

Pushing state-of-the art in transcriptomics and metagenomics on the road to personalized medicine

Paweł P Łabaj

Małopolska Centre of Biotechnology

Jagiellonian University Kraków

MetaSUB International Consortium

OeAW APART Fellow

Chair of Bioinformatics RG, Boku University Vienna



MAŁOPOLSKA
CENTRE OF BIOTECHNOLOGY



Personalized Medicine



Personalized Medicine

Technological innovations

accelerated advances in biomedical research

promising high impact findings in

basic science as well as

applied or clinical settings



Personalized Medicine

These underpin the development of

- novel approaches in diagnosis
- novel treatments

*tailored towards **individual patients** or patient groups*

Personalized Medicine

„All happy families are alike,
each unhappy family is unhappy in its own way”

Leo Tolstoy, Anna Karenina



Personalized Medicine

the WHITE HOUSE PRESIDENT BARACK OBAMA

Contact Us ▾ Get Email Updates ▾ 

 BRIEFING ROOM ISSUES THE ADMINISTRATION PARTICIPATE 1600 PENN Search 

THE PRECISION MEDICINE INITIATIVE



Personalized Medicine

nature International weekly journal of science

[Home](#) | [News & Comment](#) | [Research](#) | [Careers & Jobs](#) | [Current Issue](#) | [Archive](#) | [Audio & Video](#) | [For](#)

[Archive](#) > [Volume 529](#) > [Issue 7584](#) > [News](#) > [Article](#)

NATURE | NEWS



China embraces precision medicine on a massive scale

Strong genomics record bodes well but a shortage of doctors could pose a hurdle.

David Cyranoski

06 January 2016



[PDF](#)



[Rights & Permissions](#)



Personalized Medicine

| A-Z index | Site map | About this site | What's New | Legal notice | Cookies | Contact | Search | English (en) ▾

 European Commission

RESEARCH & INNOVATION

Health

European Commission > Research & Innovation > Health > Policies > Personalised Medicine

Home Policies Key Research Areas Funded Projects

Policies

Personalised Medicine

Many of our most common medicines are not effective as intended. For example, one in five medicines are supposed to help and more than six percent of all patients experience serious side effects or adverse reactions to medicines. Moreover healthcare systems are under pressure as the population ages and chronic diseases become more prevalent. Personalised medicine offers the opportunity to develop tailor-made prevention and treatment strategies that are better suited to individual patients. As a result, patients receive the specific therapies that work best for them, reducing the risk of side effects and error treatments. Personalised medicine is a fast-growing field of research and development. The industry has the potential to build on its leading position and contribute to the EU's competitiveness.

| A-Z index | Site map | About this site | What's New | Legal notice | Cookies | Contact | Search | English (en) ▾

 European Commission

RESEARCH & INNOVATION

Conferences and events

European Commission > Research & Innovation > PerMed2016

Home Practical Information Programme Speakers Participants



Personalised Medicine Conference 2016

1-2 June, Brussels



MAŁOPOLSKA
CENTRE OF BIOTECHNOLOGY

ÖAW

ÖSTERREICHISCHE
AKADEMIE DER
WISSENSCHAFTEN



Personalized Medicine

H2020 report after 2016-2017 perspective with suggestions for goals for 2018-2020 perspective

Specific impacts

Strengthening the International Consortium on

Personalised Medicine by:

- (i) establishing Europe as a global leader in personalised medicine research,
- (ii) supporting the personalised medicine science base through a coordinated approach to research,
- (iii) providing evidence to policy makers of the benefit of personalised medicine to citizens and healthcare systems

Personalized Medicine

vs

Precision Medicine



Personalized Medicine

vs

Precision Medicine



Personalized Wellness/Wellbeing



Challenge



Challenge

need to identify **individual variability** via
characterizing **individual baseline health state** instead of resorting to population-based variable distributions

Challenge

classical medical records not enough to define **baseline**

- mostly gathered during patient visits in hospital
 - **not when patient is healthy**
- focused on a specific disease
 - **not the overall health**
- from a specific time point
 - **no longitudinal data**

Additional sources of biomedical data

Opportunities created by recent technological advances:

- mobile medical devices for monitoring dedicated health parameters (insulin, heart rate, etc), and
- wearables



Additional sources of biomedical data

Translational Bioinformatics using Real-time Data Streams | 5

Table 2. Features of consumer health-monitoring devices

Consumer device	Health features monitored	Medical field(s)	Source
Basis B1 wrist band	Heart rate, accelerometer, body temperature, ambient temperature, skin conductance, caloric burn	CV, Endo, Psych	https://www.mybasis.com/
BodyMedia Link Armband	Heat flux, body temperature, motion and skin conductance, activity level, calorie burn and sleep	CV, Endo	http://www.bodymedia.com/
Fitbit Aria	Weight, body fat %, BMI	CV, Endo	https://www.fitbit.com/aria
Fitbit Surge	GPS, altimeter, heart rate, accelerometer, activity, caloric burn and sleep	CV	https://www.fitbit.com/surge
Hexoskin smart shirt	ECG, respiratory rate, tidal volume, accelerometer, position, sleep	CV, Pulm	http://www.hexoskin.com/
iHealth BPS	Blood pressure	CV, Renal	http://www.ihealthlabs.com/
iHealth Glucometer	Blood glucose	Endo	http://www.ihealthlabs.com/
Jawbone UP3	Accelerometer, heart rate, respiratory rate, skin conductance, skin temperature and ambient temperature, activity, sleep and caloric intake	CV, Endo, Pulm, Psych	http://jawbone.com/store/buy/up3
MapMyFitness	Record activity, food intake	CV	http://www.mapmyfitness.com/
Melon Headband	Three-channel EEG, infer concentration, relaxation	Neuro, Psych, Devel	http://www.thinkmelon.com/
Muse headband	Seven-channel EEG, infer concentration, relaxation	Neuro, Psych, Devel	http://www.choosemuse.com/
Nike Fuelband	Activity	CV	http://www.nike.com
Scanaudu Scanaflo	Urinalysis	Renal, Endo	https://www.scanadu.com/scanaflo
Scanaudu Scout	Temperature, blood pressure, heart rate, blood oxygenation and ECG	CV, Pulm	https://www.scanadu.com/scout
Sensimed Triggerfish	Eye shape and blinking, infer intraocular pressure	Ophtho	http://www.sensimed.ch/
Withings BP Monitor	Blood pressure, heart rate	CV, Renal	http://www.withings.com/
Withings Pulse	Accelerometer, heart rate, blood oxygenation, activity, sleep and caloric burn	CV, Pulm	http://www.withings.com/
Zephyr BioPatch	Heart rate, respiratory rate, accelerometer, ECG, activity	CV, Pulm	http://zephyranywhere.com/

CV, cardiovascular; Devel, development; Pulm, pulmonary medicine; Endo, endocrinology; Neuro, neurology; Ophtho, ophthalmology.

