

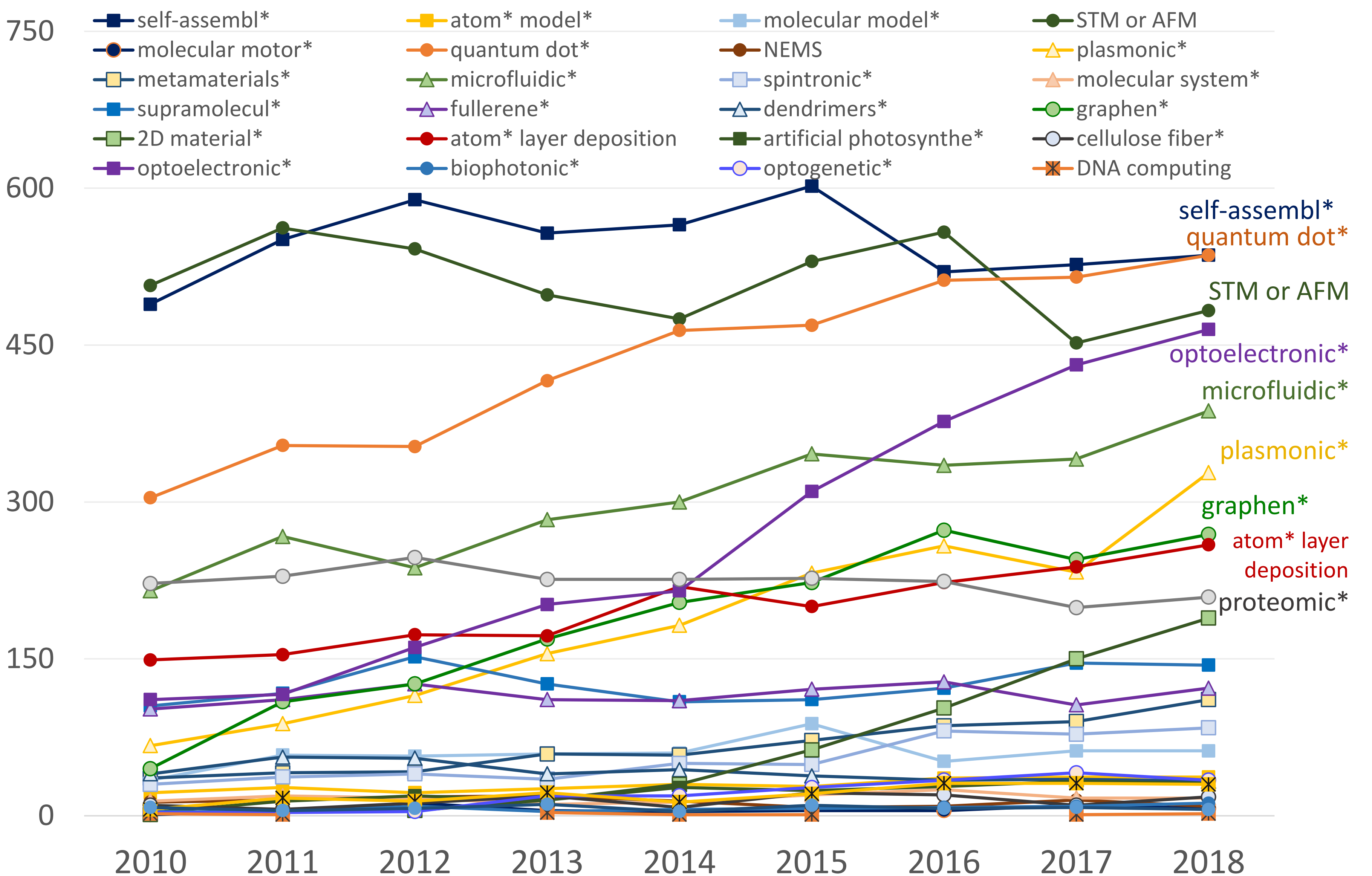
"Title-abstract" search in WoS by individual keywords: nano + 27 (method Nano2020, Ref 3)*



