



Entering the DNA information age and the Impact on Science and Society

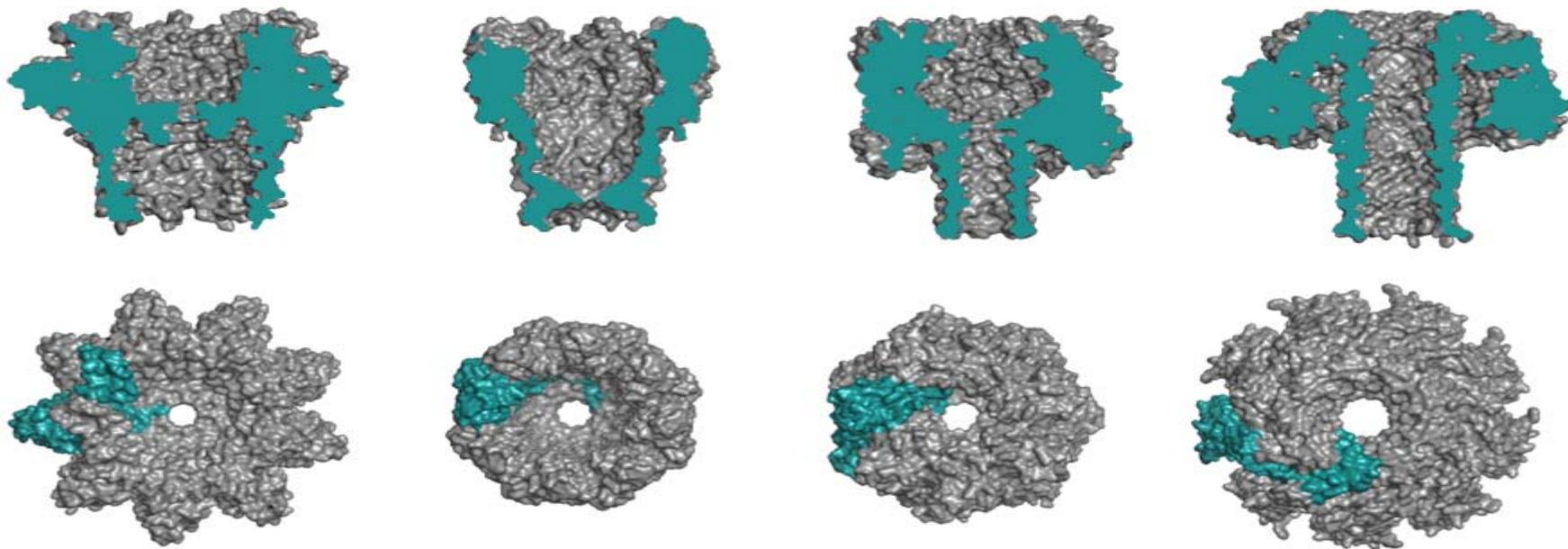
Jim McDonald
CEO, Oxford Nanopore

14 February 2017

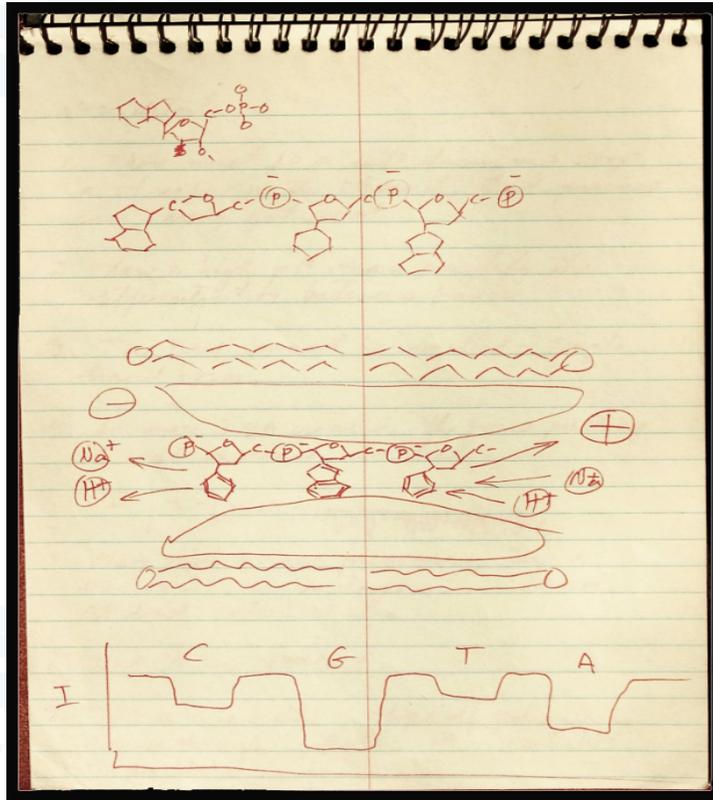
MANY NANOPORES FOR SEQUENCING CHEMISTRIES

DIFFERENT SHAPES AND SIZES HAVE BEEN ENGINEERED FOR SEQUENCING

- Some public crystal structures available, others obtained by ONT and collaborators



Nanopore Concept



- Deamer & Branton *et al*
- ~20 years ago
- Hundreds of papers and patents since

Deamer's Notebook

Company Overview



- Formed in 2005 to develop a novel single-molecule sensing system for DNA sequencing, proteins and other analytes
- Products: MinION™ series electronic devices + others
- DNA 'strand sequencing' approaching the market
- Total investment to date > £350M
- Experienced management and Board, 300 employees



GLOBAL, LONG TERM IP STRATEGY FOR LEADERSHIP IN NANOPORE SENSING



UNIVERSITY OF OXFORD

Bayley Group Pioneers of modified protein nanopores



HARVARD UNIVERSITY

Branton & Golovchenko State of the art solid state nanopore with nanotubes



UNIVERSITY OF CALIFORNIA SANTA CRUZ

Deamer & Akeson Pioneered the use of nanopores for DNA



BOSTON UNIVERSITY

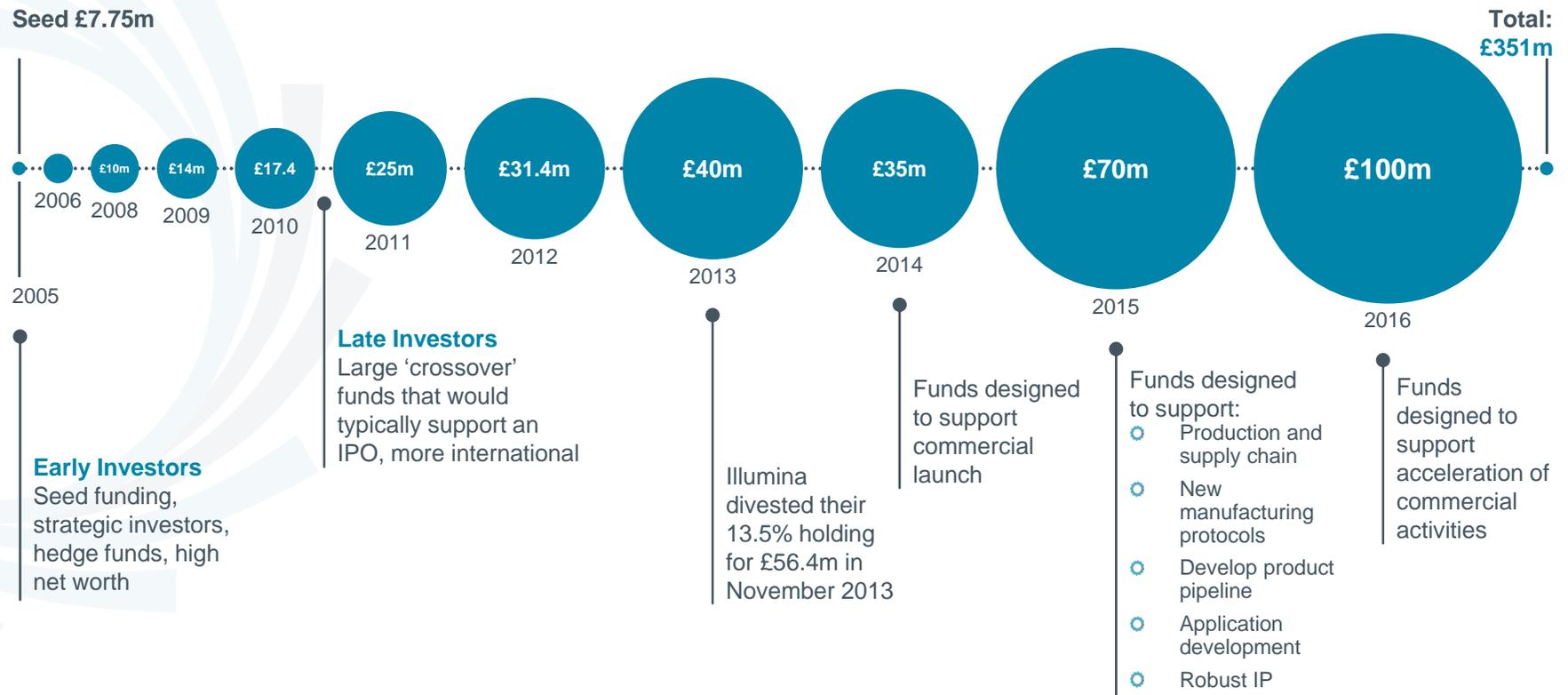
Meller Group Combining solid state holes with proteins

Broad range of agreements include

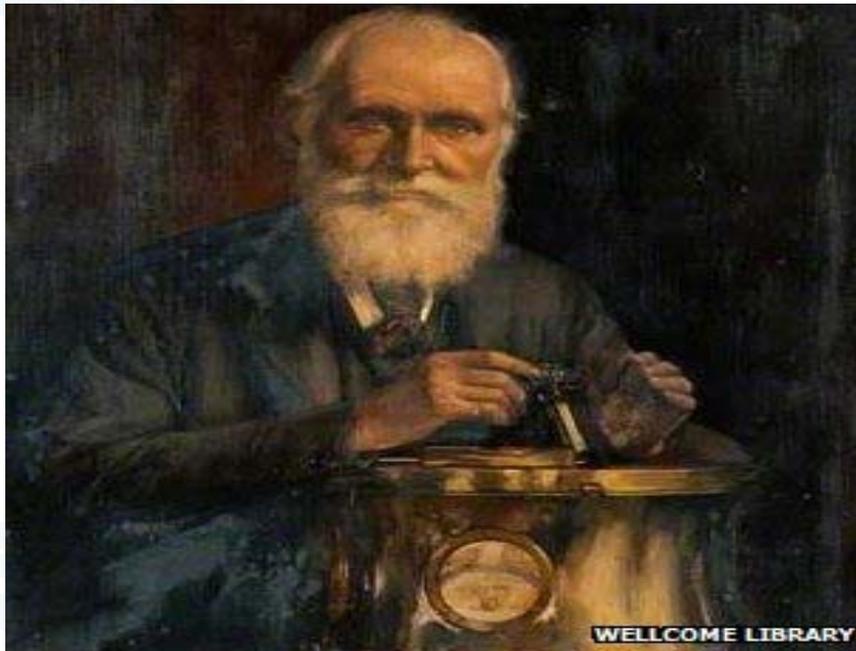


- Adds to substantial internal IP
- In total: more than 600 issued patents and patent applications, in over 137 patent families
- Research funding for continued access to cutting edge technology
- Today, 36 exclusive license agreements with 32 institutions