Additional sources of biomedical data

Table 2. Features of consumer health-monitoring devices

Consumer device	Health features monitored	Medical field(s)	Source
Basis B1 wrist band	Heart rate, accelerometer, body temperature, ambient temperature, skin conductance, caloric burn	CV, Endo, Psych	https://www.mybasis.com/
BodyMedia Link Armband	Heat flux, body temperature, motion and skin conductance, activity level, calorie burn and sleep	CV, Endo	http://www.bodymedia.com/
Fitbit Aria	Weight, body fat %, BMI	CV, Endo	https://www.fitbit.com/aria
Fitbit Surge	GPS, altimeter, heart rate, accelerometer, activity, caloric burn and sleep	CV	https://www.fitbit.com/surge

K Shameer et al. (2016) *Brief in Bioinformatics*
doi: 10.1093/bib/bbv118

Additional sources of biomedical data

Hexoskin smart shirt	activity, caloric burn and sleep ECG, respiratory rate, tidal volume, accelerometer, position, sleep	CV, Pulm	http://www.hexoskin.com/
iHealth BP5	Blood pressure	CV, Renal	http://www.ihealthlabs.com/
iHealth Glucometer	Blood glucose	Endo	http://www.ihealthlabs.com/
Jawbone UP3	Accelerometer, heart rate, respiratory rate, skin conductance, skin temperature and ambient temperature, activity, sleep and caloric intake	CV, Endo, Pulm, Psych	http://jawbone.com/store/buy/up3
MapMyFitness	Record activity, food intake	CV	http://www.mapmyfitness.com/
Melon Headband	Three-channel EEG, infer concentration, relaxation	Neuro, Psych, Devel	http://www.thinkmelon.com/
Muse headband	Seven-channel EEG, infer concentration, relaxation	Neuro, Psych, Devel	http://www.choosemuse.com/
Nike Fuelband	Activity	CV	http://www.nike.com

K Shameer et al. (2016) *Brief in Bioinformatics*
doi: 10.1093/bib/bbv118

Additional sources of biomedical data

the **second data stream** of

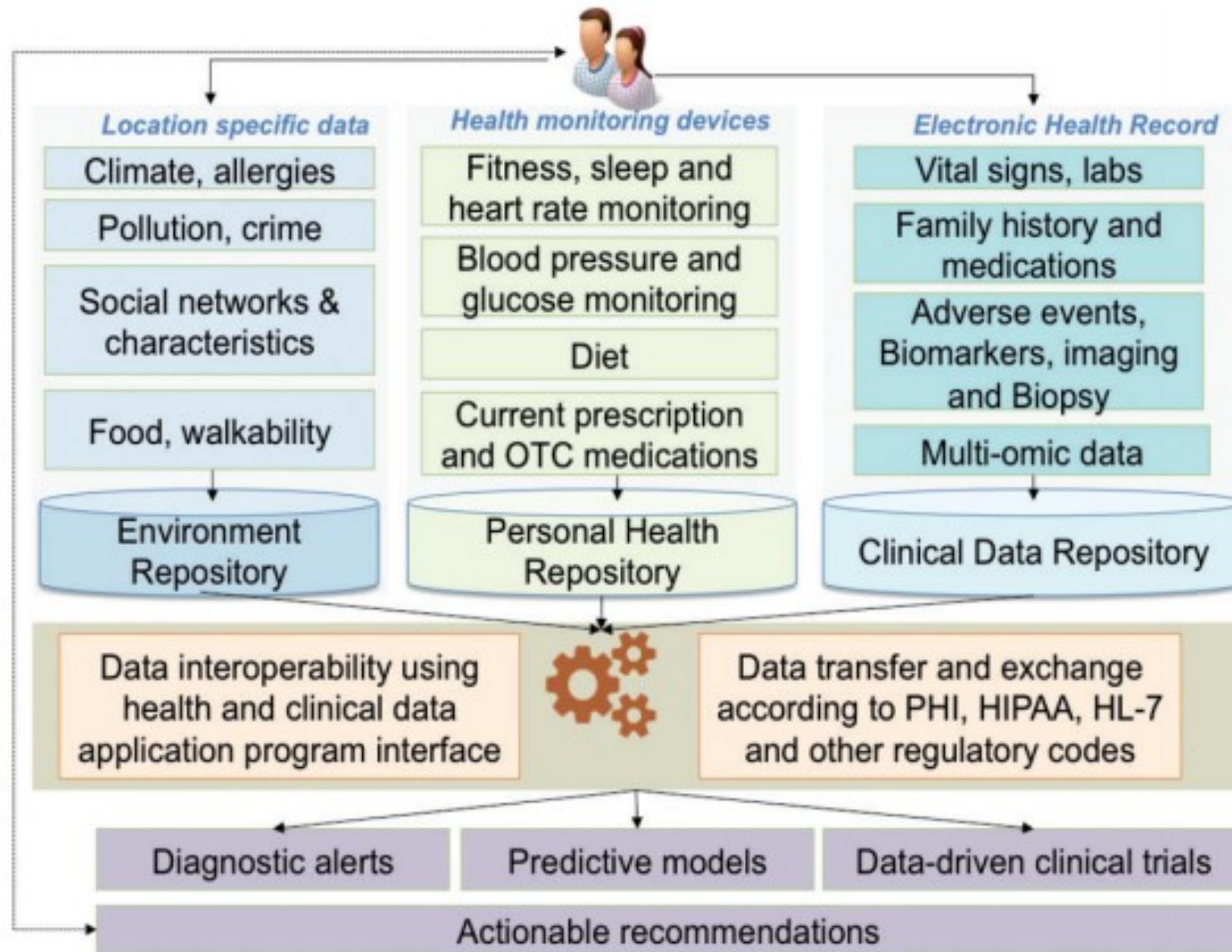
real-time biomedical, healthcare and wellness data

a synergy of these two streams should provide a
good estimate of the **health state baseline**

Additional sources of biomedical data?



Additional sources of biomedical data



Additional sources of biomedical data

Exposome

“the measure of all the exposures of an individual in a lifetime and how those exposures relate to health”



Exposome

Lifeless component:

temperature, humidity, pollution, allergens etc.

BreezoMeter

The first real time
AIR QUALITY
DATA PLATFORM

at street resolution

5th Ave, New York, NY

SEARCH



Exosome

Living component:

air / surface / water / ...

microbiome



Exosome



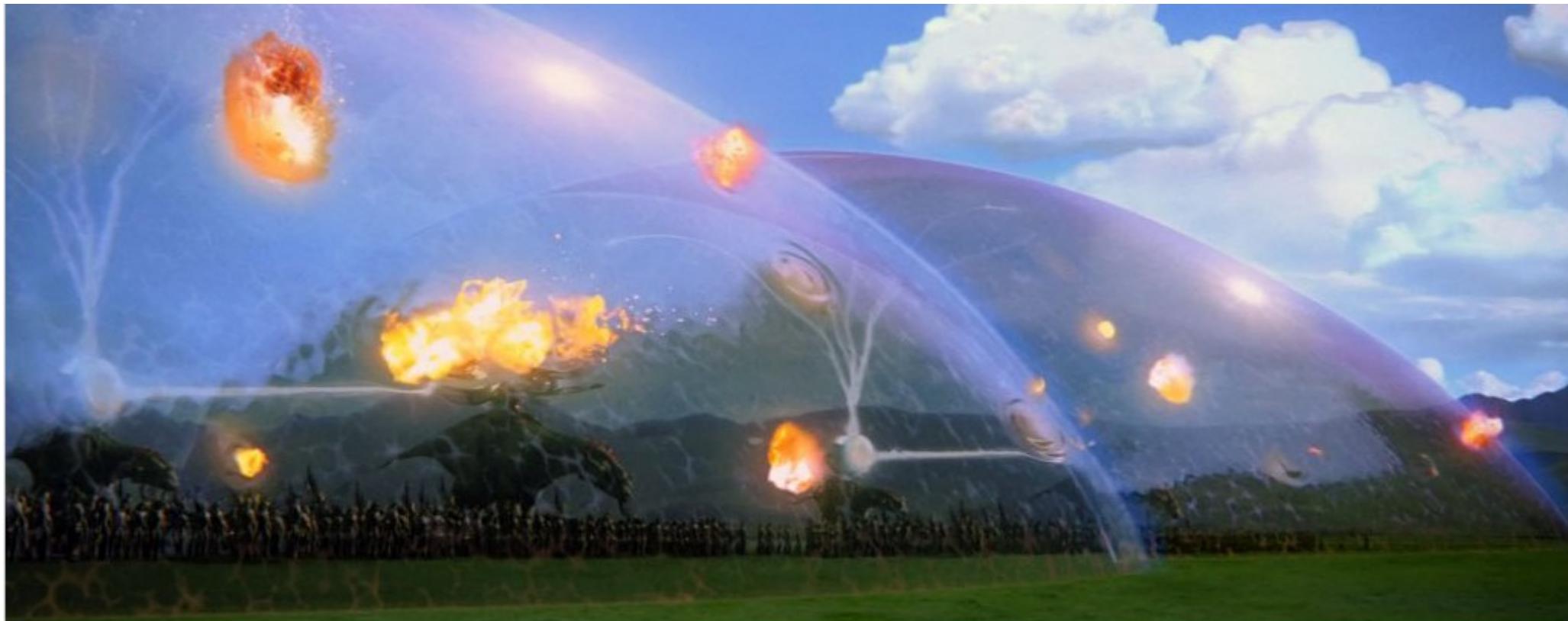
<http://www.thisiscolossal.com/2015/06/germ-handprint/>