MC Roco, Sep 23 2019

Nanotechnology publications in South Korea 2010 - 2018

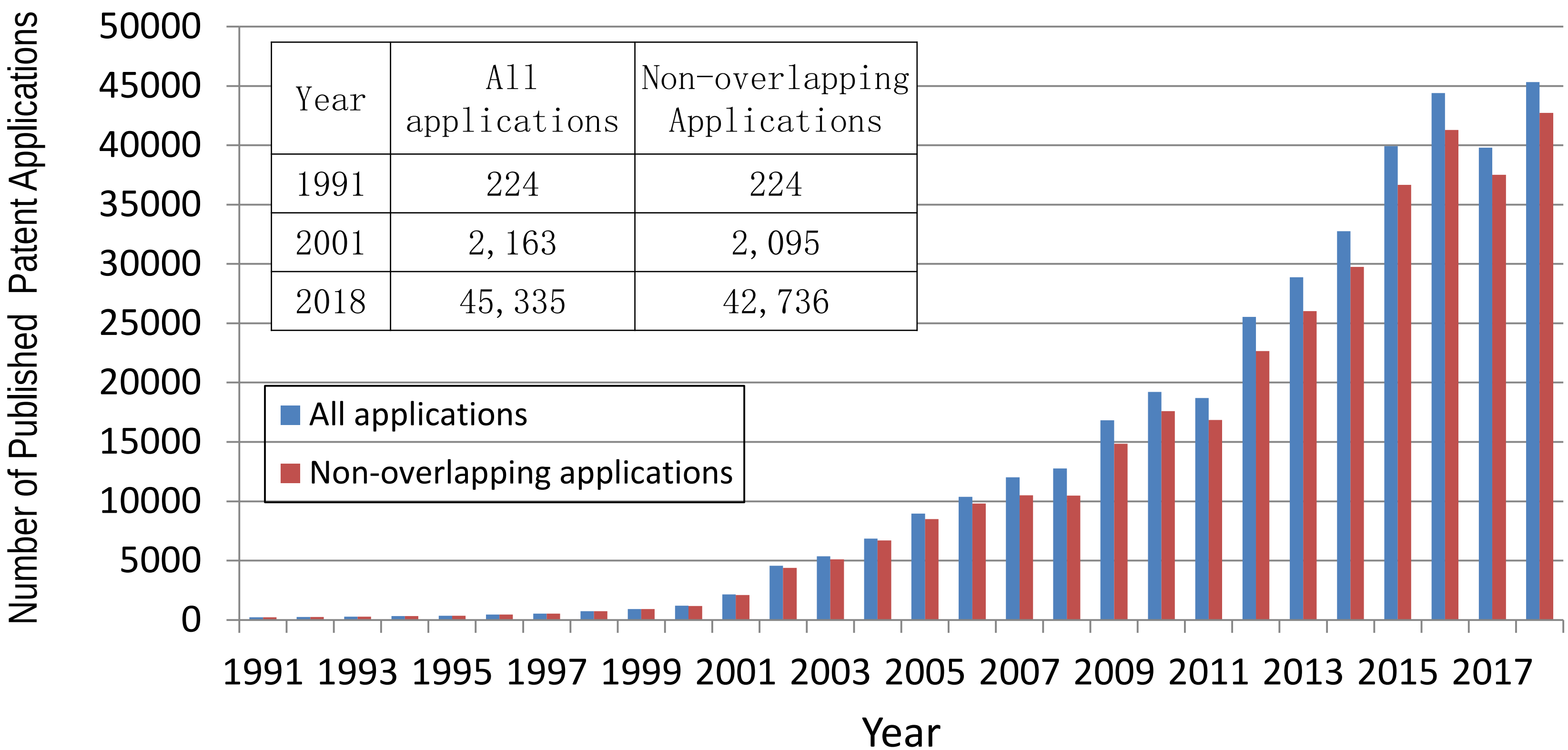
"Title-abstract" search in WoS by individual keywords: nano + 27 (method Nano2020, Ref 3)*