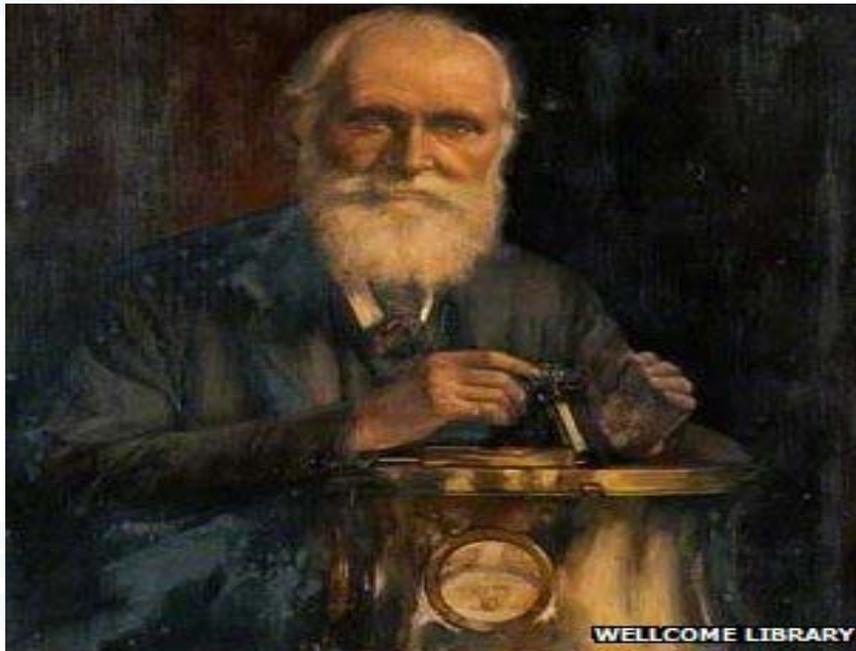
FUNDS RAISED TO DATE



WHO IS THIS



LORD KELVIN

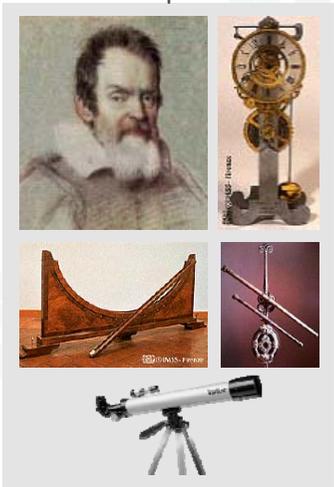


“When you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot measure it, when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind; it may be the beginning of knowledge, but you have scarcely in your thoughts advanced to the state of Science, whatever the matter may be.”

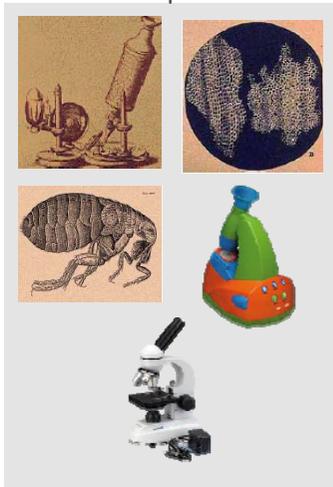
Lord Kelvin, British Scientist, 1824-1907

MEASUREMENT IS CRITICAL TO SCIENTIFIC PROGRESS

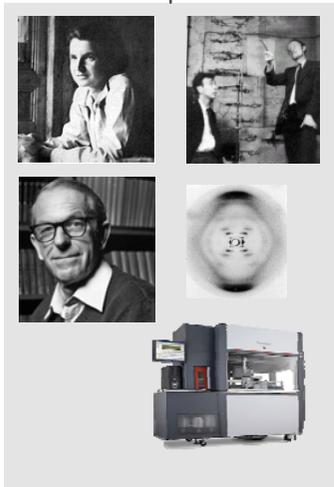
Galileo
Looking to the skies



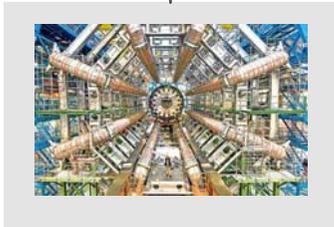
Robert Hooke
Looking to the micro-scale



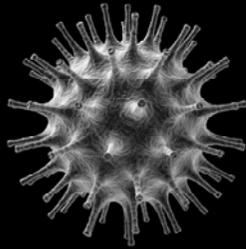
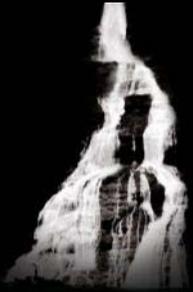
Franklin, Watson, Crick, Sanger,
Looking at biology



And of course



DNA IS IN EVERY LIVING THING



What is it?
What is *in*
it?

Is it changing?
Responding?

Is it healthy or
diseased?

What is the
disease?

Is it harmful?

How does it
vary from
others?

Human genome

3 billion base pairs (Gb) x 2
(=3,000,000,000 base pairs x 2)
Individual genes ~10,000s

Personalised Medicine

What is this disease?
What is the genetic contribution?

What is the best treatment strategy and medication for this person?

How is this person responding to treatment?
Is the disease starting to reappear?

Research

How do peoples' biology vary and why?

Human ID

E.g. Who is this?

Self-quantification

E.g. Has my biology changed? Do I need to seek advice?

Mammalian genome

3 billion base pairs (Gb) x 2
 (=3,000,000,000 base pairs x 2)
 Individual genes ~10,000s



Food

What species is present in this food and in what amounts? Is that what I was expecting?

Is it safe?

Livestock

How is this population managing? Healthy or declining? What is the movement of this species between areas? Has this changed?

How should I be breeding this livestock?

Wheat genome

17 billion base pairs

Research

How do plant species' biology vary and why?
What properties do those variations concur?

What are the mechanisms of its molecular biology?

Crop science

Where has this plant variety come from?
Is it drifting from nearby crops? Has its genome changed?

Can I specifically prevent this pest from growing/
being able to infect this crop?

Can I create strains with certain properties?



Bacterial genome

E.Coli 4.6 million base pairs (4.6Mb)

Food

Is this food safe to eat?
What food do we need to recall?

Research

Which genes are responsible for making this strain pathogenic?

Infectious diseases

Is this patient's wound infected? If so, what is the variety of the infection and how should we

Who else has this infection? How did it spread and what can we do to prevent further

Which species are this one related to/derived from?

Security and defence

Where did the pathogen come from and how has it spread/changed? What strategies are needed to stop its further spread?



Metagenome

Mixed species

Environmental

What organisms are present in this environment?

Has a species disturbed the ecological balance of this environment?

Is this water supply safe?

Is this hospital ward clean?



THE CONVERGENCE OF SCIENCE AND TECHNOLOGY

A profound impact in the past, even more in the future

Education

Research

Health

Consumer

Industry

Security

THE CONVERGENCE OF SCIENCE AND TECHNOLOGY

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Oxford Nanopore is developing a platform to enable

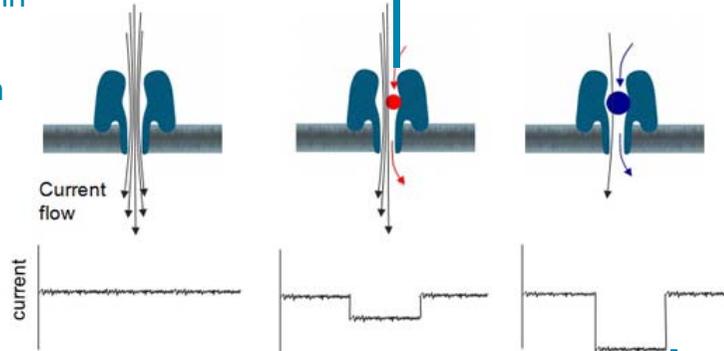
The analysis of any living thing

By any user

In any environment

NANOPORE SENSING

1 Nanopore creates hole in membrane
Current passes through nanopore

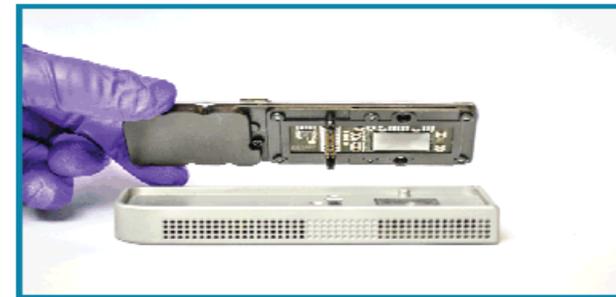
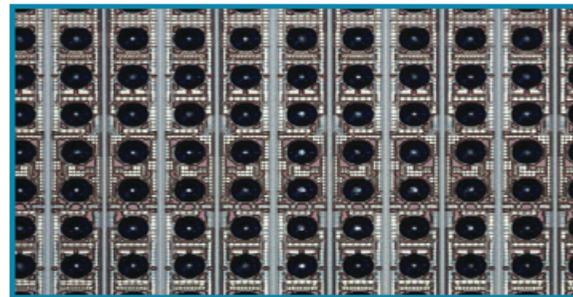
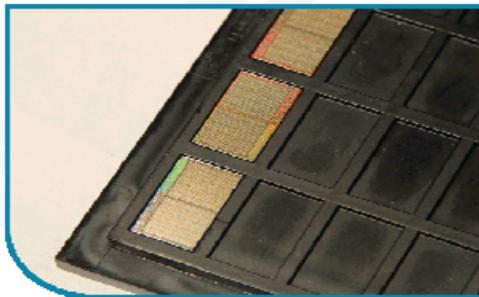
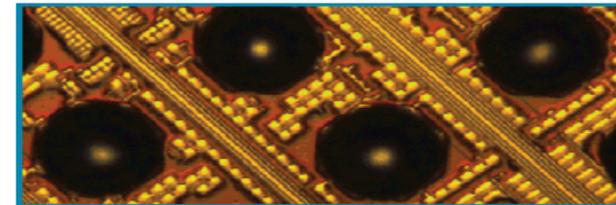