Exosome



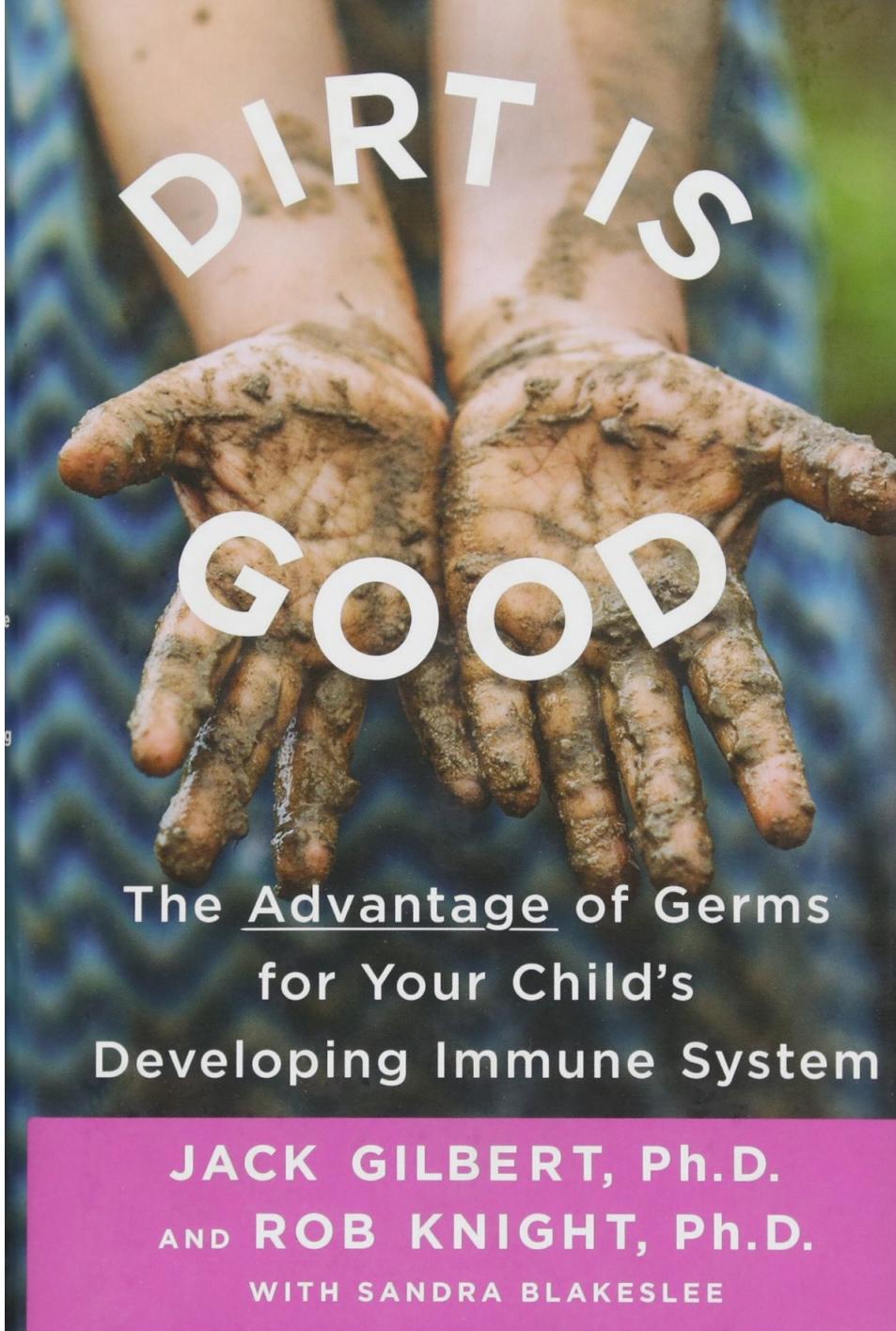
<http://www.thisiscolossal.com/2015/06/germ-handprint/>

Exosome



Lucas Films Star Wars

Boeing has patented a plasma 'force field' to protect against shock waves



MAŁOPOLSKA
CENTRE OF BIOTECHNOLOGY

ÖAW

ÖSTERREICHISCHE
AKADEMIE DER
WISSENSCHAFTEN



Exposome

„I would advise any new parent to roll their child on the floor of the New York subway.”

Chris E Mason



Exosome: City Microbiome

As dense human environments such as cities account for **over a half of the world population** (in EU ~80%) there is a need to **build a molecular portrait of cities** in order to study *what lives around us and how it affects our health and wellbeing*

Exposome: City Microbiome



The image shows the header of the Cell Systems journal website. The title "Cell Systems" is prominently displayed in white on a blue background. To the right, there are links for "All Content", "Cell Systems" (which is selected), and "All Journals". Below the main title, a navigation bar includes links for "Explore", "Online Now", "Current Issue", "Archive", "Journal Information", and "For Authors".

< Previous Article

Volume 1, Issue 1, p72–87, 29 July 2015

Article

Switch to Enhanced View

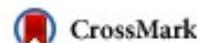
Geospatial Resolution of Human and Bacterial Diversity with City-Scale Metagenomics

Ebrahim Afshinnekoo²¹, Cem Meydan²¹, Shanin Chowdhury, Dyalal Jaroudi, Collin Boyer, Nick Bernstein, Julia M. Maritz, Darryl Reeves, Jorge Gandara, Sagar Chhangawala, Sofia Ahsanuddin, Amber Simmons, Timothy Nessel, Bharathi Sundaresan, Elizabeth Pereira, Ellen Jorgensen, Sergios-Orestis Kolokotronics, Nell Kirchberger, Isaac Garcia, David Gandara, Sean Dhanraj, Tanzina Nawrin, Yogesh Salelore, Noah Alexander, Priyanka Vijay, Elizabeth M. Hénaff, Paul Zumbo, Michael Walsh, Gregory D. O'Mullan, Scott Tighe, Joel T. Dudley, Anya Dunaif, Sean Ennis, Eoghan O'Halloran, Tiago R. Magalhaes, Braden Boone, Angela L. Jones, Theodore R. Muth, Katie Schneider Paolantonio, Elizabeth Alter, Eric E. Schadt, Jeanne Garbarino, Robert J. Prill, Jane M. Carlton, Shawn Levy, Christopher E. Mason✉

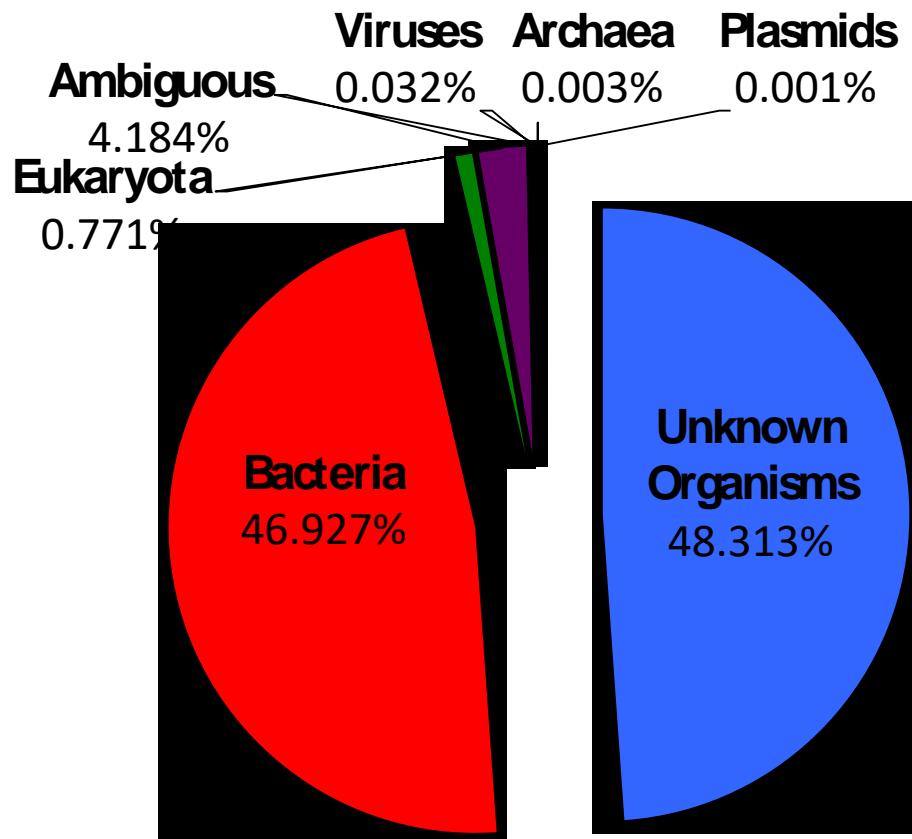
²¹ Co-first author

Open Access

DOI: <http://dx.doi.org/10.1016/j.cels.2015.01.001>

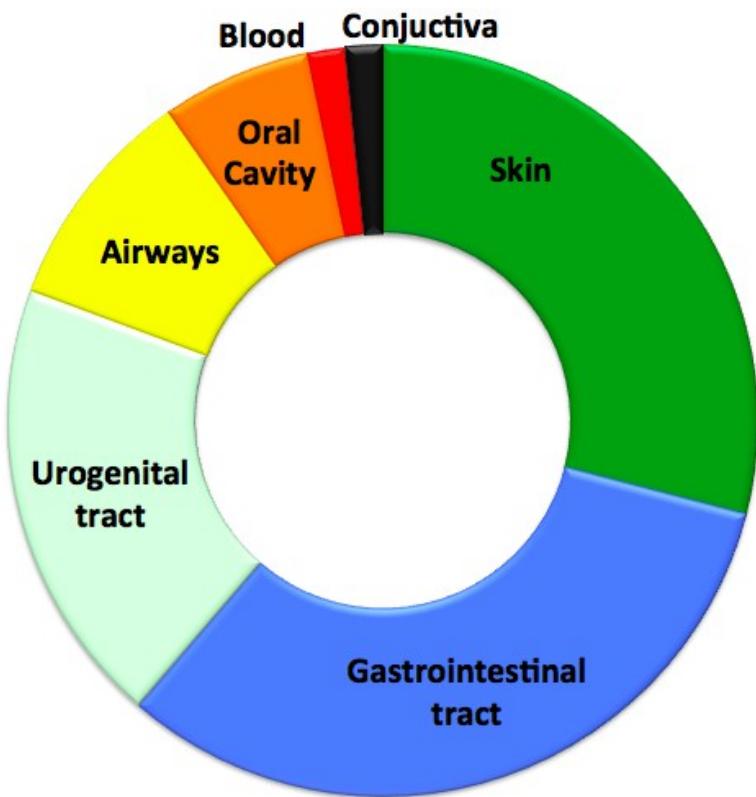


Exosome: City Microbiome

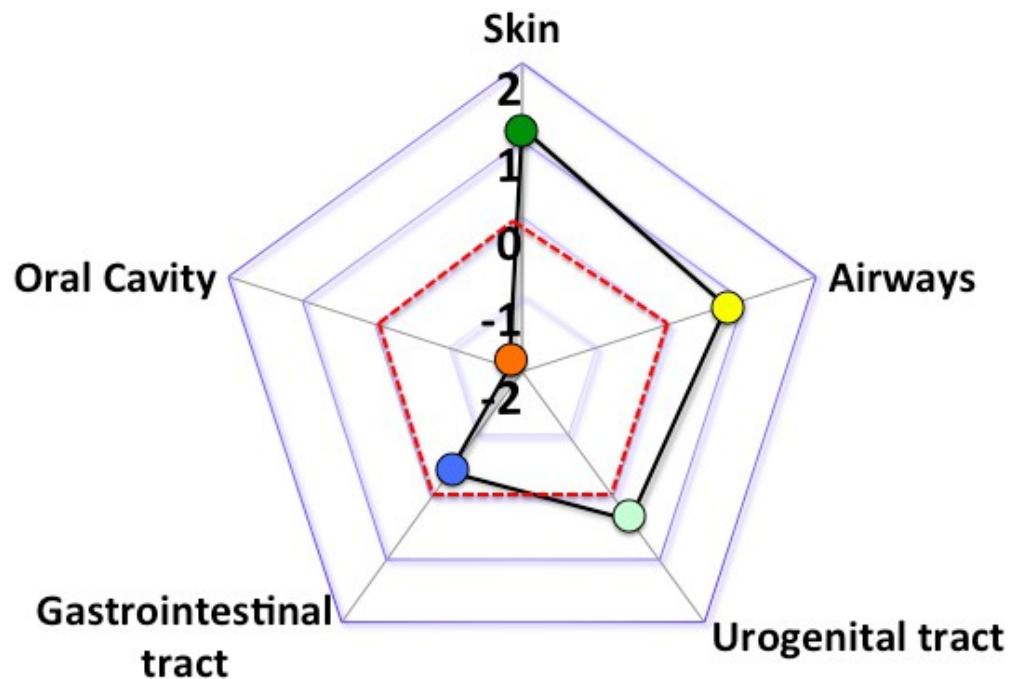


Afshinnekoo, et al. 2015, Cell Systems, 1(1), 72-87

Exposome: City Microbiome



**HMP Comparison Shows
That the Subway
“Looks Like Skin”**



Exosome: City Microbiome

Data → Information → Knowledge → Wisdom (DIKW).

Just because you have *data*, it takes some processing to get quality *information*, and even good information is not necessarily *knowledge*, and knowledge often requires context or application to become *wisdom*.