MC Roco, Sep 23 2019

Total number of nanotechnology applications per year in the World 1991-2018

Number of nanotechnology applications per year



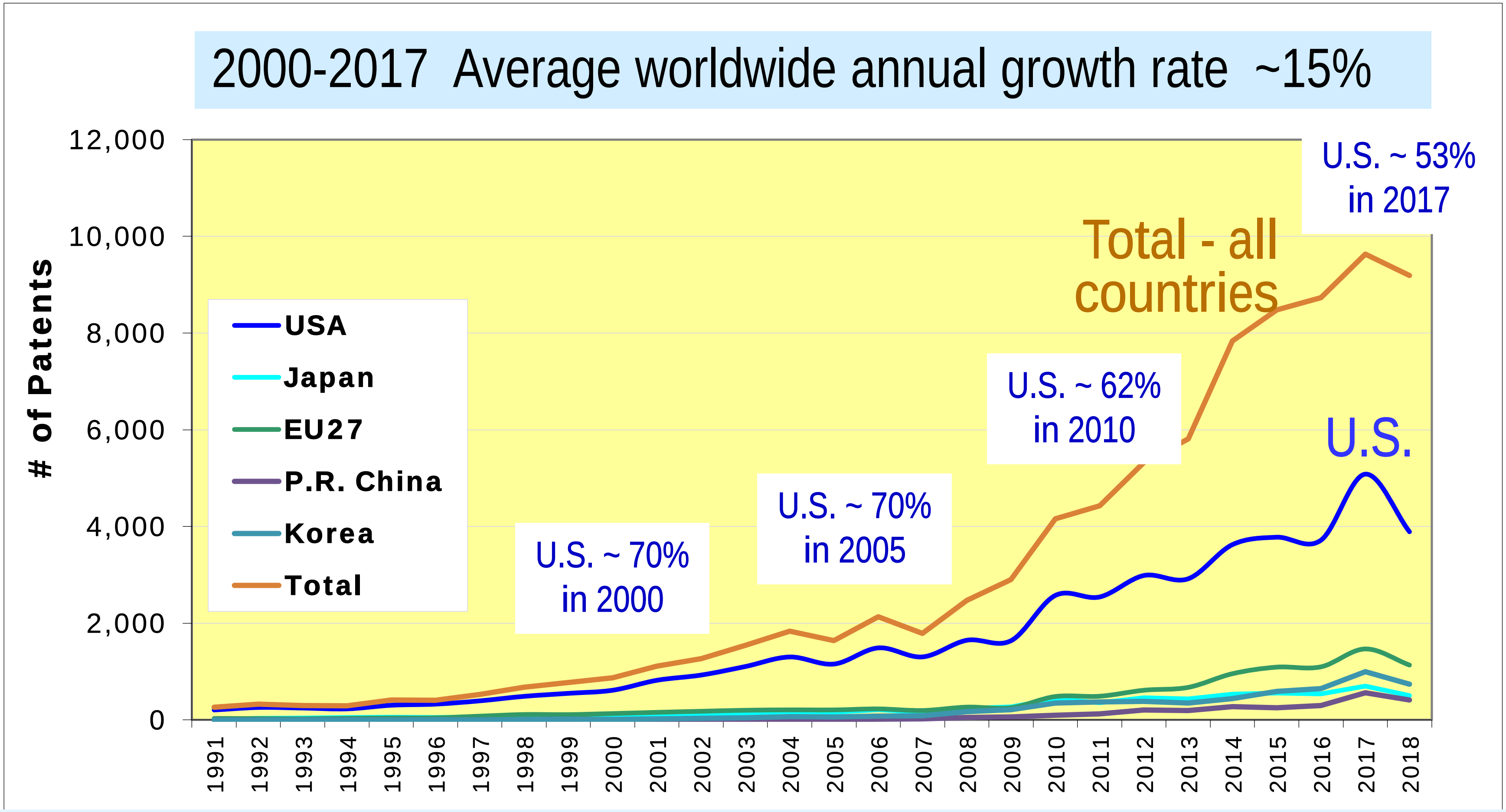
Year	All applications	Non-overlapping Applications
1991	224	224
2001	2,163	2,095
2018	45,335	42,736

Longitudinal evolution of the total number of nanotechnology patent applications in the 15 largest repositories per year ("title abstract," 1991–2018). *The numbers are based on "publication of patent application" in respective years. Data was obtained from UA NSE database (crawled from Espacenet) and EPO's PATSTAT Online service (2012-2018).

** Started using Combined Keywords from 2014

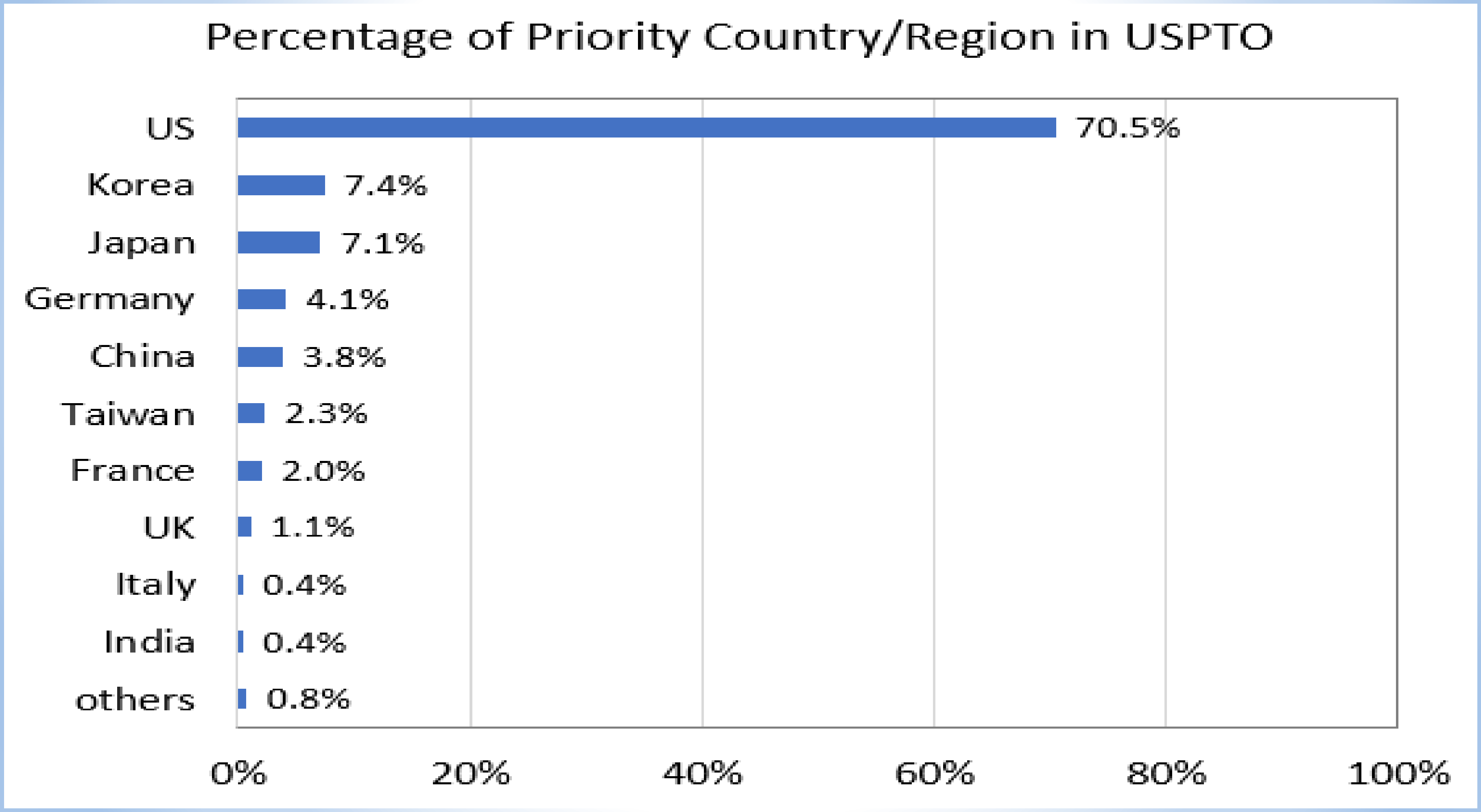
Nanotechnology patents at USPTO: 1991-2018 (data May 2019)

"Title-abstract" search of nanotechnology by keywords (update Chen and Roco [7])



U.S. patent authors maintain the lead at USPTO in 2018

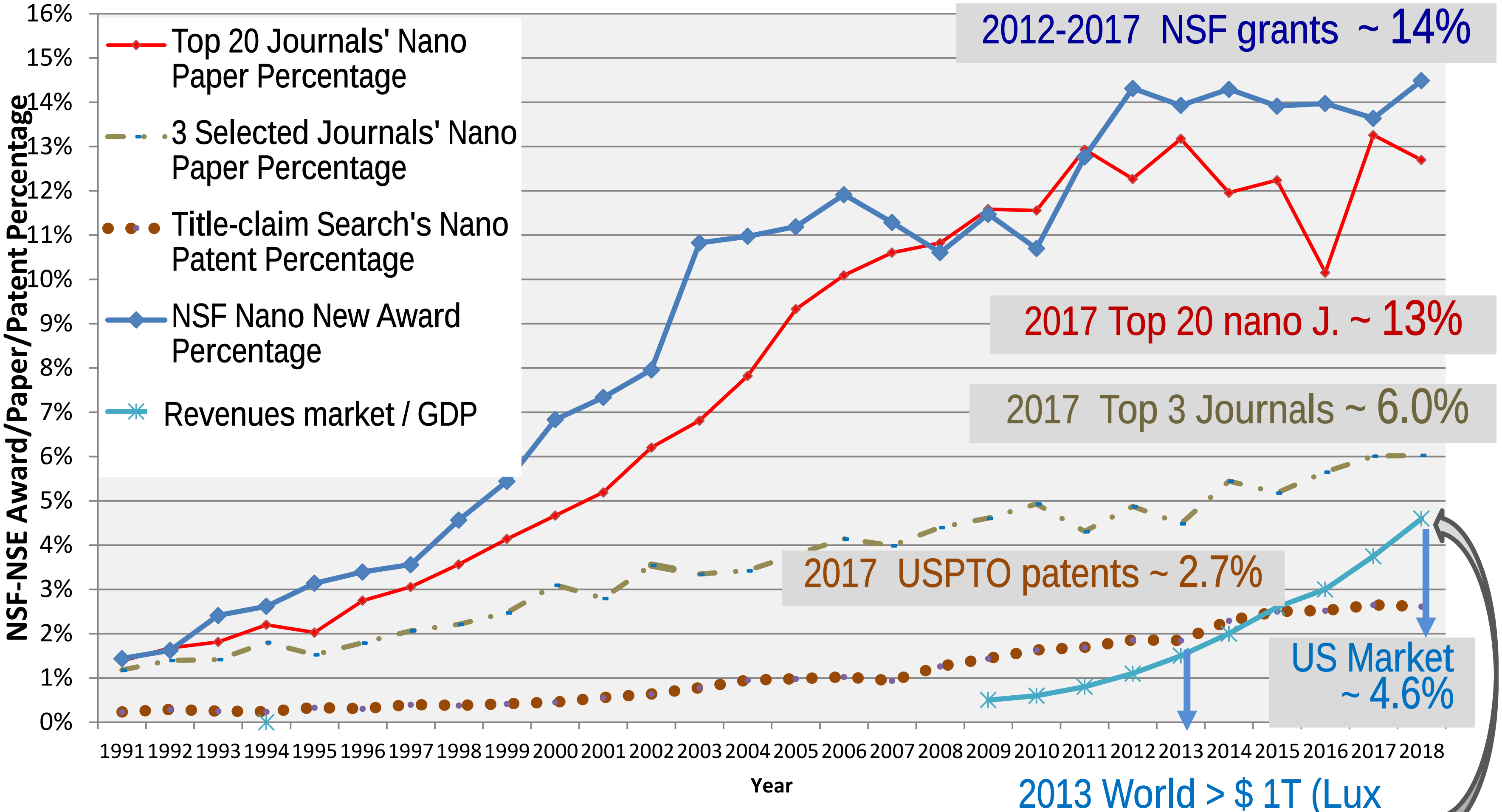
Country/region distribution in the USPTO in 2001-2017



Comparing Nanotechnology Landscapes in the US and China: A Patent Analysis Perspective, JNR, Springer, 2019

Percentage rate of penetration of nanotechnology in NSF awards, WoS papers and USPTO patents (1991-2018)

Searched by keywords in the title/abstract/claims (update Encyclopedia Nanoscience, Roco, 2016)



Est. US Market / US GDP: 2014 ~ 2%; 2018 ~ 4.6%

MC Roco, Sep 23 2019

Nanotechnology - Several trends *(1)*

- **Develop generalized theories, models and tools** for larger nanostructures (with complex information contents and interacting phenomena), and control of fundamental processes (such as self-assembling and quantum transition)

- Create hierarchical, modular, nano-precise **NBICA integrated design and manufacturing**

- **Emphasize nanotechnology for sustainability:** recyclability, water, energy, food, improve carbon-cycle

- **Nano-controlled gene editing** for medicine, agric., energy

Nanotechnology - Several trends *(2)*

- Brain–to-brain, -machine, -like devices and systems
- Develop hardware for quantum entanglement, communication and computing
- Nanotechnology for smart systems: general purpose AI & Intelligence Augmentation (IA); Intelligent Cognitive Assistants; cyber-physical-human systems; personalized education, healthcare and other services.
- Convergence with other foundational technologies to create new emerging S&T platforms

Related publications

(4 reports with R&D recommendations for 2020)

1. *"Coherence and Divergence of Megatrends in Science and Engineering" (Roco, JNR, 2002)*
2. *"Nanotechnology: Convergence with Modern Biology and Medicine", (Roco, Current Opinion in Biotechnology, 2003)*
3. *NANO1: "Nanotechnology research directions: Vision for the next decade" (Roco, Williams & Alivisatos, WH, 1999, also Springer, 316p, 2000)*
4. *NANO 2020: "Nanotechnology research directions for societal needs in 2020" (Roco, Mirkin & Hersam, Springer, 690p, 2011a)*
5. *NBIC: "Converging technologies for improving human performance: nano-bio-info-cognition" (Roco & Bainbridge, Springer, 468p, 2003)*
6. *CKTS: "Convergence of knowledge, technology and society: Beyond NBIC" (Roco, Bainbridge, Tonn & Whitesides; Springer, 604p, 2013b)*
7. *The new world of discovery, invention, and innovation: convergence of knowledge, technology and society"* (Roco & Bainbridge, JNR 2013a, 15)
8. *"Principles and methods that facilitate convergence" (Roco, Springer Reference, Handbook of Science and Technology Convergence, 2015)*
9. *"Science and technology convergence, with emphasis for nanotechnology-inspired convergence" (Bainbridge & Roco, JNR, 2016)*
10. *HSTC: "Handbook of Science and Technology Convergence" (Bainbridge & Roco, Springer Reference, 2016)*

This Nanotechnology Forum

- Exchange recent scientific results in both countries in the topics selected for 2019:
  - *single cell research*
  - *sensors for cognition and brain research*
- Explore new research trends
- Facilitate collaborative opportunities