2 As analyte passes through or near the nanopore, this created characteristic disruptions in the current

3 Current disruption is interpreted to understand the identity of the analyte

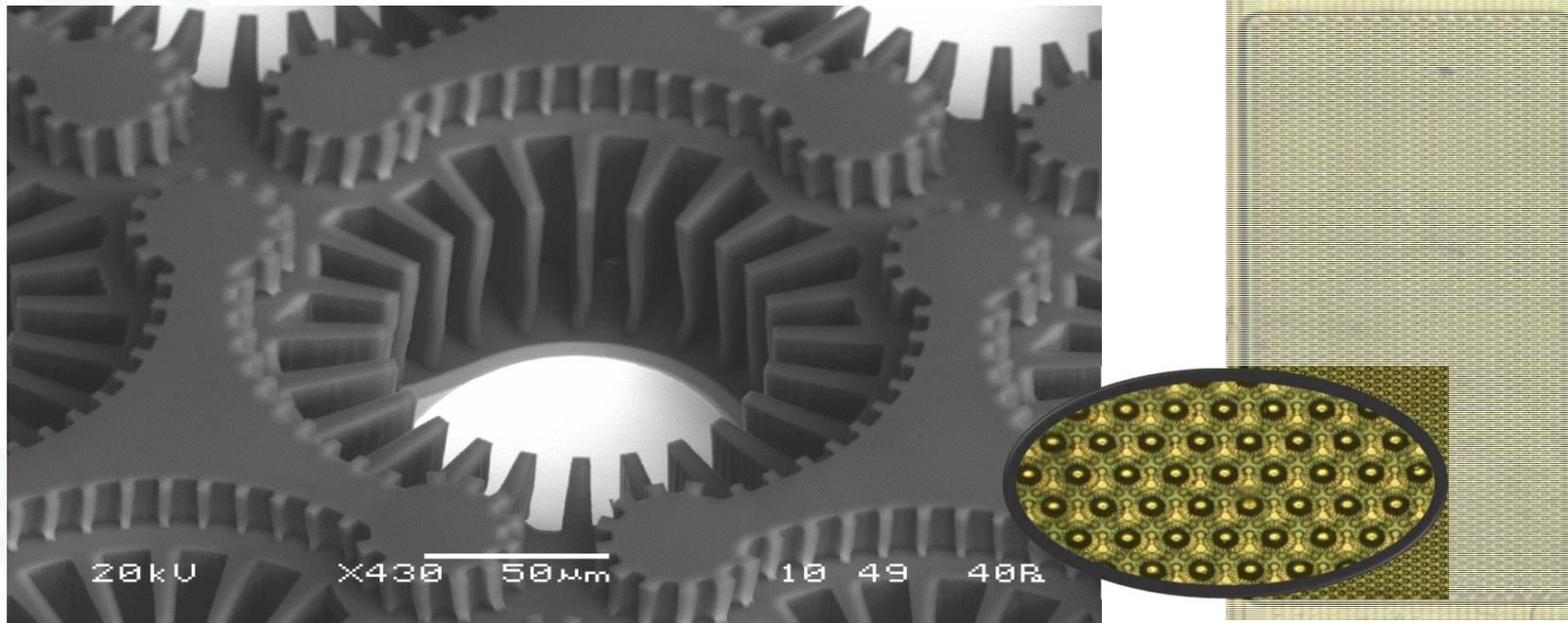
Inside the MinION: (1) ASIC

- Application specific integrated circuit
- Multiplexed to maximise yields
- System can do 1000 bases per second
- Quality similar to “Axopatch” gold standard
- Single MinION chip = 1,000s of Axopatches



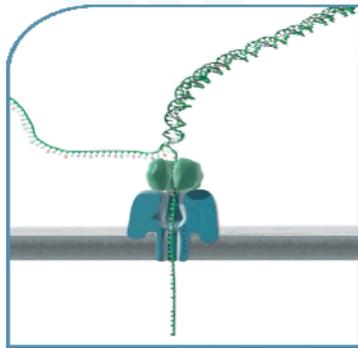
Inside the MinION: (2) Individual Well

- Current device structure for MinION

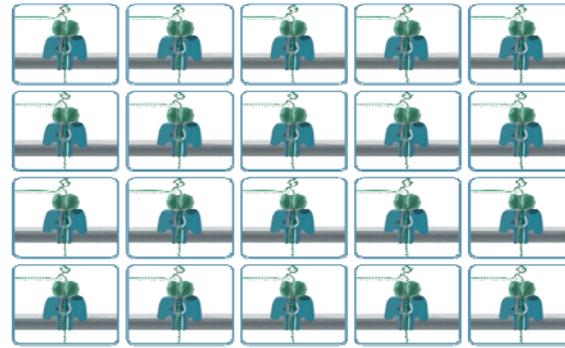


Inside the MinION: (3) Sensor Array

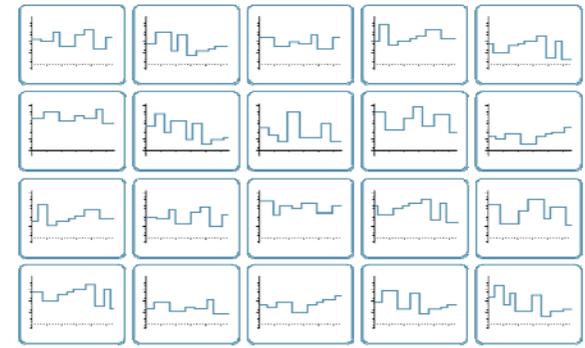
- ⦿ Sensor array connected to the ASIC



Pore



Membrane array

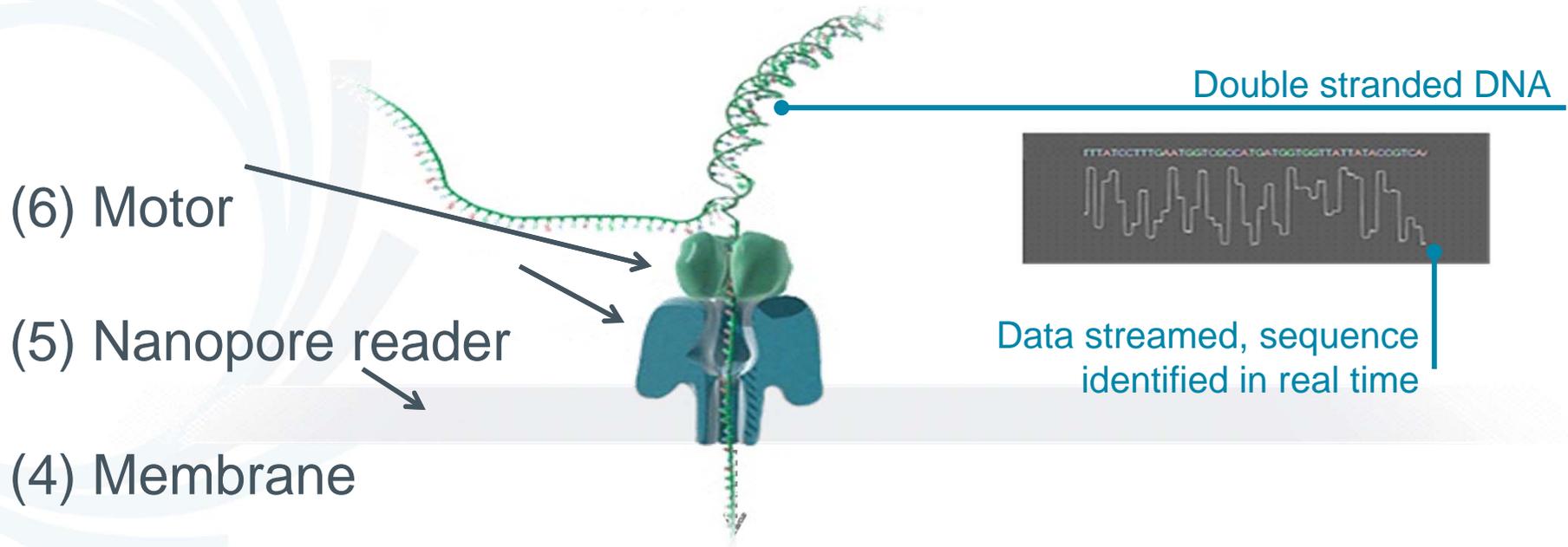


ASIC Channels

- ⦿ A single nanopore per well
- ⦿ 100s to 1000s of channels
- ⦿ Many analytes per pore, per channel, per run
- ⦿ Channels/pores asynchronous – no ‘cycles’