Exosome: City Microbiome

Data → Information → Knowledge → Wisdom (DIKW).

Just because you have *data*, it takes some processing to get quality *information*, and even good information is not necessarily *knowledge*, and knowledge often requires context or application to become *wisdom*.

DNA → Species → Organism → Pathogen (DSOP)

Even if you have *DNA* fragments, and you correctly match it to the right *species*, and you have evidence that it is coming from a *living organism*, this still does not mean you have a *pathogen*.

Mason CE. The long road from Data to Wisdom, and from DNA to Pathogen. MicroBEnet, Feb 2015



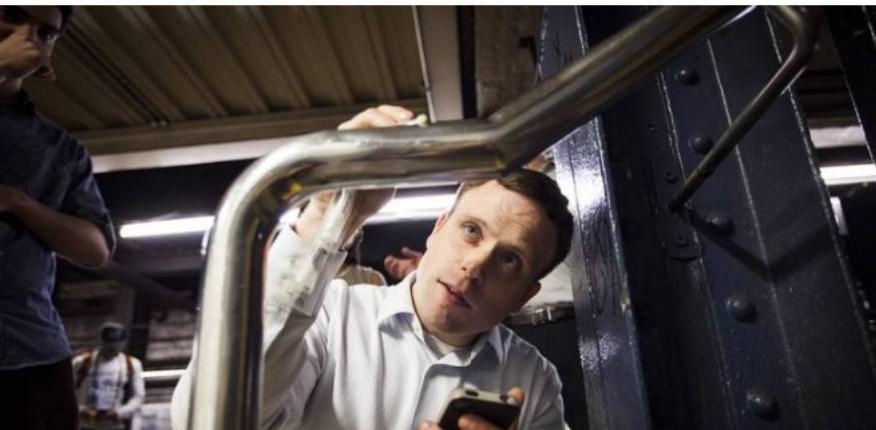
Exosome: City Microbiome



CITY PROFILES ABOUT MAP METHODS PEOPLE MEETINGS LINKS CONTACT

Building a Molecular Portrait of Cities

Subway surfaces define the daily commute for billions of people each year, and yet there is almost nothing known about the impact of surface type, season, commuter type, or subway design on their commute. We aim to bring a molecular view of the cities to improve their design, use, and impact on health.



About MetaSUB

The Metagenomics and Metadesign of the Subways and Urban Biomes (MetaSUB) International consortium is a novel, interdisciplinary initiative made up of experts across many fields, including genomics, data analysis, engineering, public health, and design. Just as there is a standard and measurement of temperature, air pressure, wind currents- all of which are considered in the design of the built environment- the microbial ecosystem is just as dynamic and just as integral and should be integrated into the design of cities. By developing and testing standards for the field and optimizing methods for urban sample collection, DNA/RNA isolation, taxa characterization, and data visualization, the MetaSUB consortium is pioneering an unprecedented study of urban mass-transit systems and cities around the world. These data will benefit city planners, public health officials, and designers, as well as discovery new species, biological systems, and biosynthetic gene clusters (BGCs), thus enabling an era of more quantified, responsive, and "smarter cities."

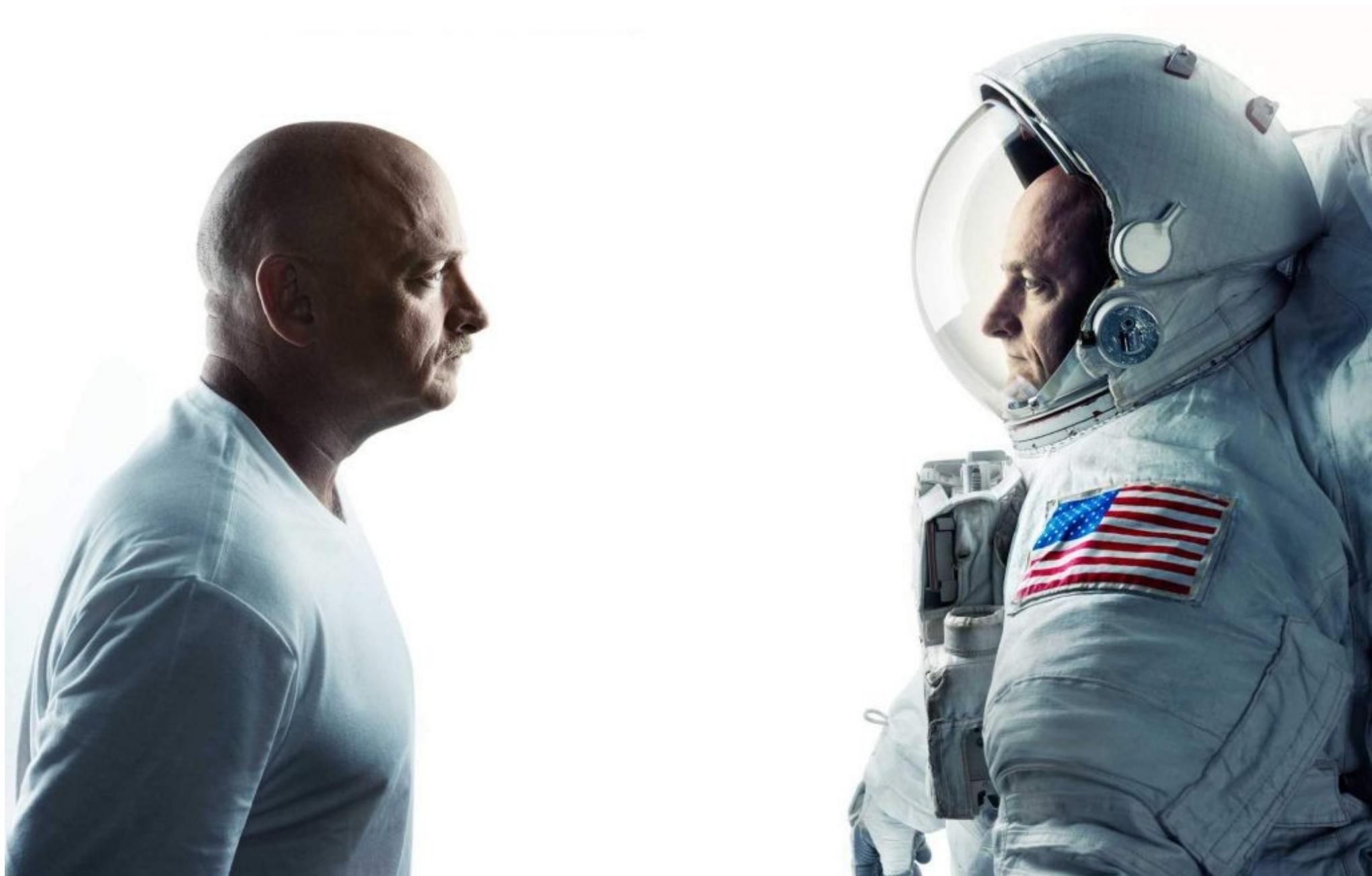
MetaSUB International Consortium www.metasub.org



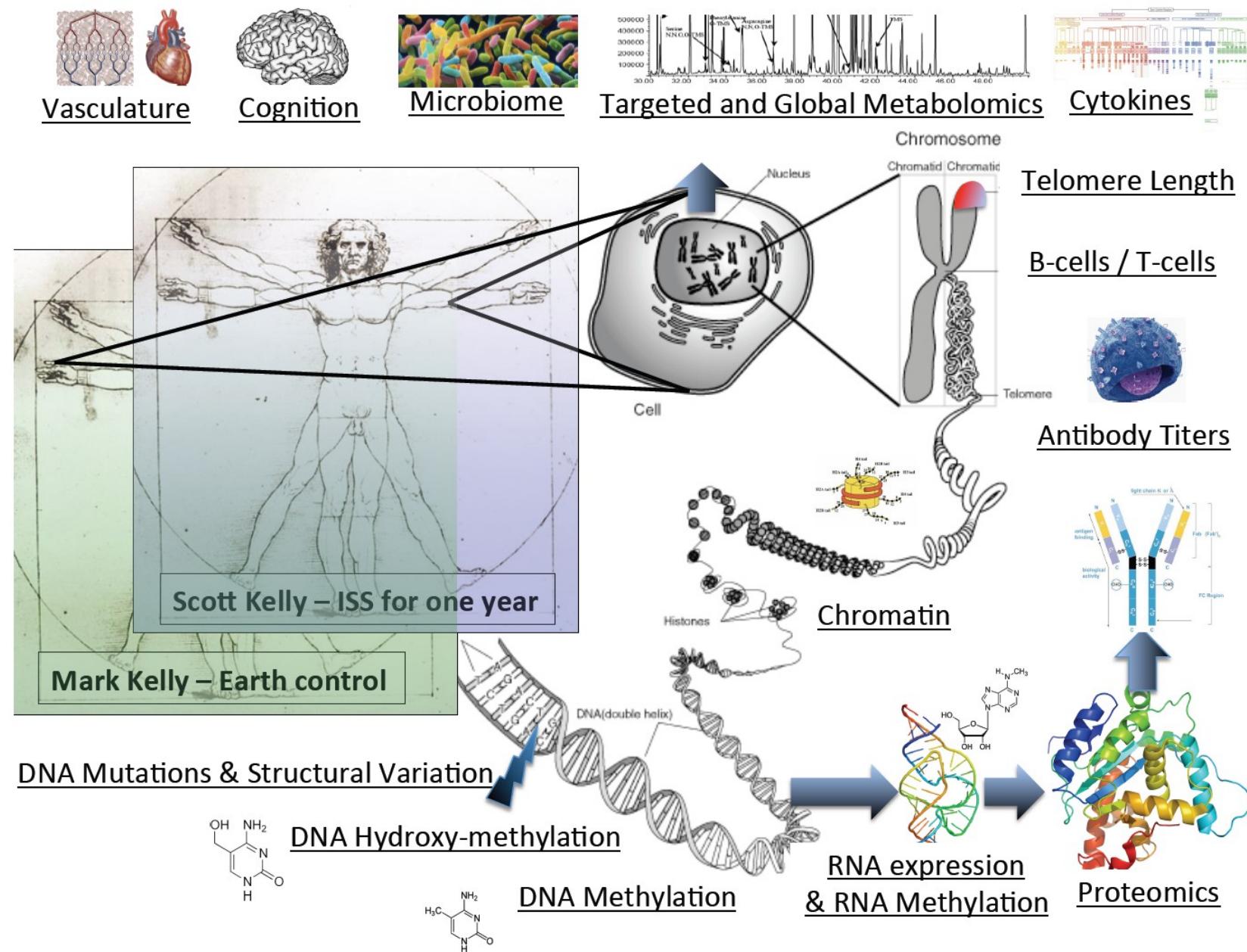
Exposome: ~~City~~ Space Microbiome



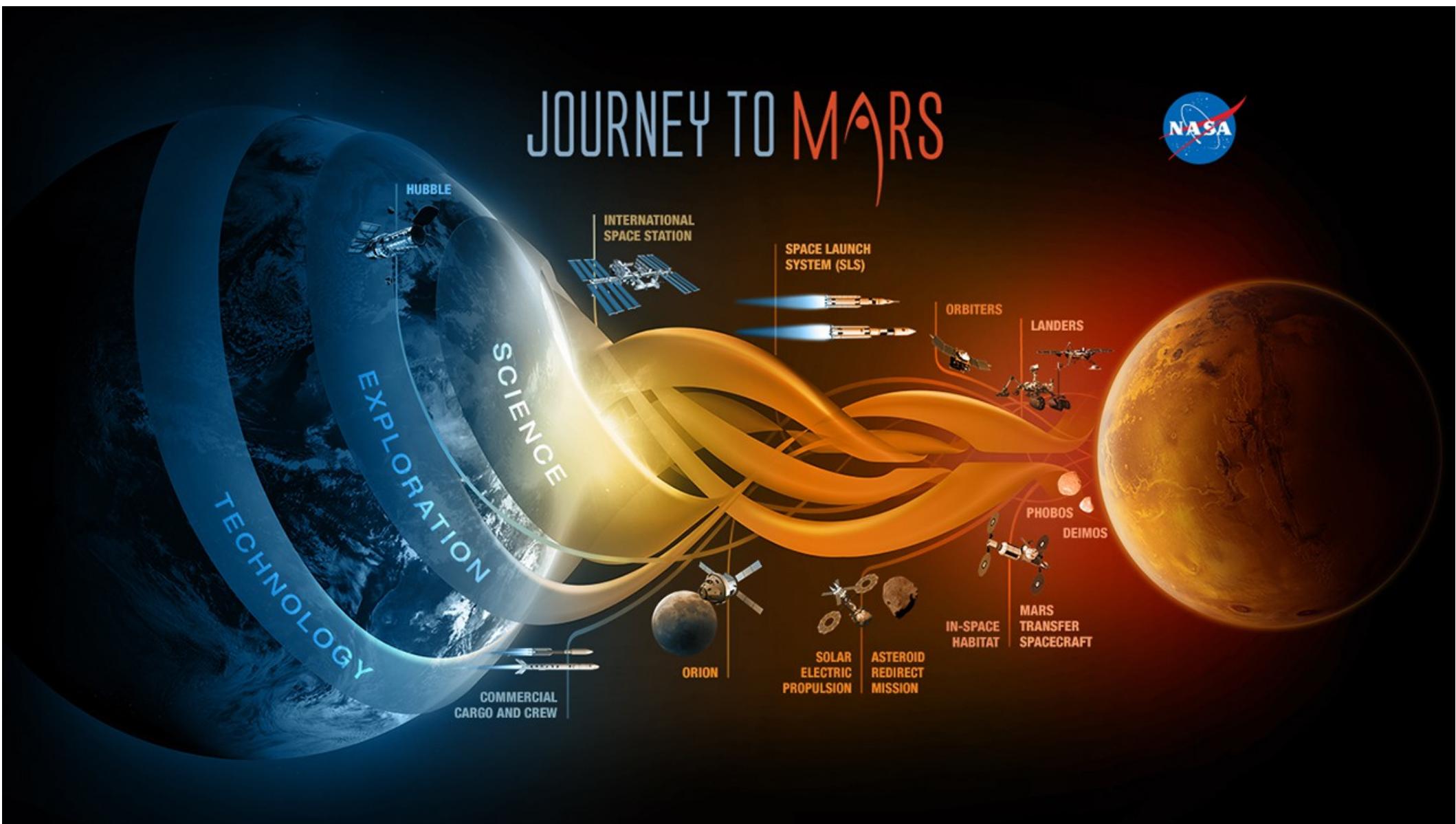
Exposome: ~~City~~ Space Microbiome



Space Personalized Medicine



Space Personalized Medicine



Exposome: City Microbiome



Explore journals

Get published

About BioMed Central



MEETING REPORT

OPEN ACCESS

The Metagenomics and Metadesign of the Subways and Urban Biomes (MetaSUB) International Consortium inaugural meeting report

The MetaSUB International Consortium¹ 

Microbiome 2016 4:24 | DOI: 10.1186/s40168-016-0168-z | © The MetaSUB International Consortium. 2016

Received: 17 December 2015 | Accepted: 15 April 2016 | Published: 3 June 2016



Exposome: City Microbiome

Five core areas:

- collection,
- **analysis**,
- design,
- **standards**, and
- education

Bioinformatics for City Microbiome

key questions about ideal methods to:

- store,
- merge,
- analyse / process
- visualise and communicate

the data

→ multiple analytical challenges in dealing with the
metagenomic data



Bioinformatics for City Microbiome

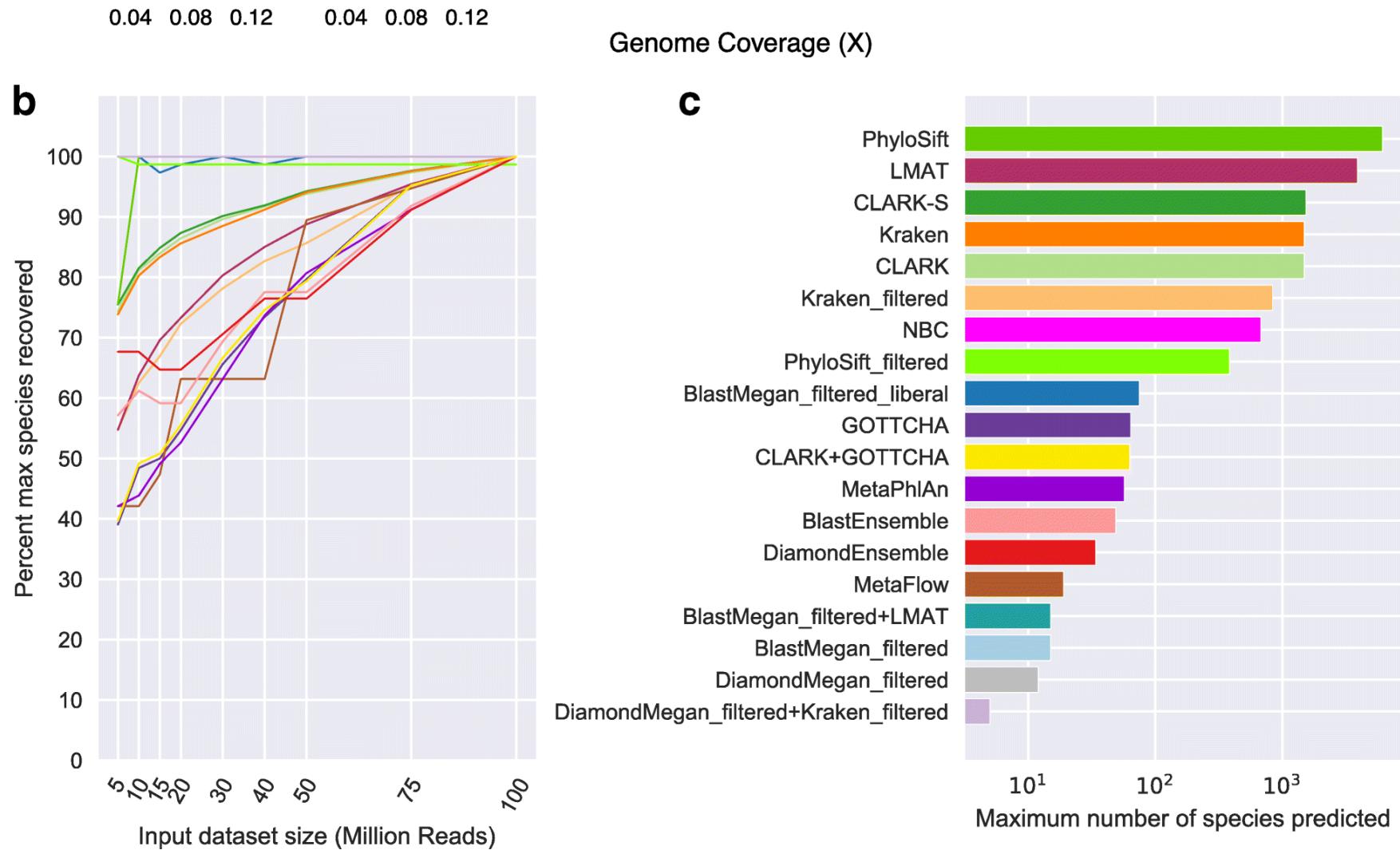
Addressing these has implications for how we **understand** and **interpret** the diversity and complexity of *urban biomes*.

there is not a definitive set of guidelines for many of these challenges

*standards, reproducibility,
open-access/data sharing, and innovation*

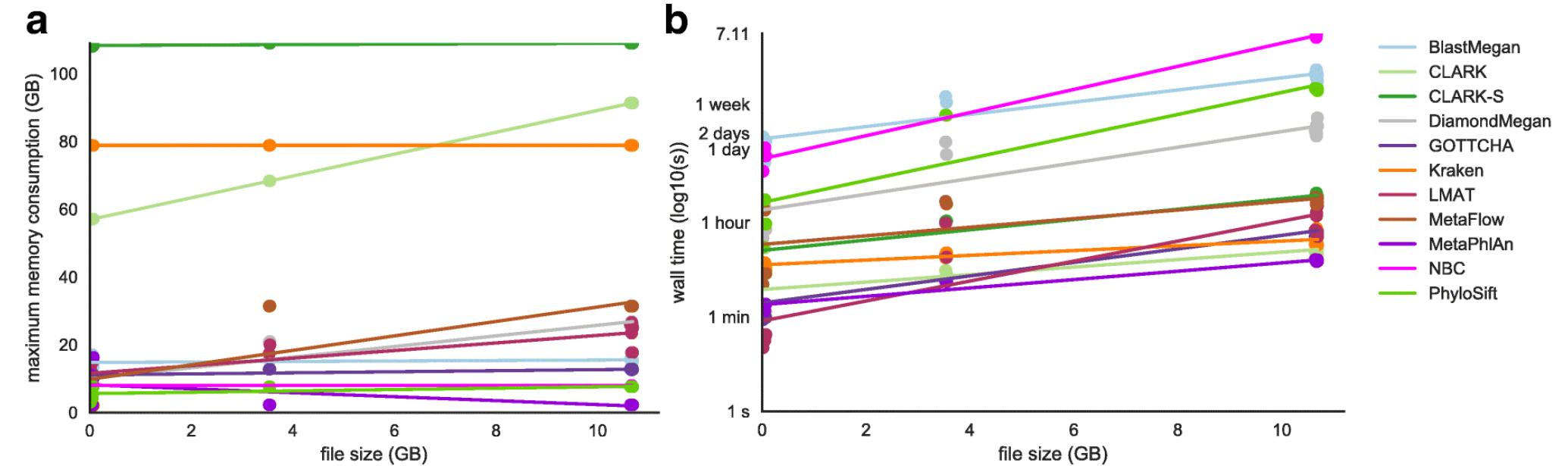


Bioinformatics for City Microbiome



McIntyre et al. Genome Biology 2017 18:182

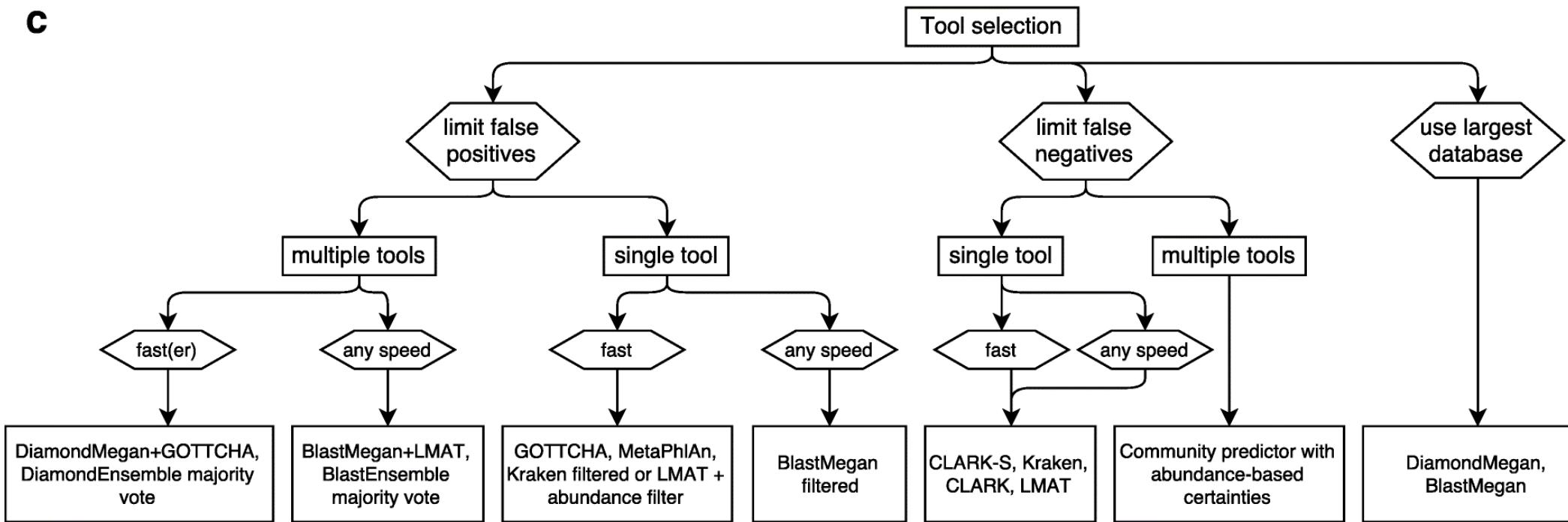
Bioinformatics for City Microbiome



McIntyre et al. Genome Biology 2017 18:182

Bioinformatics for City Microbiome

C



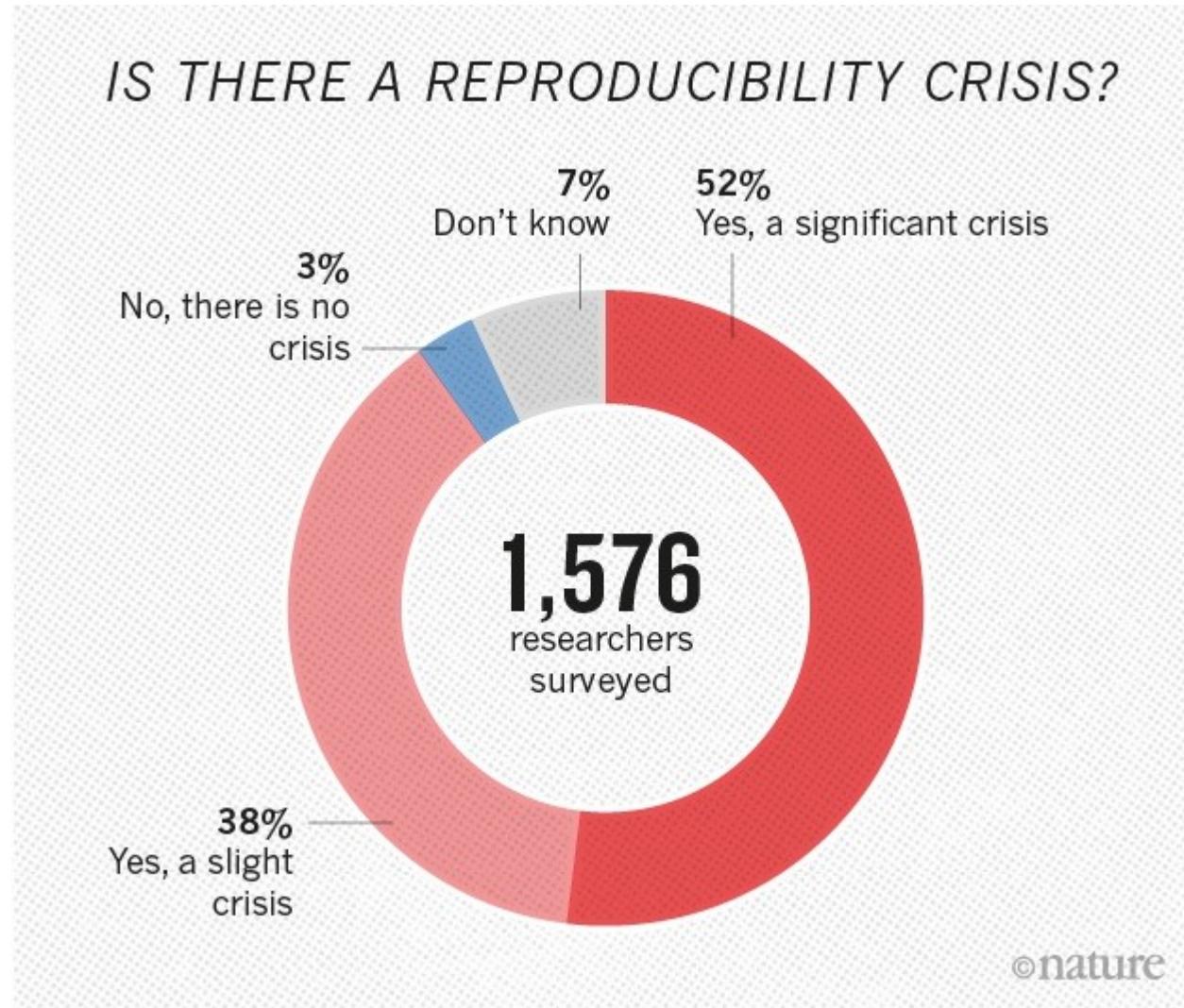
McIntyre et al. Genome Biology 2017 18:182

Bioinformatics for City Microbiome

There is a lot to do !!!



Reproducibility in science?



Baker, M. (2016). 1,500 scientists lift the lid on reproducibility. *Nature*, 533(7604), 452-454.

Reproducibility in science?

SIGNAL PODCAST

Episode 3: Should we believe published scientific research?

By LUKE TIMMERMAN and MEG TIRRELL / DECEMBER 3, 2015

*Currently, many published research findings are **false** or **exaggerated**, and an estimated **85%** of research resources are **wasted**.*

JPA Ioannidis (2014) How to Make More Published Research True, *PLOS Medicine*



Reproducibility in science?

NATURE | EDITORIAL

Journals unite for reproducibility

Consensus on reporting principles aims to improve quality and encourage public trust in science.

05 November 2014

NATURE | COMMENT

Reproducibility: The risks of the replication drive

Mina Bissell

20 November 2013



EDITORIAL



REPRODUCIBILITY IN CANCER BIOLOGY

The challenges of replication

Interpreting the first results from the Reproducibility Project: Cancer Biology requires a highly nuanced approach.



nature International weekly journal of science

Home | News & Comment | Research | Careers & Jobs | Current Issue | Archive | