

Opportunities and Challenges for HEI's in the SA Medical Device Industry



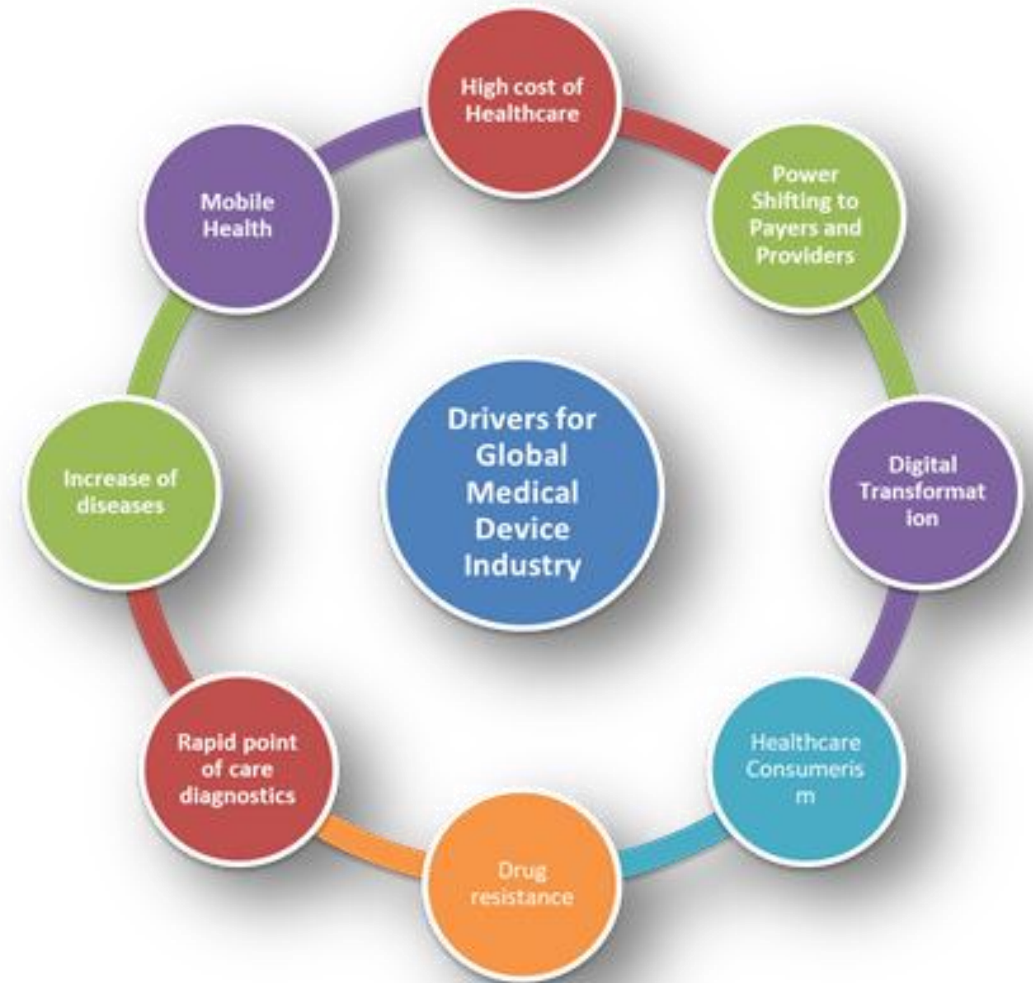
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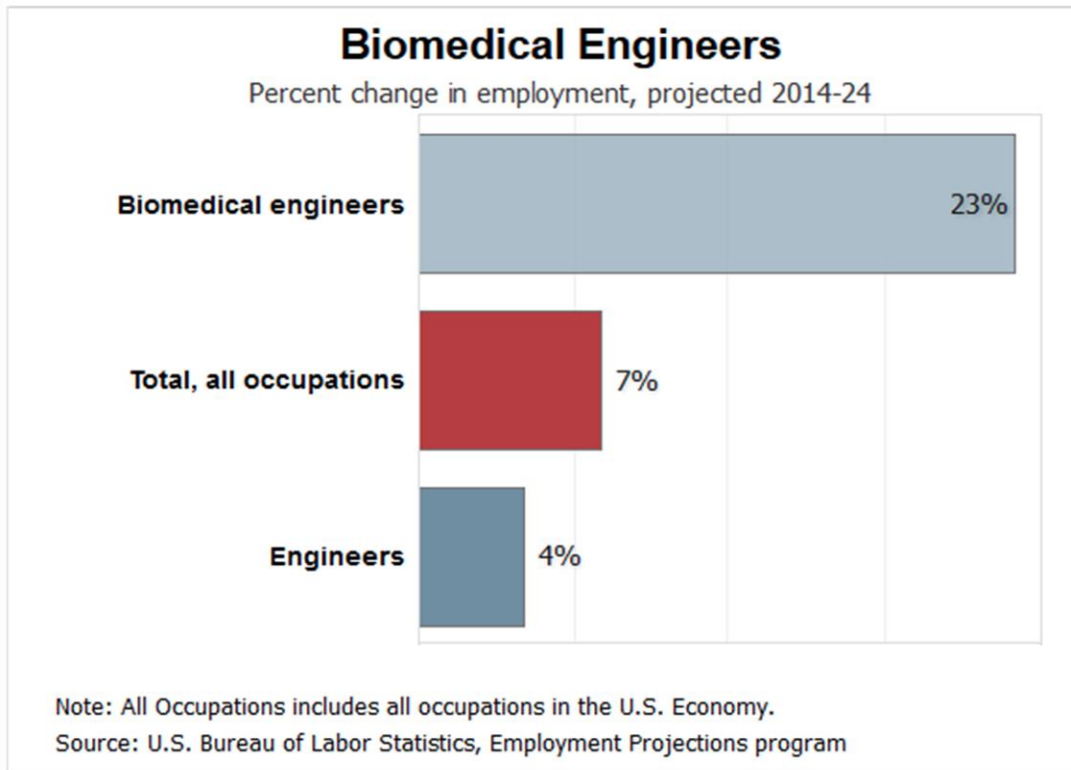
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Director: Martin Nieuwoudt

Key Global Drivers of Change in Med Devices

- Increased drug resistance of diseases
- Deployment of rapid point of care diagnostics at low costs
- Climate change, leading to an increase in the number of diseases and emergence of new diseases
- Healthcare consumerism, moving to a patient centric model
- Digital transformation of products and processes
- Explosion of mobile health, with the availability of smart phones to the poorest people
- High cost of healthcare, which is driving new innovation in diagnostics
- Power is shifting to medical aid companies and service providers



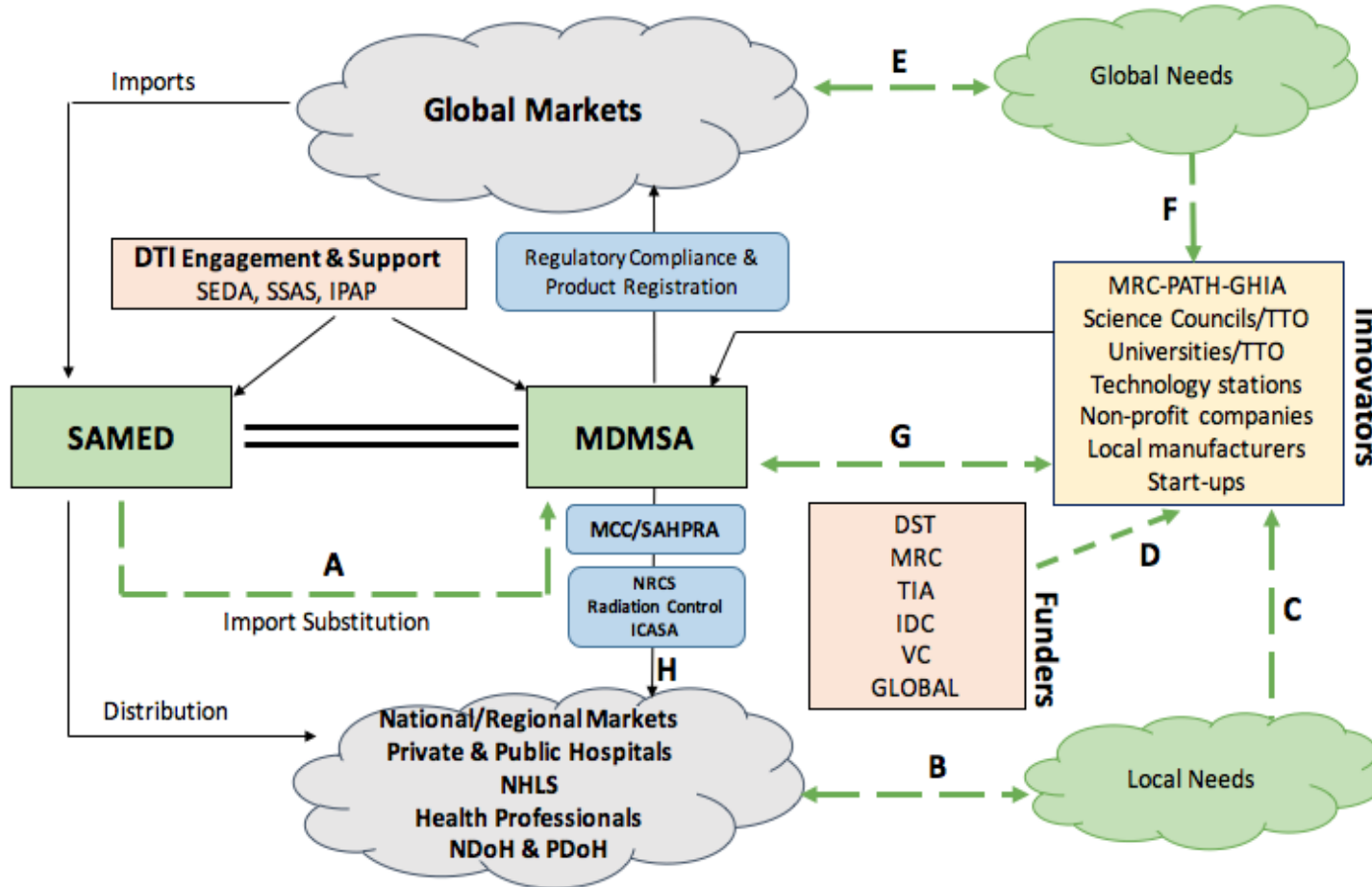


Medical Devices South Africa landscaping reports:

- BMI-Research SA Medical Devices report (BMI, 2016)
- The South African Medical Device Industry – Facts (SAMED, 2015)
- Medical Devices Sector Report (Wesgro, 2015)
- SAMED Business Monitor International, (2014)
- Developing an Ecosystem to support the local Medical Device & Diagnostics Industry in South Africa: (MRC-PATH Medtronic, March 2014)
- Research to Guide the Development of Strategy for the Medical Devices Sector of South Africa (Deloitte, commissioned by IDC/DTI, 2014)
- Situational Analysis of the RSA Medical Device Innovations Landscape (Acorn Technologies, 2008)

All projections from all reports predict a rapidly growing local Medical Device Industry sector.

THE SA MEDICAL DEVICE ECOSYSTEM



List of Abbreviations

ASSOCIATIONS & INNOVATORS

| | |
|---------------|---|
| SAMED | South African Medical Device Industry Association |
| MDMSA | Medical Device Manufacturers South Africa |
| MRC-PATH GHIA | MRC-PATH Global Health Innovation Accelerator |
| TTOs | Technology Transfer Offices |

GOVERNMENT BODIES

| | |
|--------------|---|
| DST | Department of Science & Technology |
| DTI | Department of Trade & Industry |
| -SEDA | Small Enterprise Development Agency |
| -IPAP | Industrial Policy Action Plan |
| -SSAS | Sector Specific Assistance Scheme |
| ICASA | Independent Communications Authority of South Africa |
| NDoH | National Department of Health |
| -MCC/SAHPRA | Medicines Control Council / South African Health Products Regulatory Agency |
| NHLS | National Health Laboratory Service |
| NRCS | National Regulator for Compulsory Specifications |
| PDoH | Provincial Departments of Health |

FUNDERS

| | |
|------------|------------------------------------|
| MRC | Medical Research Council (SHIP) |
| TIA | Technology Innovation Agency |
| IDC | Industrial Development Corporation |
| VC | Venture Capital |

The South African View

Sector Economic Indicators

- **Sector Size:** ~ R16.9bn
- **Imports:** R14.6bn
- **Exports:** R2.3bn
- **CAGR on exports:** 14%
- **CAGR for Africa and Asia:** 163%
- **Global Market share:** 0.4%
- **Jobs:** 20 945

Key Economic Indicators for the Medical Devices Sector

- SA med devices market (consumption, production and trade) estimated at US\$1.2 billion in 2013.
- Forecast to grow at a CAGR of 7.74% between 2013 and 2018. 2017 value close to US\$1.6B or R20B.
- Reasons: population growth, increased life expectancy, growing quadruple disease burden and increased domestic healthcare spend due to the introduction of the NHI.
- SA's spend on medical devices per capita = US\$24, comparable to fellow BRICS countries.
- But, compared to more mature markets, e.g USA, Germany, per capita spends stand at US\$399 and US\$313
- *Suggests ample room for growth.*
- SA's domestic medical device industry remains underdeveloped, **imports cater for 90% of market by value.** As such the 90/10 ratio of imports to exports creates a large balance of trade deficit currently estimated at R15B pa.



Much of materials taken from proceedings of SA Medical Device Stakeholder meetings 2017/18



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South African medical device industry association (SAMED):

- 160 manufacturers. Supply approx. 300,000 diff. med devices.
- Ave 2 new companies join SAMED monthly.
- Of > 700 local industry players, < 5% actually manufacture.
- Local firms, mostly SMME's < 50 employees. Industry employs approx. 4,000 people total.
- Often combine distribution activity with manufacturing.
- Multinational companies present in South Africa often operate in a joint venture capacity with local firms.

Weaknesses:

- Diverse product ranges, little opportunity for products + technology collaboration/clustering.
- Poor Industry-University + Industry-Science Council collaboration is. Few university-based medical technology innovations taken up by local industry + commercialized.
- Many companies operate in 'boot-strap' mode - under-financed.
- Lack of clusters due to small size of sector, low product diversity and lack of common value chains.



Industry Pain Points in order of priority:

1. Highly 'siloed' industry. Need for greater industry/community cohesion along the value chain (public & private)
2. Regulatory and quality management challenges/constraints
3. A lack of policies that support local industry competitiveness (preferential procurement)
4. Insufficient or poorly capacitated R&D and manufacturing incentives (costs related to raw material & labour)
5. Need for interventions aimed at maintaining and building a skilled labour force
6. Insufficient efforts and interventions aimed at stimulating local innovation and technology development (localisation & other financial & non-financial support is required). Should technology development be stimulated per disease focus areas, enabling technologies and inputs/ components would be required.
7. Lack of strategic integrated infrastructure required by the industry.



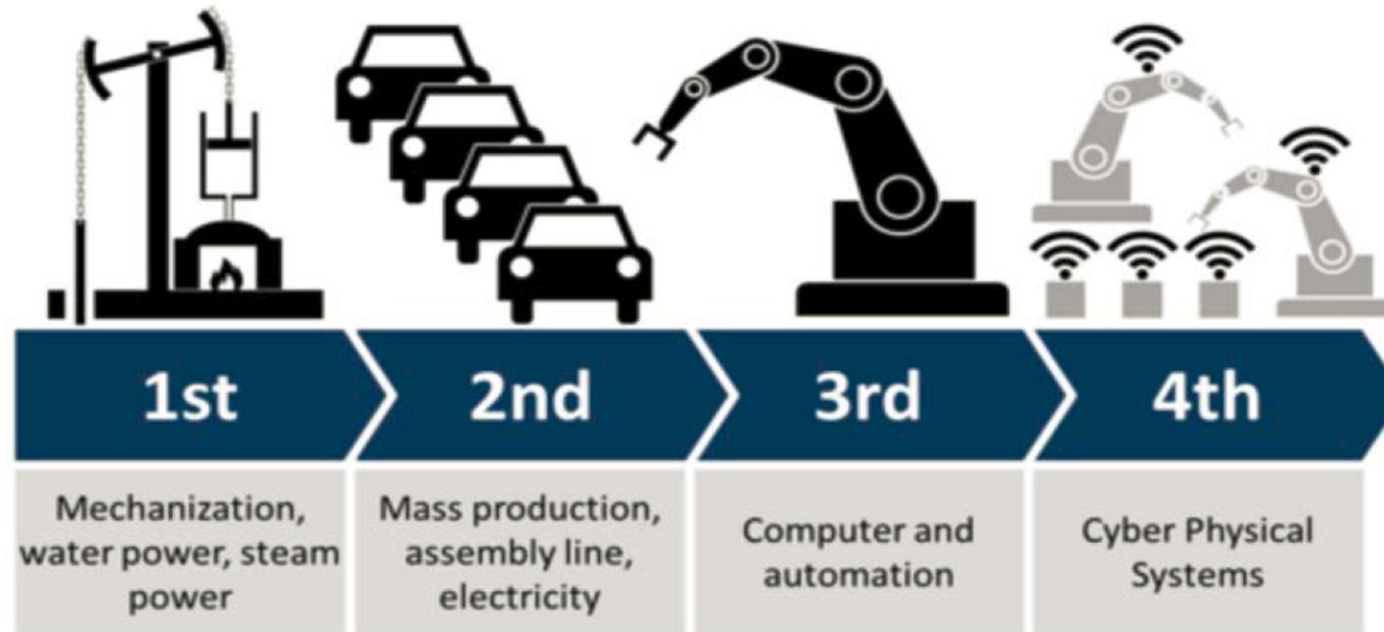
- https://www.usb.ac.za/usb_reports/innovation-in-sa-organisations-driven-by-c-level-support-new-report-finds/
- <https://www.usb.ac.za/wp-content/uploads/2019/02/The-State-of-Innovation-Report-Capabilities-2018%E2%80%932019.pdf>



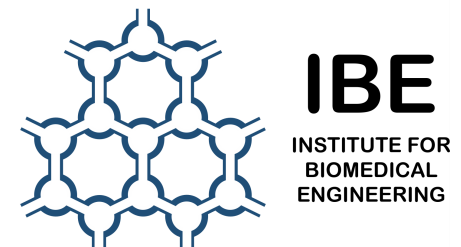
The time we find ourselves in:

What is the “4IR”? - *Klaus Schwab (2016), Founder and Executive Chair of World Economic Forum*

Industry 4.0 - current trend of automation and data exchange in manufacturing technologies: Includes, Cyber-physical systems, the Internet of things (IoT), cloud computing, cognitive computing, additive manufacture, autonomous vehicles.



- Schwab, Klaus (January 11, 2016). *The Fourth Industrial Revolution*. World Economic Forum. ISBN 1944835008
- https://en.wikipedia.org/wiki/Fourth_Industrial_Revolution



The 4IR is unique - speed, breadth and depth of changes caused by introduction of emerging technologies. Affecting more people & faster than ever.

- **Emerging set of industrial technologies** dependent on their interoperability and combinatory capacities
A disruption and blurring of lines between industry sectors
- **Societal transformation** made possible by new technologies. Impact more than economics. Values, identities and possibilities for future generations
- **Systemic change** driven by emerging technologies. Will impact business, society and politics & will require new regularity frameworks to mitigate the unintended social, economic and environmental consequences.

Characteristics:

- **Non-linearity:** Exponential businesses
- **Convergence:** Interface of digital and non-digital technologies. Incremental encroachment of global influence, culture and technologies on one another. Overlap of technological fields
- **Re-emergence:** Integration of digital into the traditional material, physical domain (e.g. 3D printing, bioprinting, neuroprosthetics etc).

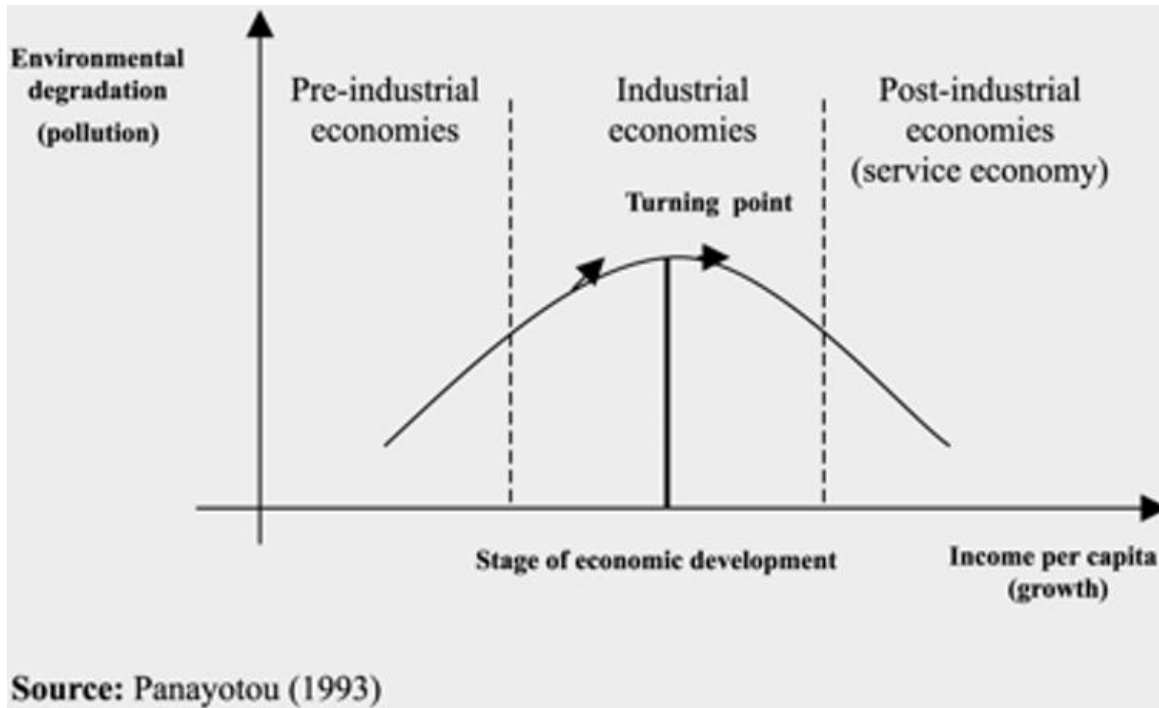


Arnaud Bernaert: The Fourth Industrial Revolution. European Medtech Forum 2016



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The historical view:



*Environmental Kuznets Curve - Income growth generates environmental degradation. Natural capital is treated as free, and carbon emission as costless, in accounting systems.

The new view:

4IR may help build a 'circular economy'† - industrial systems are restorative and regenerative by intention.

- IoT enables material & energy flow for greater efficiencies along product value chains.
- Development of service industries
- Less reliance on fossil fuels
- Renewable energy and Smart grids

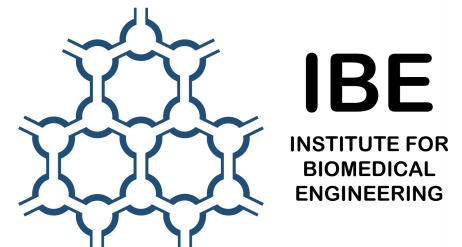
Industry 4.0 and impact on Medical Devices

Digital concepts and solutions previously considered *SCIFI* only a few decades ago are now real. Mobilization and integration of computing power, the power to handle + analyze masses of data, electronics shrinking in cost and size, global communication, global data access. Products and services can be connected to systems from anywhere. Removes geographic limitations of scheduling, controlling, and tracking manufactured products. Minimizes cost and maximizes production efficiency:

- Internet of Things (IoT)
- Big Data
- Cloud computing
- Machine Learning/Artificial Intelligence
- Mobile technology
- Microelectronics
- Low cost sensors

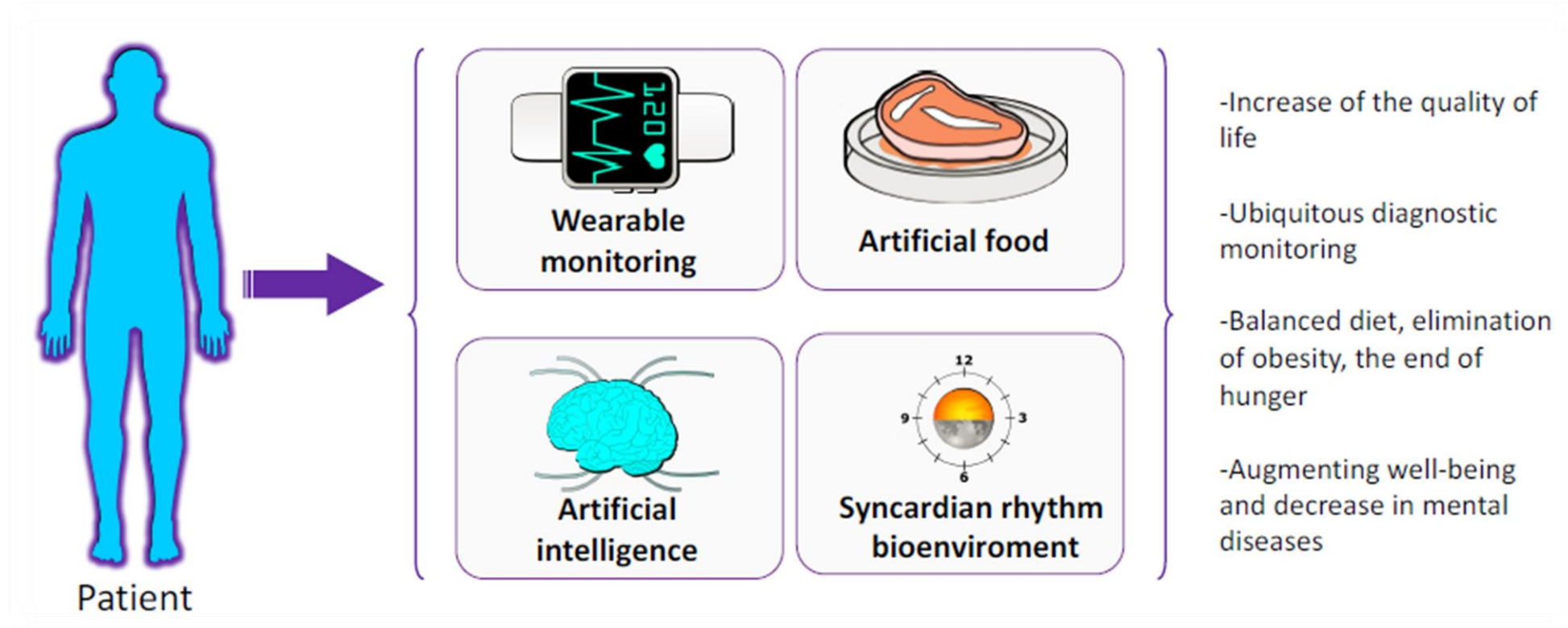


‘Production of medical devices is poised for revolution’.

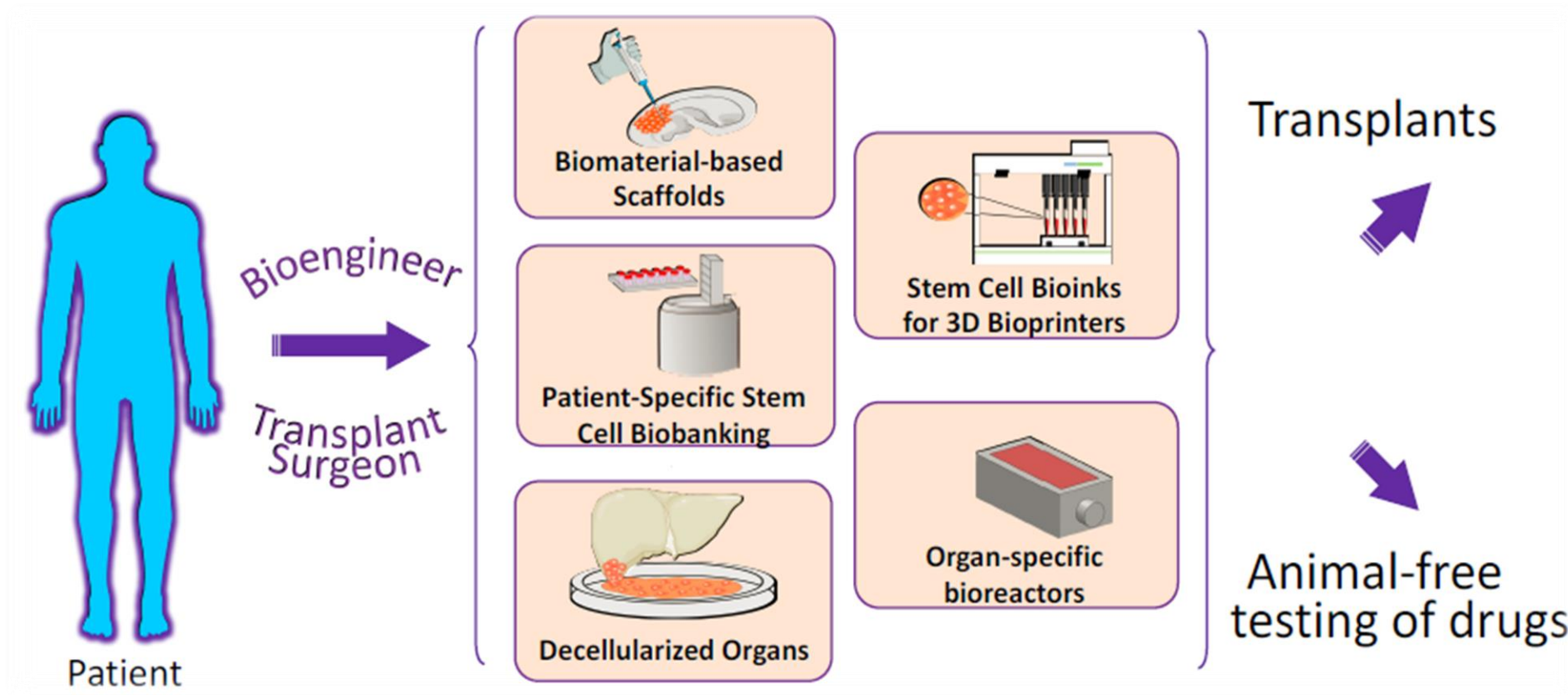


Health Domains:

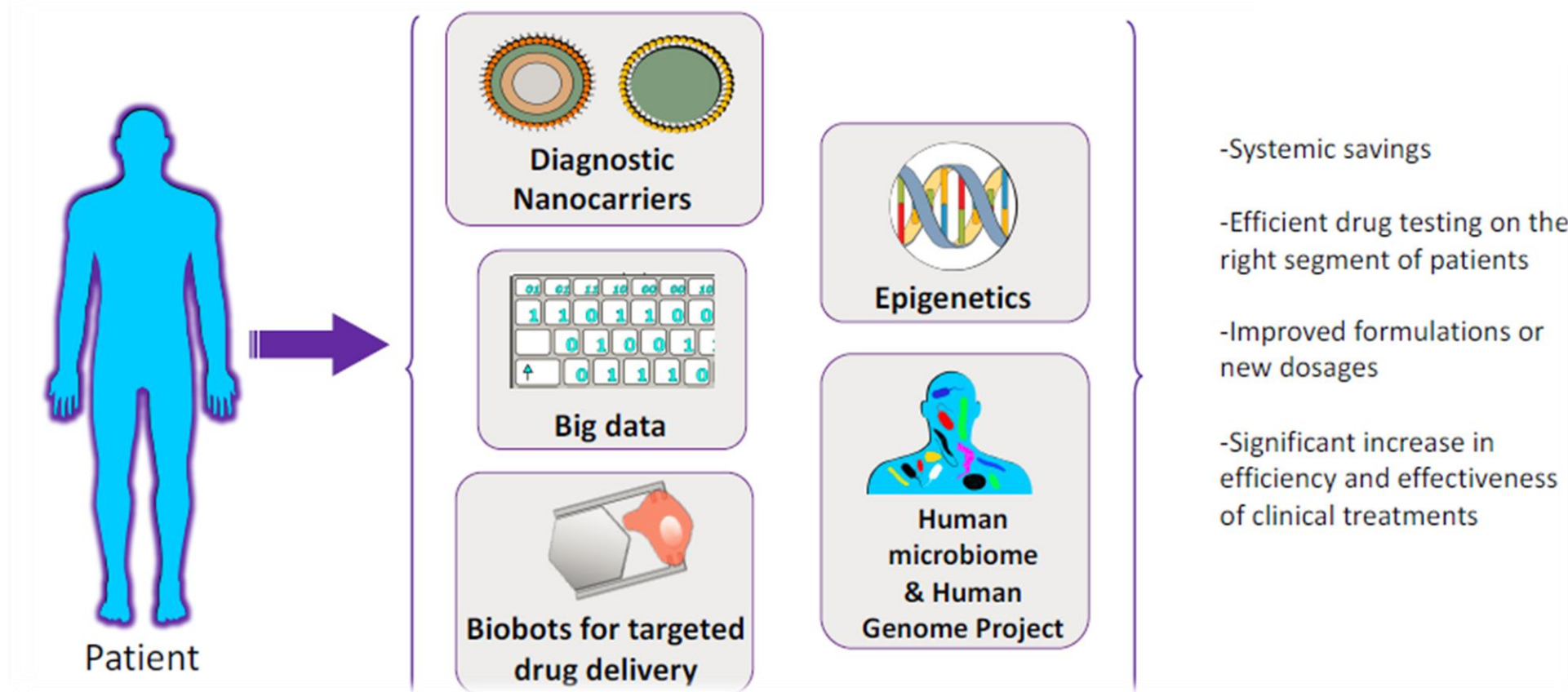
Preventative Medicine and eHealth



Artificial Organs and Regenerative Medicine

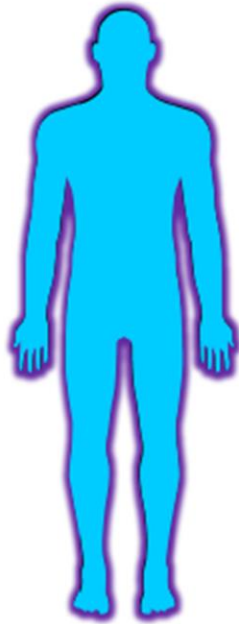


Personalized Medicine and Nanotechnology

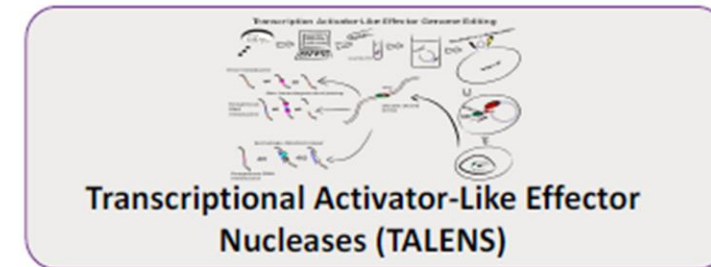
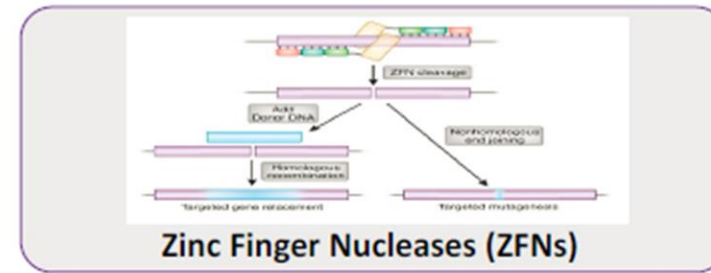
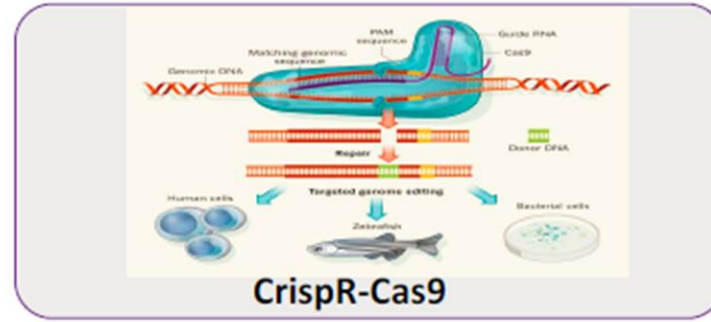


Gene Editing

*Special note: Immunotherapies,
+ *Off-target* CRISPR

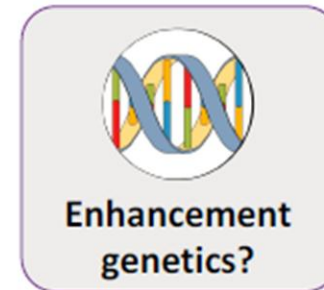


Patient



-Different types of therapeutic editing

- Specificity: A pre-requisite for broad clinical application



- “It seems that for the first time in human evolution, the speed of change is outpacing our evolutionary brain capacity to cope with it.”
- Four dimensions of big data: **volume, variety, velocity and veracity**. Rapid growth in health data facilitating an unprecedented understanding of health and wellbeing like no other in human history.
- Current **ethical, legal, and regulatory frameworks not sufficient to regulate** new data or speed of change.

Problems/challenges associated with the 4IR(a):

1. With increased data access

- With big data- Privacy, confidentiality, ethics. Who owns our data? Who has access to the data? How will the data be regulated?
- With AI – Is the data meaningful? What biases are in the data? Who gets access to the data?
- Trend among global tech giants and insurance companies towards the privatisation of health data. Methods treated as proprietary trade secrets. *‘Its about commerce, not health’*
- Data security –Facebook scandal, Breaches of Dropbox, Adobe, LinkedIn, Myfitness pal, Verifications.io, Ster Kinekor
- Blockchain as a security/privacy solution

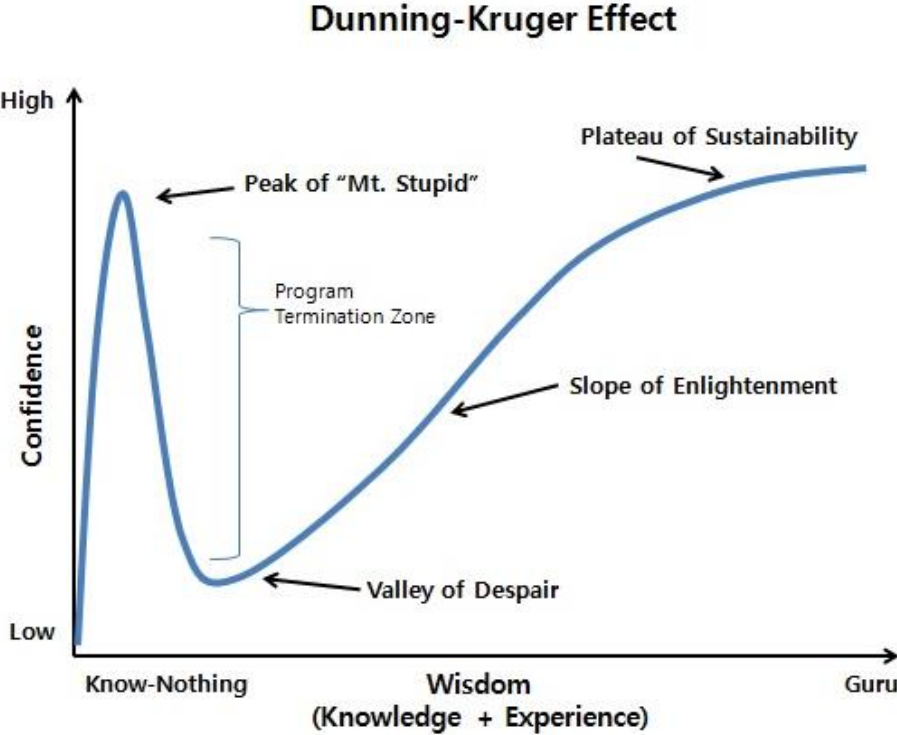
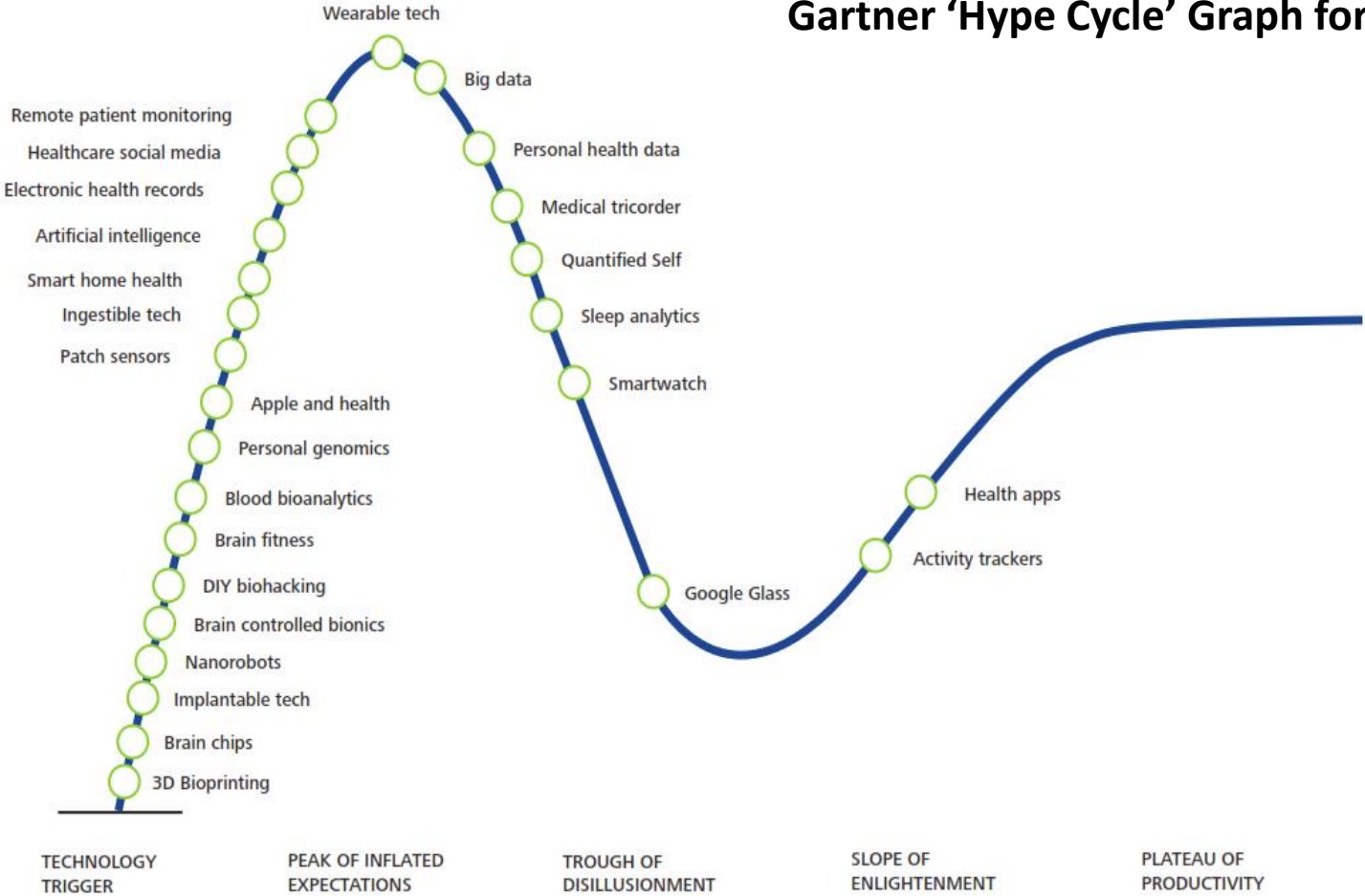


*Zajfman D. Curiosity driven research as driver for high value innovation.
Presentation at 5th Agora round-up held in Zürich on 3 September 2018.

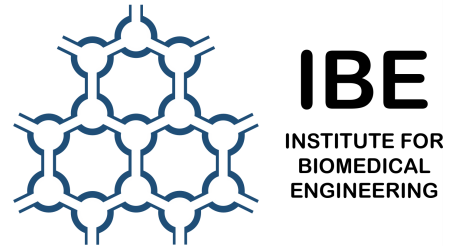


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A word of caution: Gartner 'Hype Cycle' Graph for Medical Devices



https://en.wikipedia.org/wiki/Dunning%E2%80%93Kruger_effect



Problems/challenges associated with the 4IR (b):

2. Joblessness

- * *'Premature deindustrialisation'* – Move from manufacturing into service industries in developing countries
- Mining – 4IR -digitized and non-invasive. Loss of low-skill labour jobs
- Rising inequality = social instability

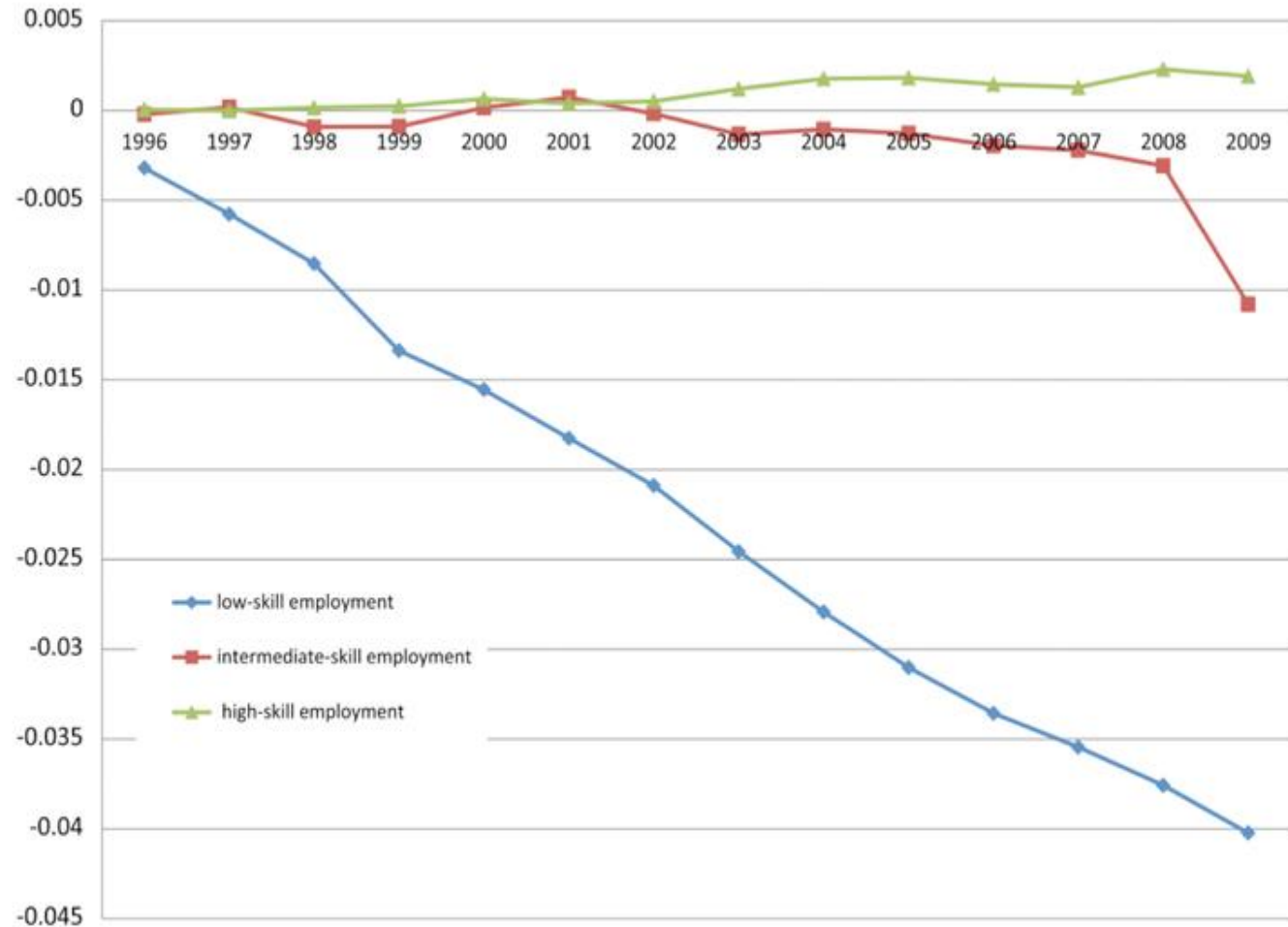


Fig. 4 Estimated year coefficients for employment of different skill types

Problems/challenges associated with the 4IR (c):

3. Regulatory Compliance in manufacture

- Medical devices demand the highest quality levels – lives depend on this
- Lacking in individuals adequately qualified to audit manage such processes
- In theory - Data from the ‘smart’ factory, proactively eliminate errors before they occur
- However, customized solutions such as patient-specific devices add complexity and cost
- Regulatory bodies (e.g. FDA, ISO etc) might need to broaden mandate – As mobile health apps or software-based medical devices perform “patient-specific analysis, diagnosis, or treatment recommendations.”



Summary: Bioethics and Biopolitics

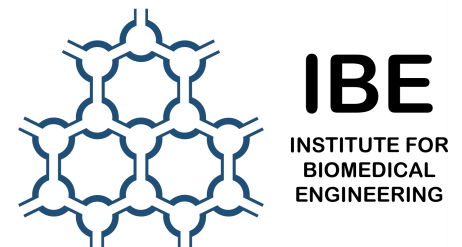
The future of healthcare holds the unprecedented opportunity to decrease inequalities

But there are Risks & Responsibilities:

- Hacking of medical devices
- Privacy and confidentiality of medical records
- Patient empowerment vs negligence in the era of digital healthcare
- Financial inequalities could lead to biological inequalities? (Gene editing is expensive)
- Ageing and overpopulation
- Bioterrorism (synthetic biotoxins)
- Transhumanism & Singularitarianism - gene editing gone astray =>



Arnaud Bernaert: The Fourth Industrial Revolution. European Medtech Forum 2016



Example: What's the worst that could happen?

He Jiankui et al: Draft Ethical Principles for Therapeutic Assisted Reproductive Technologies. The CRISPR Journal, Volume 1, Number 6, 2018, Mary Ann Liebert, Inc. DOI: 10.1089/crispr.2018.0051

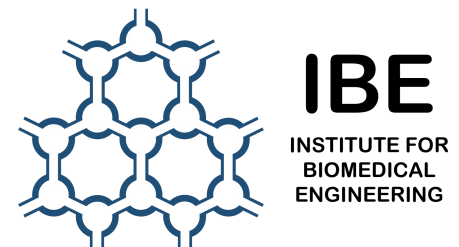
“Crispr Babies, IVF, and the Ethics of Genetic Class Warfare” - Chinese national He Jiankui headed a team that used CRISPR editing to modify the *CCR5* gene in human embryos that were then implanted, resulting in the birth of twin girls who He believes will be immune to infection by HIV. (It was later revealed that the trial also resulted in a second pregnancy.)

The news brought widespread condemnation from researchers and bioethicists who said the risks of editing human babies, particularly to head off a disease that can be prevented in other ways, are too great.

He Jiankui, claimed in various documents that the experiment was backed by Chinese government funding



- <https://www.wired.com/story/crispr-babies-ivf-and-the-ethics-of-genetic-class-warfare/>
- <https://www.the-scientist.com/news-opinion/crispr-babies-trial-may-have-been-government-funded-65523>



BME is inherently inter-disciplinary. It involves any applications of Physics, Mathematics, Sciences and Engineering at the intersections of Biology, Medicine and Health Sciences, aimed at solving or improving health-related problems.

INSTRUMENTATION, SENSORS, AND MEASUREMENT

BIOMATERIALS

BIOMECHANICS

BIO-INFORMATION TECHNOLOGY AND TELEMEDICINE

CLINICAL ENGINEERING AND HEALTH SYSTEMS

REHABILITATION ENGINEERING

SYSTEMS PHYSIOLOGY

**MOLECULAR BIOLOGY, BIOCHEMISTRY
AND DIAGNOSTIC TECHNOLOGY**

NANOTECHNOLOGY

- the use of electronics, computer science, and measurement principles to develop devices used in the diagnosis and treatment of disease. Biosignal processing falls within this area.
- the study and development of naturally occurring or laboratory-designed materials for use in medical devices or as implantation materials.
- the study of mechanics, including device design and thermodynamics, to solve biological or medical problems.
- uses modern computer and networking technology to solve medical problems or create health-monitoring applications.
- the development, repair and optimization of healthcare delivery systems.
- the study of engineering and computer science to develop devices that assist individuals with physical and cognitive impairments.
- the use of engineering methods to understand how living systems function and respond to changes in their environment and thereby to enable interventions.
- the use of modern molecular techniques for understanding biological systems and to develop, for example Point of Care, diagnostic applications.
- the use of nanoscale instrumentation in diagnostic and medical

Western Cape - 45% of companies commercialising Med Device inventions have come from universities:

Stellenbosch

- Diacoustic Medical Devices – Automated Paediatric Cardiac Auscultation (APCA) system is a portable hand-held device providing healthcare providers with clinical decision support to distinguish between pathological and physiological heart murmurs
- Surfactant Medical Technologies (SMT) – a synthetic surfactant formulation consisting of a combination of readily accessible phospholipids and synthetic peptides
- Stellenbosch Nanofibres – some products of which are intended for medical applications
- Azargen – plant genetic engineering for human protein production
- Unistel Medical Labs – Genetic DNA profiling
- Kathleho Biomedical – a recent platform for the R&D and commercialisation of innovative biomedical engineering concepts.



Materials from Innovus



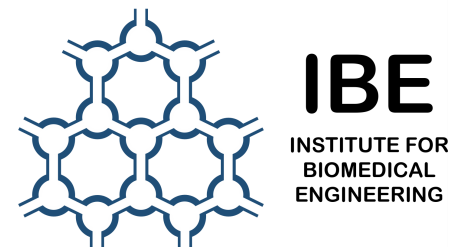
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- Lodox – low radiation dose X-ray and Ultrasound imaging applications
- Cell-Life – e-Health technology development company
- Cape Ray Medical – low dose x-ray coupled with ultrasound or breast cancer detection
- Strait Access Technologies – heart valve and deployment device for heart valve repair
- Serapix CC – biosensors/diagnostic
- Antrum Biotech – extra-pulmonary TB diagnostic test – rapid bedside testing
- Attri Orthopedics – design of orthopaedic implants exclusively for people who have suffered loss of bone tissue due to surgery.

UWC

- Hyrax Biosciences – clinical DNA analysis and drug resistance genotyping

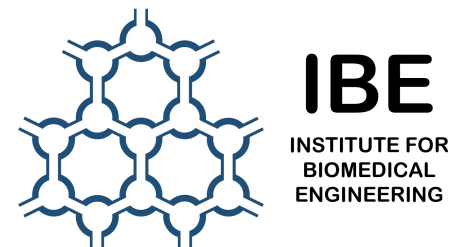


The Problems: Constraints to innovation for HEI's

- Critical skill/human-capacity shortages. Sustained investment required in, e.g student bursaries, staff compliment to train students + the underlying infrastructure.
- Historic notion of government + industry = 'Education and innovation are mutually exclusive'. Government incentives + job performance => research output metrics, i.e. awarded degrees + journal publications. But, technological innovations widespread + common. See above lists + Google is an excellent example!
- Funding for innovations focussed on project-by-project approach. Does not build sustainable long-term pipelines for innovation. Investment required in human capacity focussed on market-driven requirements. Government funding instruments require synchronization with private sector.
- 'Technology-push' rather than 'market-pull' strategy of HEI R&D innovations. Research doesn't address needs of the market. Also, a lack of knowledge regarding medical device regulation. Compliance often sought at great expense *after* R&D
- A one-size-fits-all solution not appropriate for all HEI's. Pronounced asymmetries between institutions in BME domain, e.g. what UCT and what SU needs is different. HEI's also in direct competition with science councils for government funding, despite councils enjoying selective advantages.



Materials from my own interviews/surveys



'Success' in SA Medical Device Innovation, as a Bayesian Optimization problem:

1. Optimization = adjust the parameters of a (high dimensional) system to achieve a desired result
2. We have a 'belief', a given prior distribution, of what success looks like
3. We have some data (D)
4. Infer a posterior distribution, given the data,

$$p(\mathbf{w} | \mathcal{D}) = \frac{p(\mathcal{D} | \mathbf{w}) p(\mathbf{w})}{p(\mathcal{D})}$$

likelihood prior distribution

data

5. Iteratively maximize an objective function, f, namely 'success' probability

$$\mathbf{x}^* = \arg \max_{\mathbf{x} \in \mathcal{X}} f(\mathbf{x}),$$

where X is the design space of interest, i.e. the SA Medical Devices Ecosystem

Algorithm

- 1: **for** n = 1; 2, **do**
- 2: select new \mathbf{x}_{n+1} by optimizing the objective probability function,
 $\mathbf{x}_{n+1} = \arg \max f(\mathbf{x}; D_n)$,
- 3: query objective function to obtain y_{n+1}
- 4: augment data $D_{n+1} = \{D_n; (\mathbf{x}_{n+1}; y_{n+1})\}$
- 5: update statistical model
- 6: **end for**

***My Actions:* Parameter adjustments to maximize success probability function:**

1. Implementation of new BME degrees
2. Implementation of training in Medical Device Regulation
3. Implementation of Product Design and Development Innovation Skills Programme/s
4. Direct Interface/Collaboration with Industry
5. 'Push' SA government to fund human capacity development in BME

Summary:

Ideally, a far greater synergy or synchronization is required between academia and industry than currently exists. e.g. in Germany more than 70% of funding for HEI engineering projects comes from partners in industry.

- In return for small investments by companies in e.g. bursaries + operating costs, receive the expert knowledge of supervisor/s, innovative HEI environment, + following project completion, a student trained specifically for the company's needs.



Thank you ! (martin.nieuwoudt@gmail.com)