Inside the MinION: Motor and Reader



MINION: PORTABLE DNA/RNA SEQUENCING

Consumable flow cell contains sensing chemistry, nanopore, and electronics

Sample added to flow cell here

Sensor chip with multiple nanopores



USB powers device

MinION docks with flow cell, data streamed to USB

Sensor chip works with custom ASIC for control and data processing

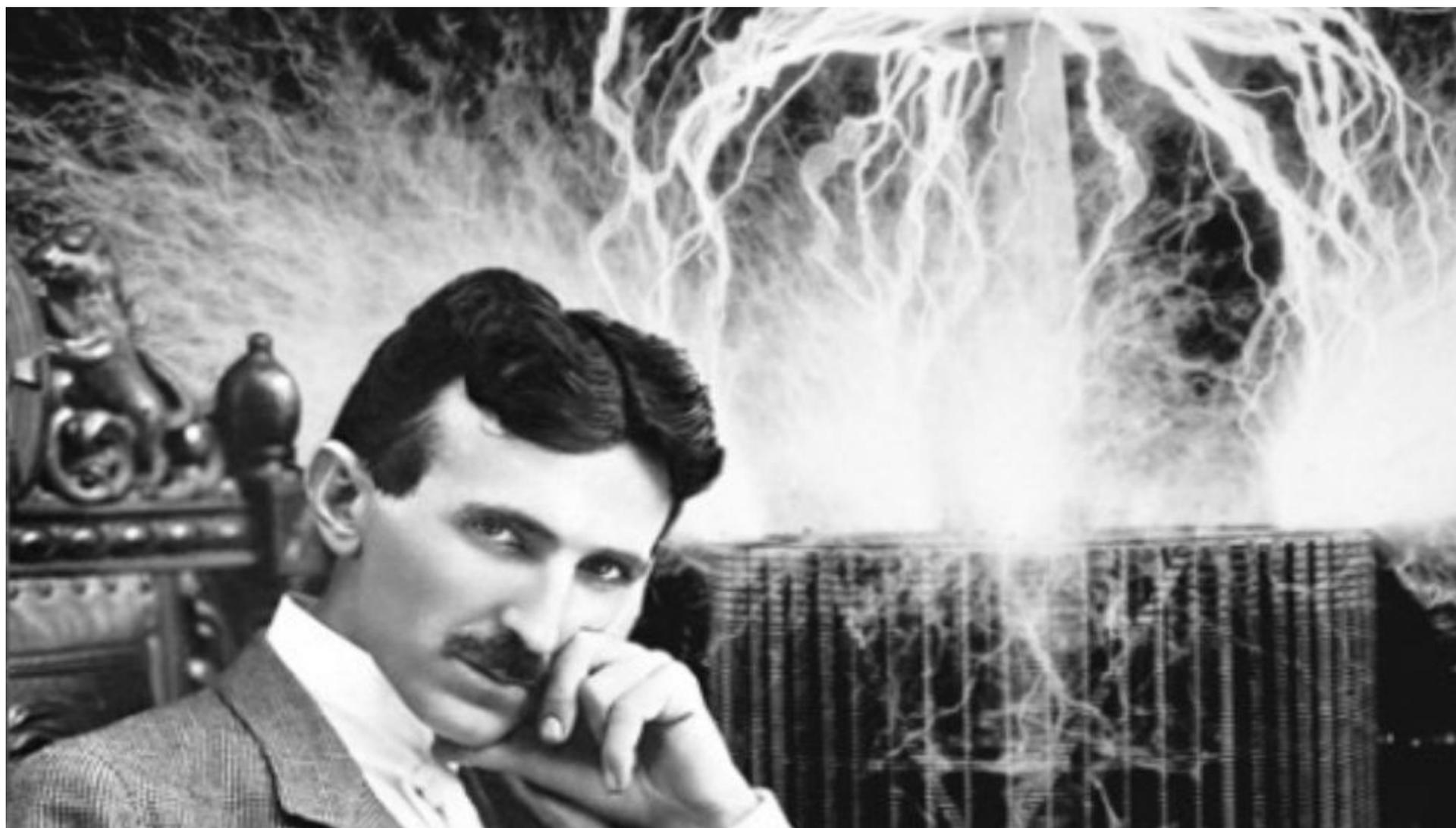
USB DEVICE AND FLOW CELL

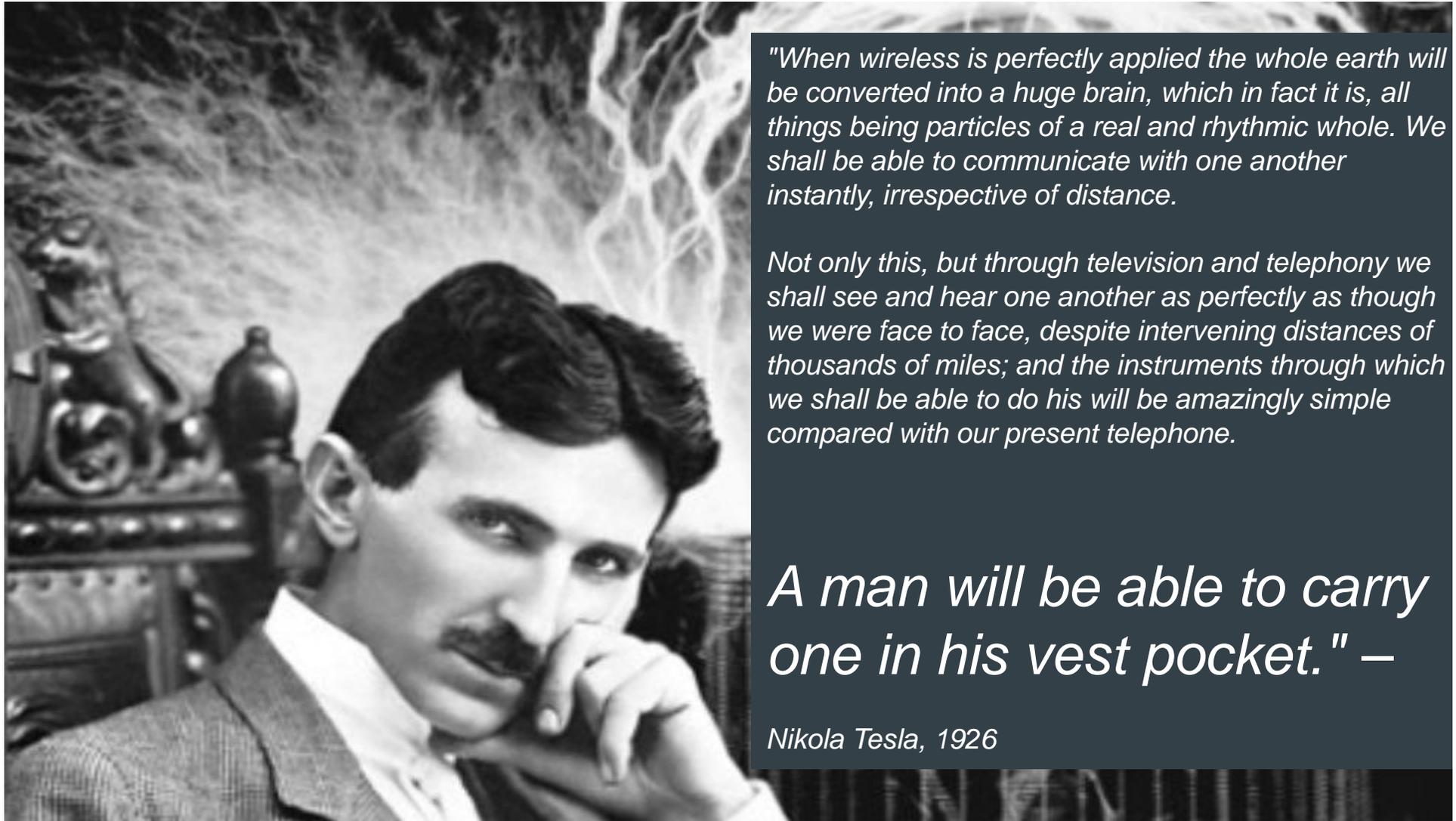
Current MinION version: Mk 1B

- Electromagnetic shielding protects sensor chip from noise
- Delivers higher accuracies at faster speeds
- Upgrade shipped together with all new consumable orders

Current flow cell version: R9.4

- 2048 wells
- 512 recording channels
- 4:1 multiplexing
- Can run at ~450 bps (bases per second per nanopore)





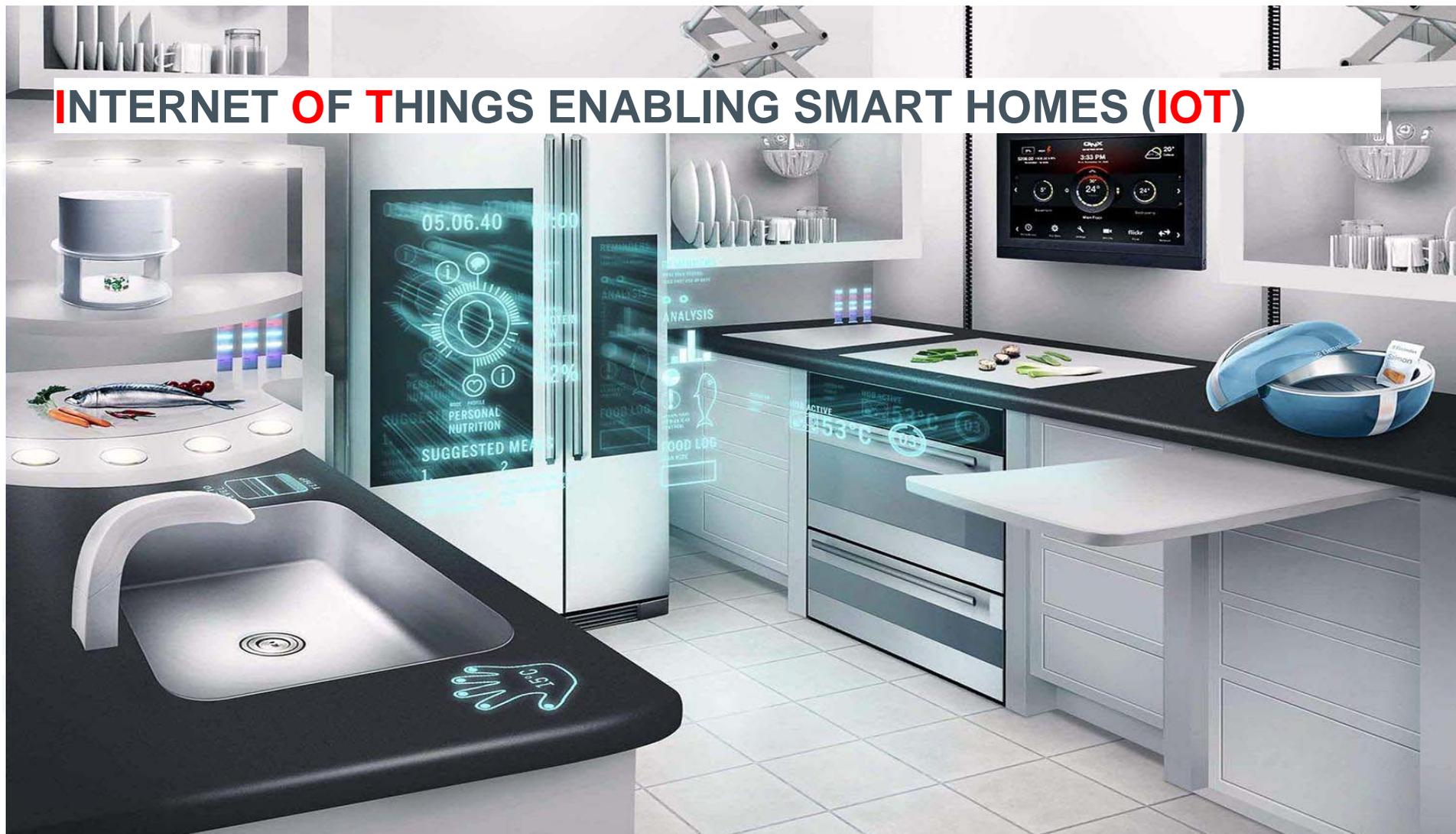
"When wireless is perfectly applied the whole earth will be converted into a huge brain, which in fact it is, all things being particles of a real and rhythmic whole. We shall be able to communicate with one another instantly, irrespective of distance.

Not only this, but through television and telephony we shall see and hear one another as perfectly as though we were face to face, despite intervening distances of thousands of miles; and the instruments through which we shall be able to do his will be amazingly simple compared with our present telephone.

A man will be able to carry one in his vest pocket." —

Nikola Tesla, 1926

INTERNET OF THINGS ENABLING SMART HOMES (IOT)



THE COMPUTING REVOLUTION

Computing
Mainframe



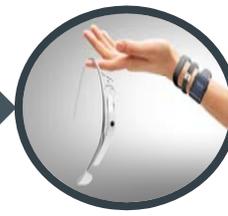
Desktop



Mobile



Wearables/sensors

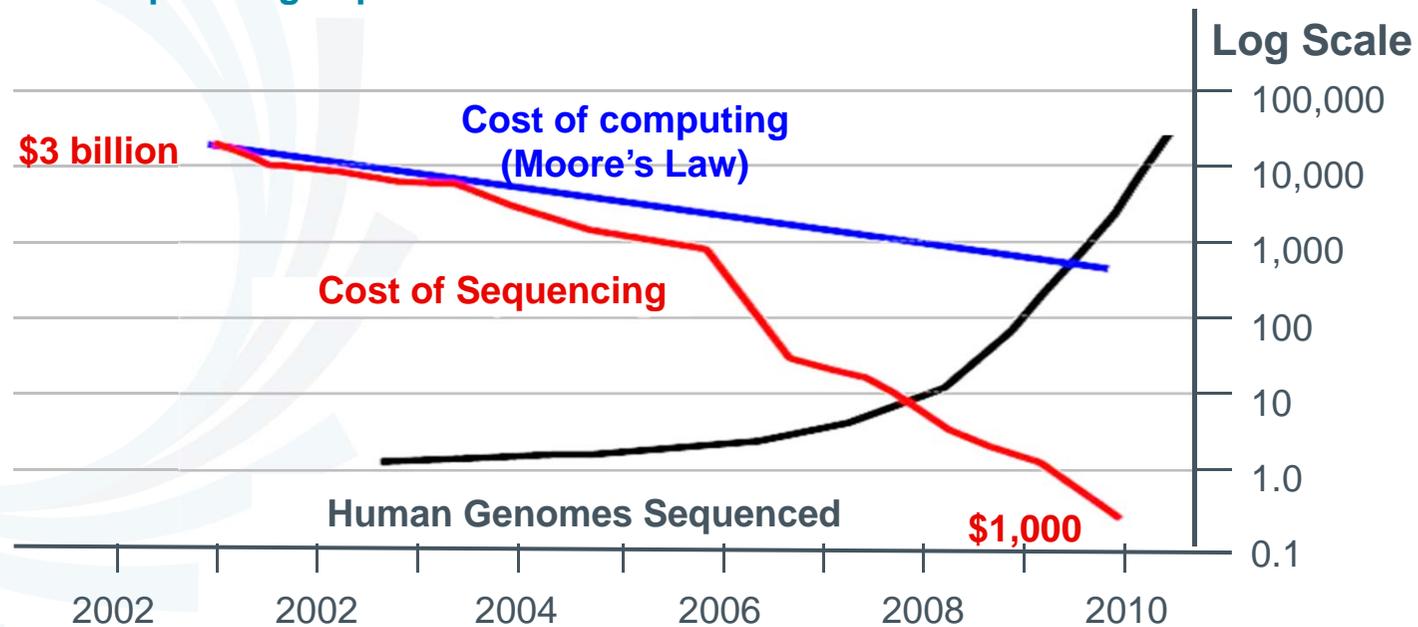


BIOLOGY IS STILL IN MAINFRAME MODE



PLUNGING SEQUENCING COSTS

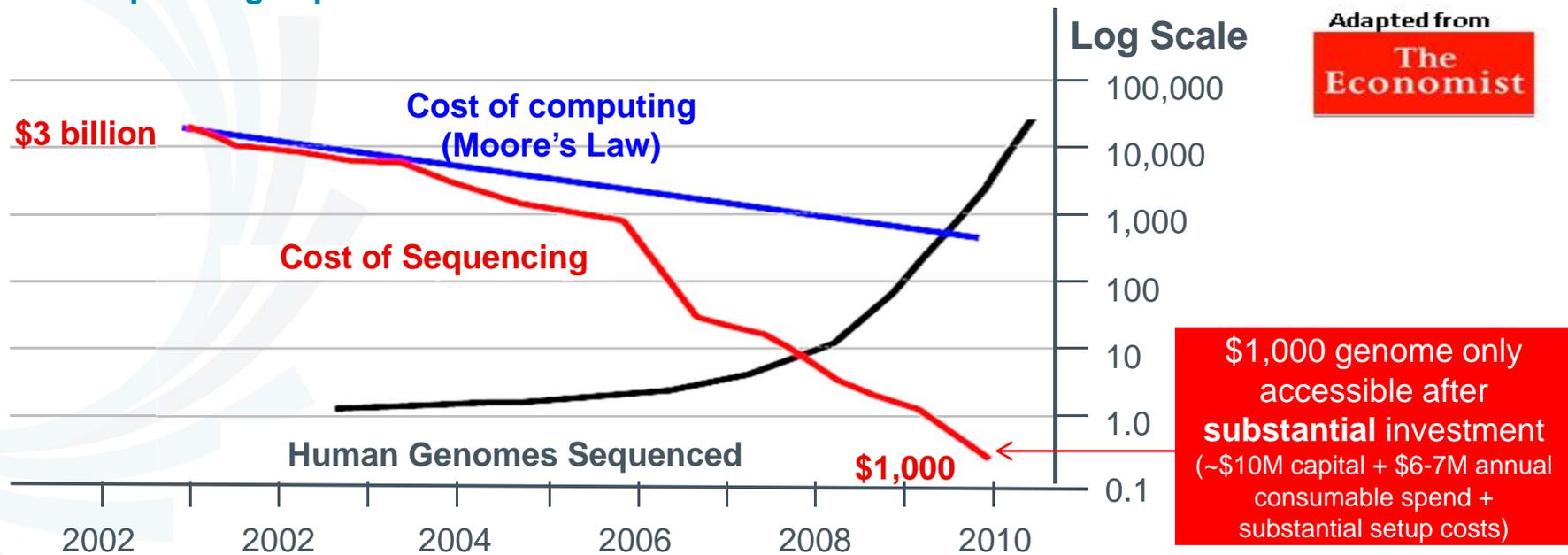
The Sequencing Explosion



Adapted from
The Economist

PLUNGING SEQUENCING COSTS

The Sequencing Explosion



DISTRIBUTING BIOLOGICAL ANALYSIS

Computing
Mainframe



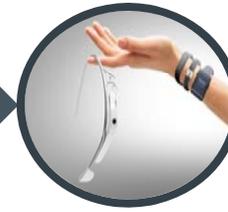
Desktop



Mobile



Wearables/sensors



Molecular Analyses
Mainframe



PromethION 2017
Desktop, high throughput



MinION 2014
Mobile



SmidgION 2017
Ultra Mobile



DNA IS AT THE CONVERGENCE OF SCIENCE AND TECHNOLOGY
IT IS BOTH BIOLOGY, AND INFORMATION



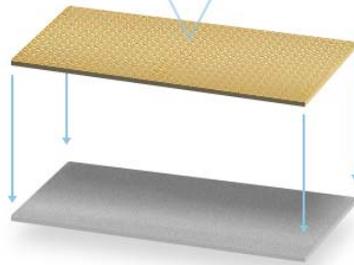
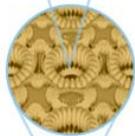
1997: DNA=



SINGLE CORE SENSING TECHNOLOGY

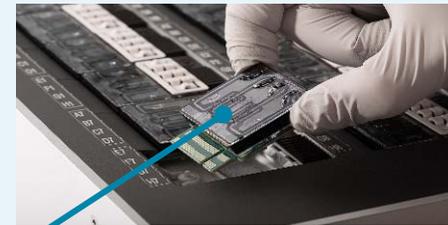
Can integrate into devices of any scale

Biological nanopore



Bespoke electronics

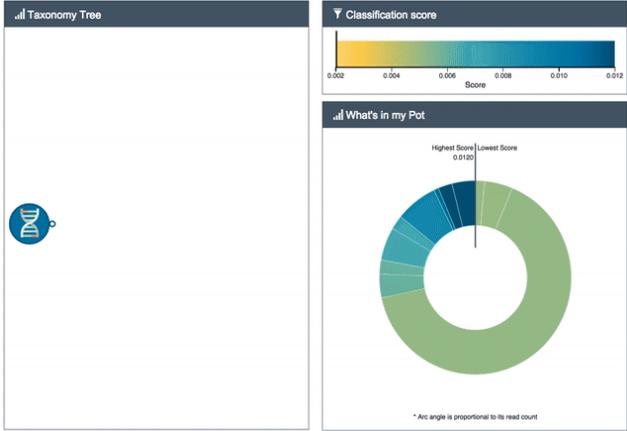
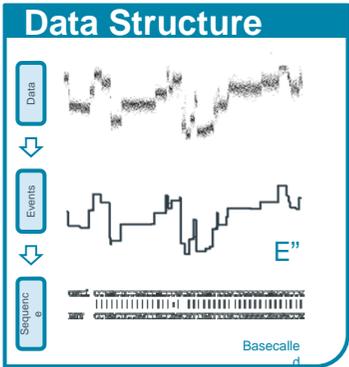
High throughput



Portable



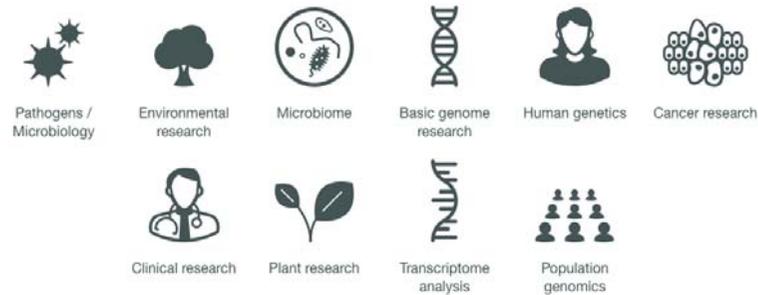
SIMPLE, SCALABLE, VERSATILE WORKFLOWS



DNA SEQUENCING: FOR WHO, AND WHY?

The research market

50-200,000 scientists



Applied markets

Everyone



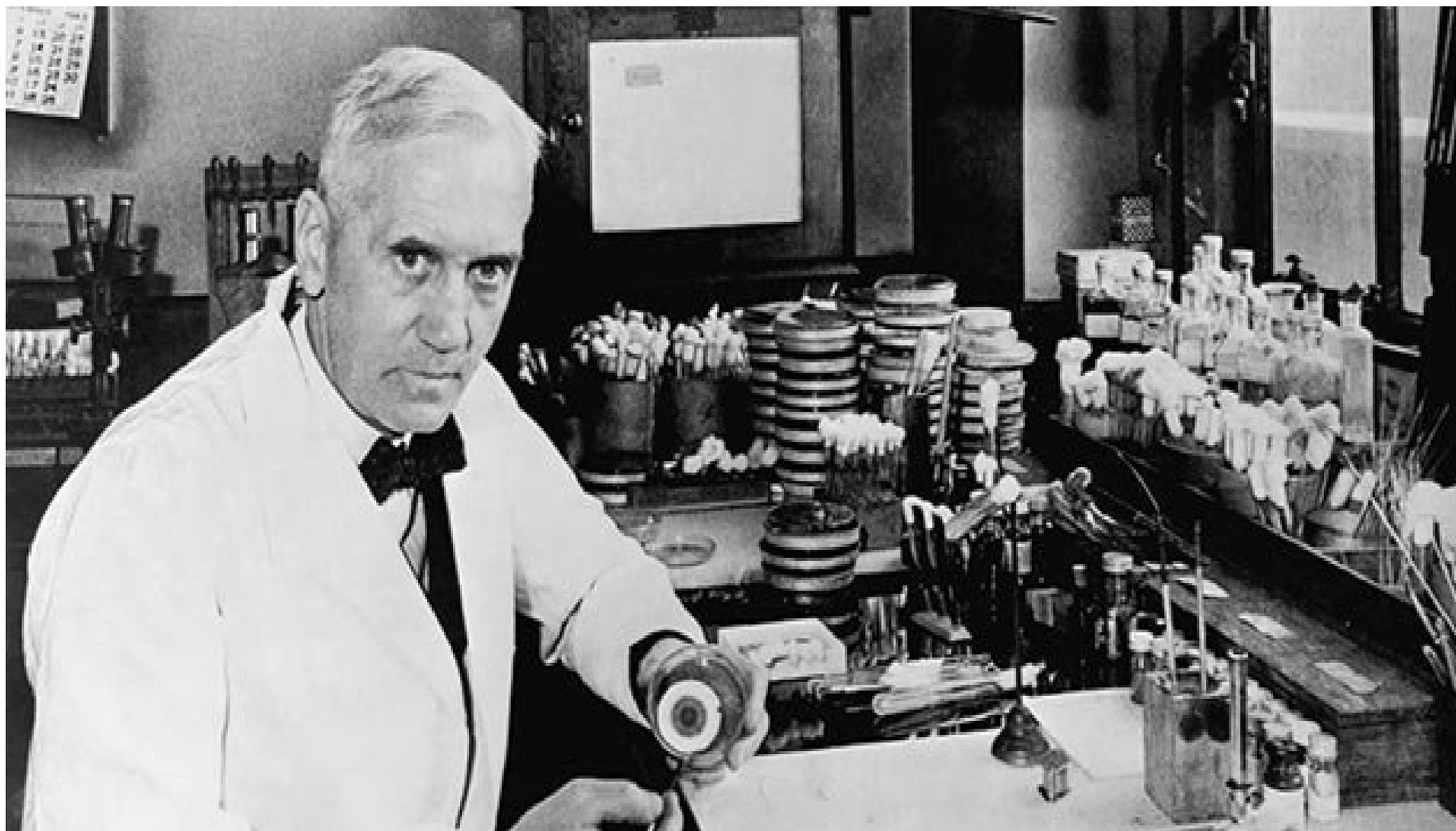
IMPACT ON SOCIETY

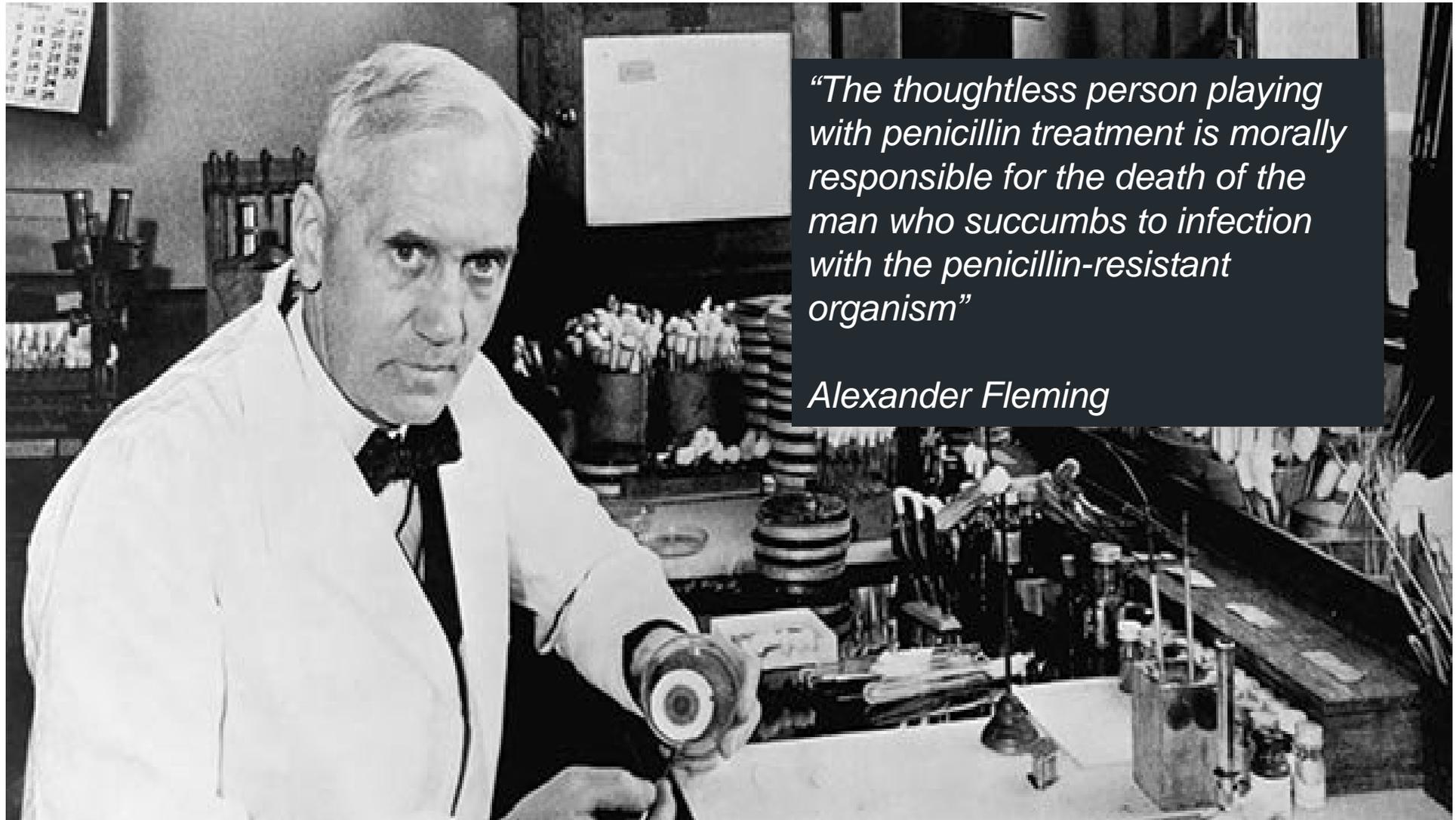
WHY ARE MOBILE, REAL TIME
DEVICES IMPORTANT?



IN TRADITIONAL LABS, IN THE CLASSROOM...







“The thoughtless person playing with penicillin treatment is morally responsible for the death of the man who succumbs to infection with the penicillin-resistant organism”

Alexander Fleming

ANTIMICROBIAL RESISTANCE (AMR)

An emerging threat that needs a rapid identification technology

The New York Times

The Opinion Pages | OP-ED CONTRIBUTORS

We Will Miss Antibiotics When They're Gone

By NICHOLAS BAGLEY and KEVIN OUTTERSON JAN. 18, 2017



A microbiologist working with tubes of bacteria as part of an antimicrobial resistance and characterization

2/3 antibiotics are needlessly prescribed

2016: 50,000 deaths

2050: 10 million deaths

Routine operations may no longer be possible – too high a risk of infection

Lifestyle > Health & Families > Health News

Woman killed by superbug resistant to every available antibiotic after visit to India

Twenty-six different antimicrobials tried, but none could halt infection

Harriet Agerholm | @HarrietAgerholm | Friday 13 January 2017 | 47 comments

TB: ANTIBIOTIC RESISTANCE IS WINNING

Time to strain ID is key

Time to ID TB and drug resistance genes now: 6-8 weeks

Now with nanopore: under 1 day (first antibiotic doses)

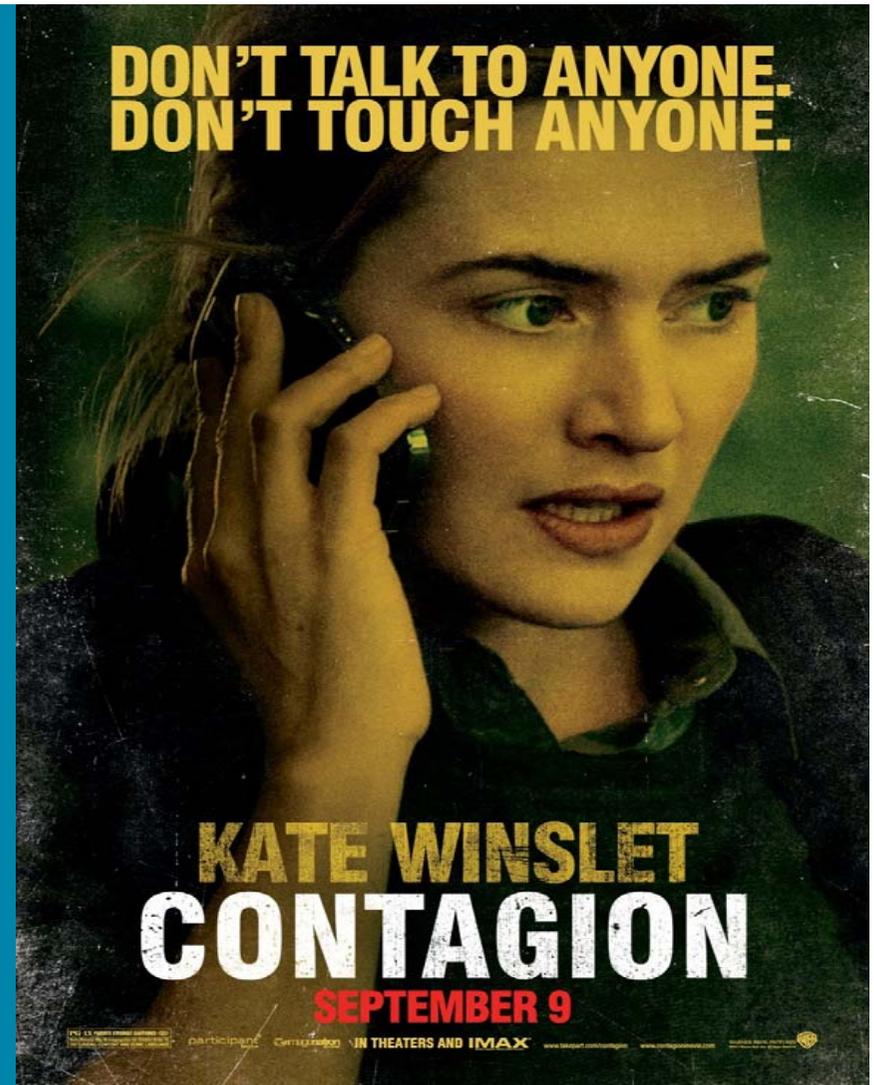
Target: 30 minutes (during visit)

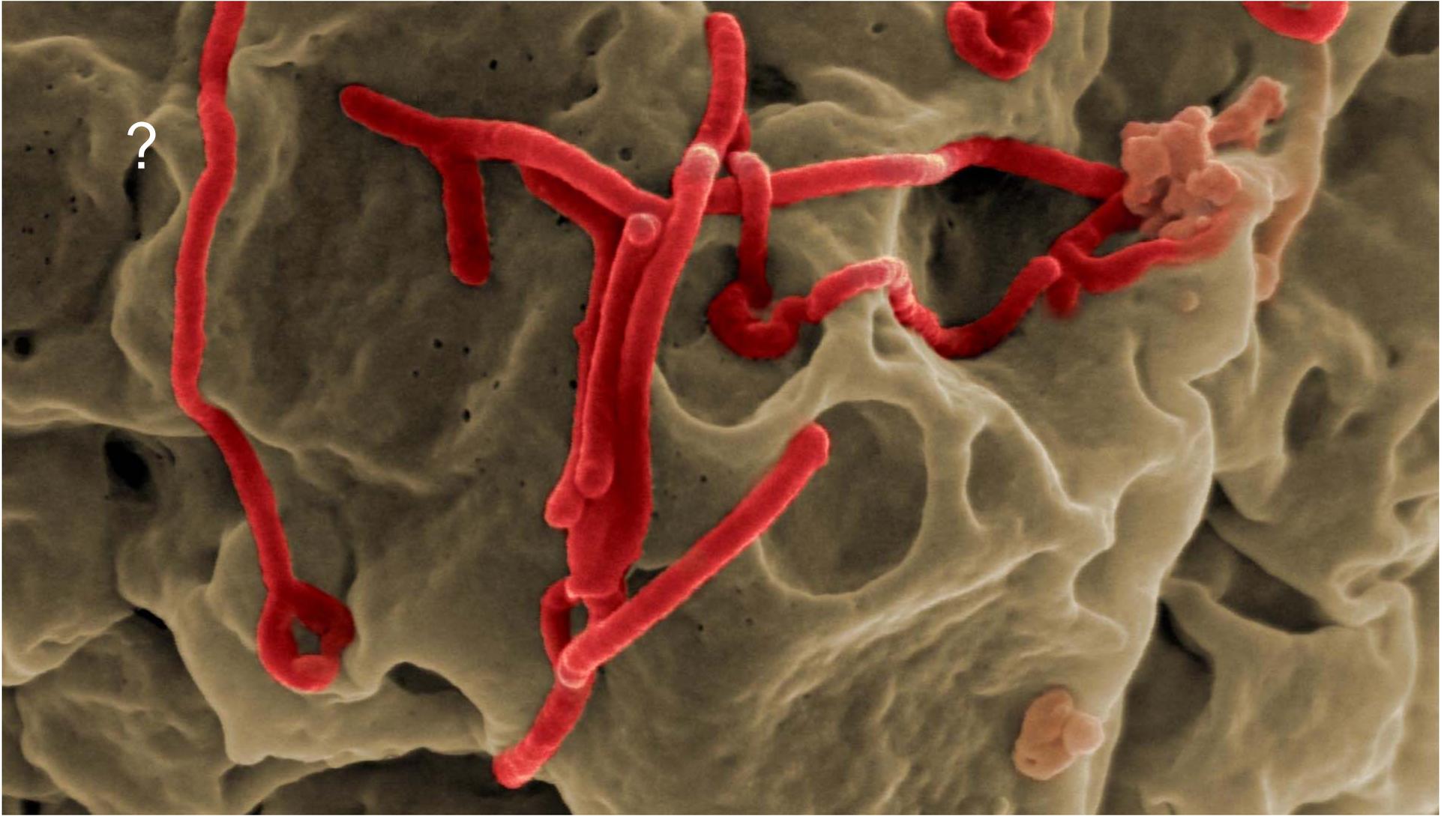
**IS THERE A PATHOGEN
HERE?**

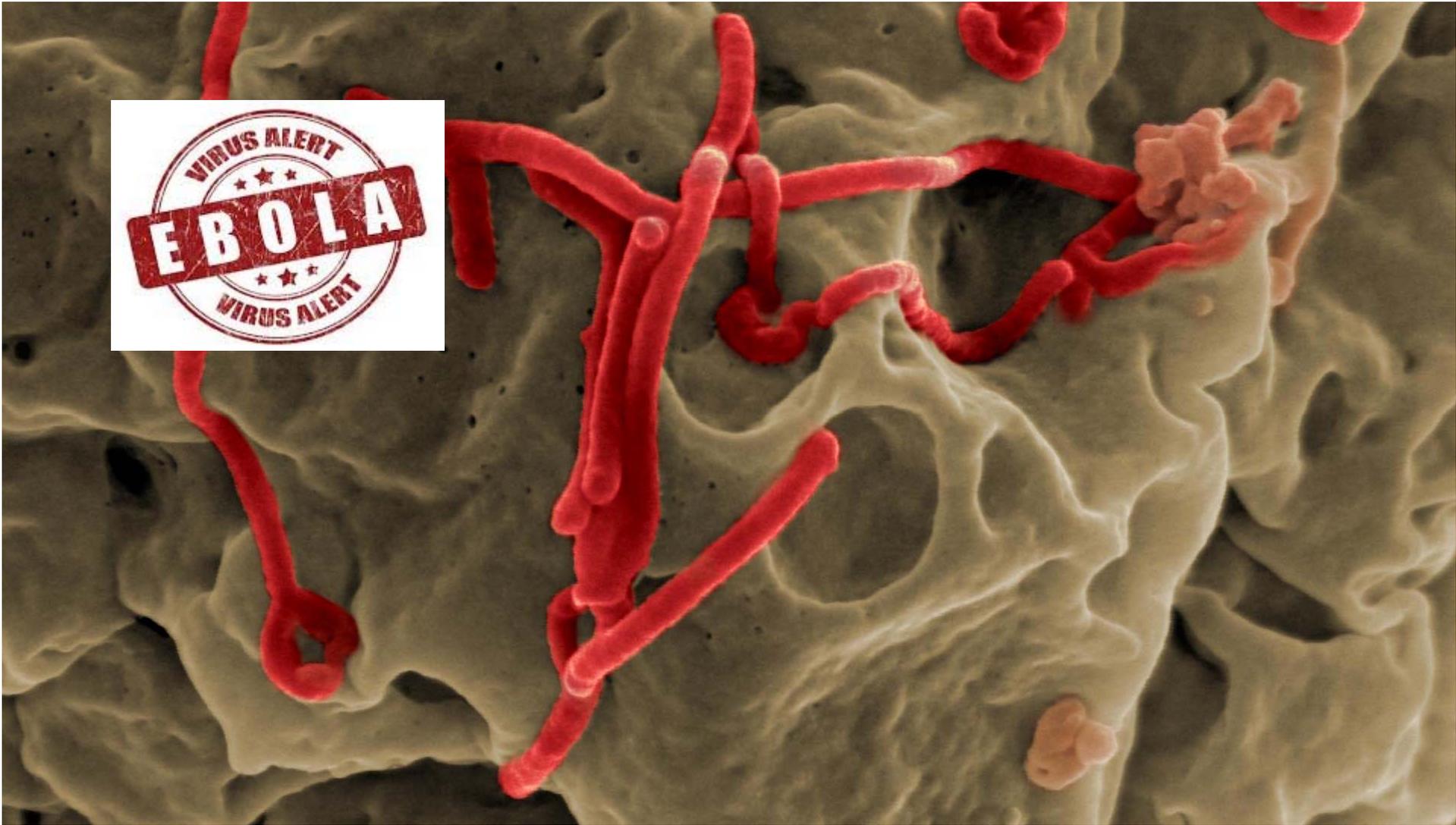
HOW HAS IT CHANGED?

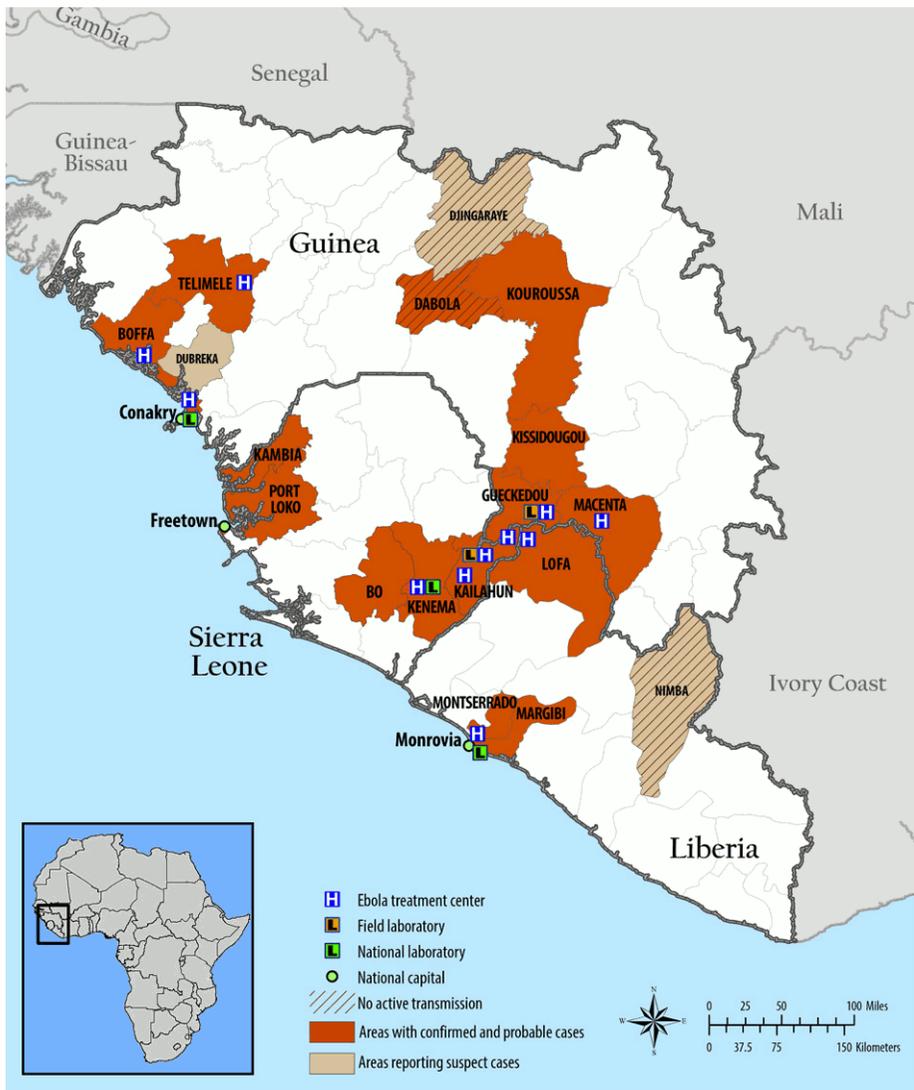
**HOW IS IT BEING
TRANSMITTED?**

**WHAT SHOULD WE DO
ABOUT IT?**









From Ebola to Zika, tiny mobile lab gives real-time DNA data on outbreaks

A genomic surveillance system which fits in a suitcase can help health workers to quickly understand the spread of viruses and break the chain of infection



The MiniON device, which weighs less than 100g, takes frequent electrical current measurements as a single strand of DNA passes through one of 2,000 pores in a plastic membrane. Photograph: Tommy Trenchard/EM Labs

A revolutionary DNA sequencing instrument which could help break the chain of transmission of viruses such as Ebola and Zika has been developed by British scientists.

?



How the Zika virus spread

Active transmission

Known previous transmission

Antibodies also detected



DISEASE SURVEILLANCE: ZIKA MONITORING

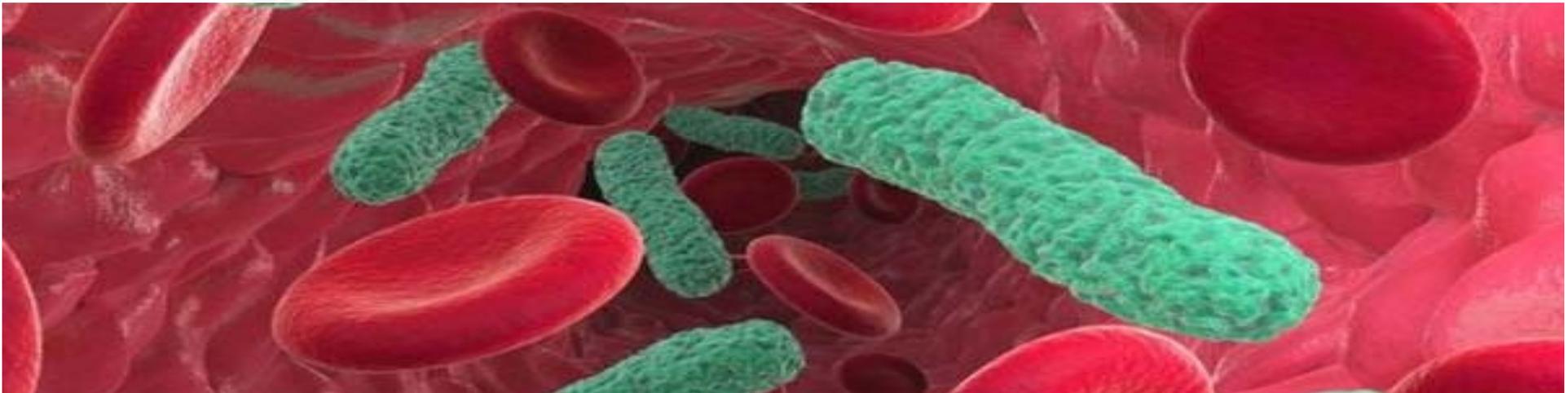
How is it moving?

Is it changing?



SEPSIS

- 1/3 patients in intensive care never leave hospital
- Deaths per year in US >200k (more than prostate, breast cancer and AIDS combined). Cost to US >\$20 billion
- Early diagnosis and evidence based treatment could → 92k fewer deaths (US)
- Diagnosis window for septic shock: 6 hours
- **MinION being explored for early identification of infection (UTI/Sepsis) by UK group**



SOLUTIONS?

No antibiotic without knowledge of the pathogen

Full DNA analysis at the point of care could fully characterise pathogens, guiding treatment options



The image is a screenshot of a BBC News article. At the top, the BBC logo is visible on the left, and navigation links for 'Sign in', 'News', 'Sport', 'Weather', 'iPlayer', 'TV', and 'Radio' are on the right. Below this is a red banner with the word 'NEWS' in white. Underneath the banner is a secondary navigation bar with links for 'Home', 'UK', 'World', 'Business', 'Politics', 'Tech', 'Science', 'Health', 'Education', and 'Entertainment'. The article is categorized under 'Health'. The main headline reads 'Sore throat sufferers urged to take pharmacy test'. Below the headline, it says '12 November 2016 | Health' and there is a 'Share' button. The article features a photograph of a male pharmacist with a beard and glasses examining a female patient's throat with a tongue depressor. The photo is credited to 'THINKSTOCK'. Below the photo, the text states: 'Sore throat sufferers will be encouraged to visit their pharmacist instead of their GP for an on-the-spot test to see if they need antibiotics. The walk-in service is aimed at reducing doctor appointments and to help reduce the over-use of antibiotics, NHS England said. It is hoped the scheme could result in fewer visits to GPs -potentially saving the NHS millions of pounds a year.'

E.G. SELF QUANTIFICATION REAL TIME MONITORING TO TRACK, TREND, PREDICT



Continuous monitoring of biological state for health or fitness



Eg microbiome: you are mainly microbes

IMPACT ON SOCIETY OF COMMUNITY SCREENING FOR INFECTIONS?

Shifts from 2' care → 1' care
→ community

Personal
responsibility
for screening
choices

Socialising
information /
privacy / data
themes

Shifts would
mirror health-
on-the-internet
introduction

OTHER IMPACTS ON SOCIETY: CONSUMER SAFETY



FOOD SAFETY AND AUTHENTICITY



Second horse meat scandal could happen because lack of routine testing, experts warn

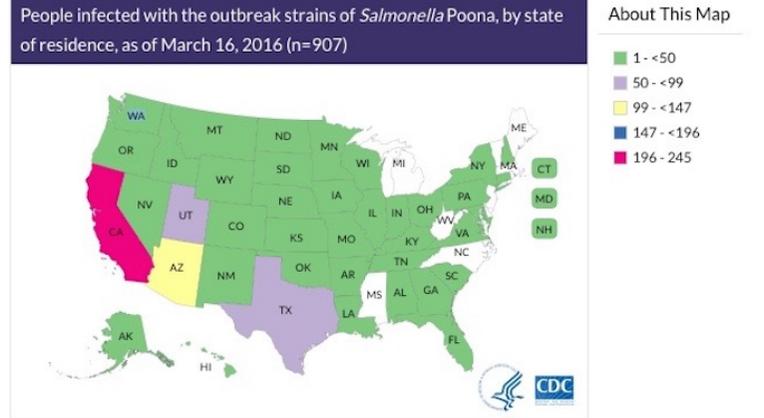


The 2013 scandal, or something equivalent, could happen again, experts warn. CREDIT: CHARLY TRIBALLEAU

Largest Food Poisoning Outbreak of 2016: Salmonella in Cucumbers

December 31, 2016 by News Desk • [Leave a Comment](#)

The largest multistate food poisoning outbreak in 2016 ended in 2016, but it started in 2015. At least 907 people were sickened with Salmonella Poona infections that were linked to **imported cucumbers**. Six people died, and 204 people were hospitalized in this massive outbreak.



The strange thing about this outbreak is that even though the cucumbers that were identified as the source of this outbreak, infections were still being reported to officials **two months** after the recall was issued. Cucumbers do not have a long shelf life.

The cucumbers in question were traced to Bancho Don Juanita de P. de C.V. in Baja, Mexico. Two import alerts

SUPPLY CHAIN MONITORING



FARM



PROCESSING



FACTORY



DISTRIBUTION



RETAIL
CONSUMER

Is it safe?

Is it actually a
beefburger?

SHIFT IN MONITORING WATER, ENVIRONMENTS, FOOD SUPPLY CHAINS



Food

Monitoring pathogens/
species ID, Farm to fork



Water

Monitoring water
networks in real time



Environment

Remote, multi-location
real time microbial &
species analysis

**SCIENCE ANYWHERE: REMOTE
ENVIRONMENTS, BY ANYONE**

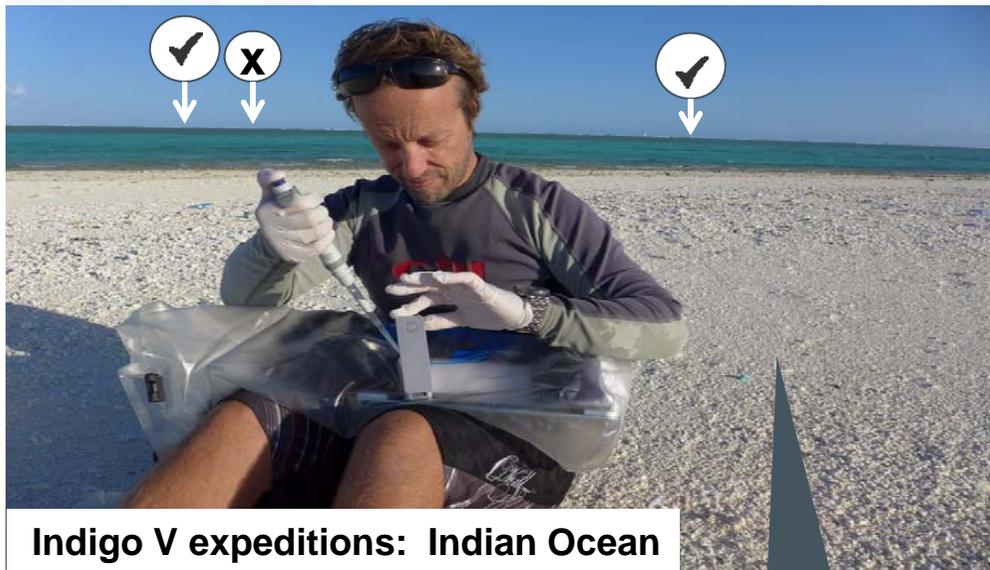


ENVIRONMENT: MONITORING, STOPPING WILDLIFE CRIME

- Using MinION in remote locations for environmental purposes eg
- Project from Leicester involving Kenya, Bangladesh
- Eg Identifying blood on a poachers machete
- Identifying bushmeat eg chimpanzee at local market
- Detect illegal substitutions in products, from protected species



REMOTE ENVIRONMENTS: EDUCATION AND CITIZEN SCIENCE



Indigo V expeditions: Indian Ocean



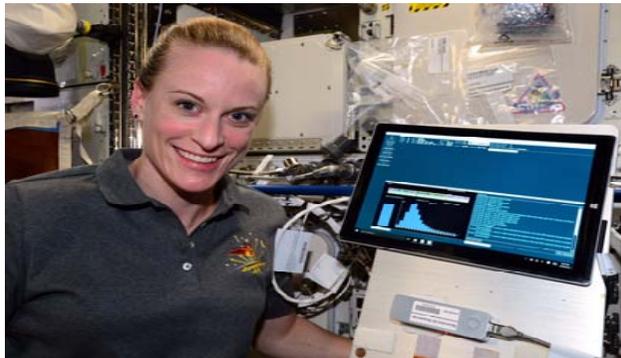
What is the biology of my backyard?

Scott Tighe and team, Extreme Microbiome Project: Antarctica

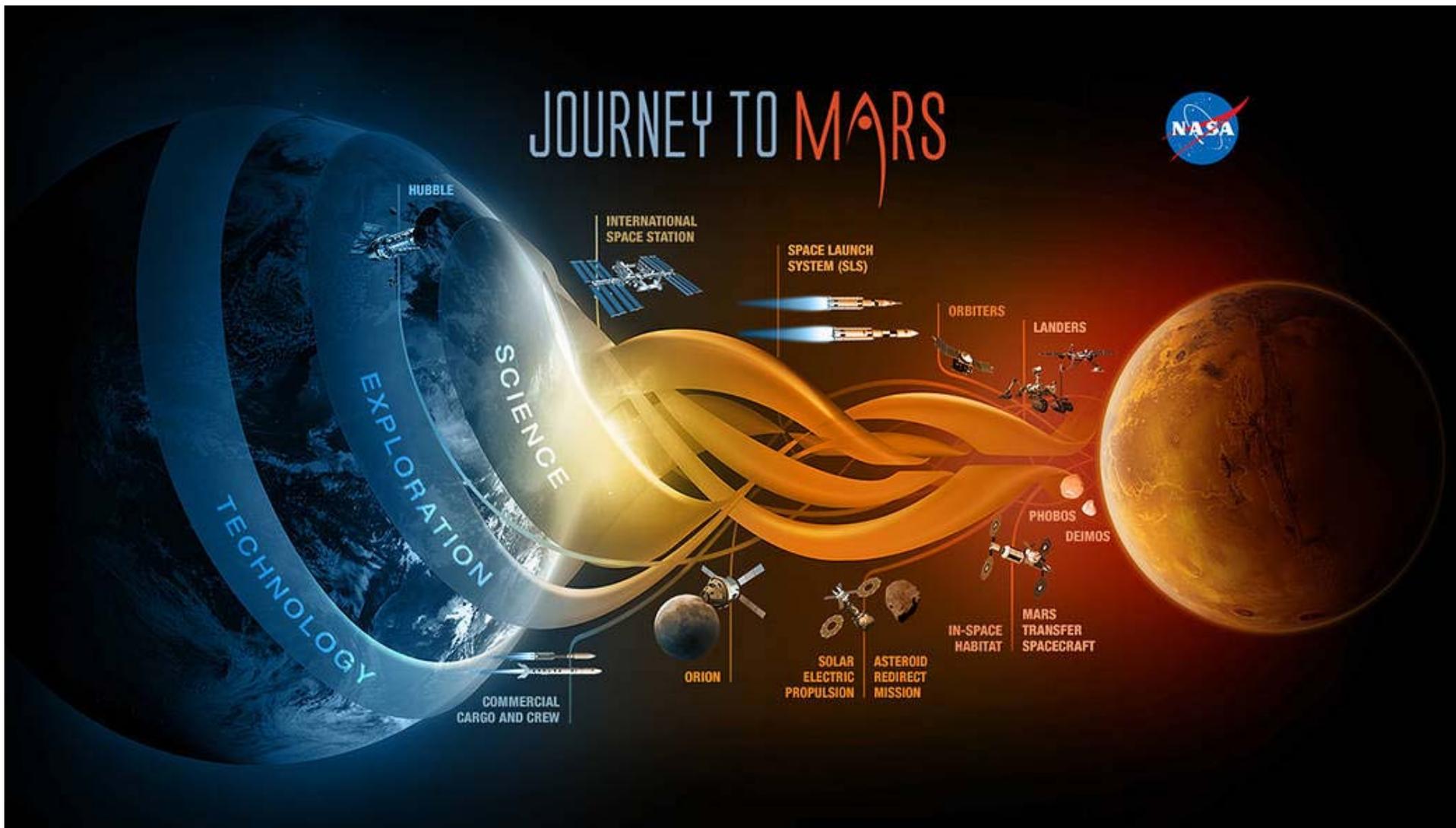
Can we join together to solve a biology problem?

NASA AND DNA SEQUENCING

- 1 Environment
- 2 Health
- 3 Life?



JOURNEY TO MARS



THANK YOU

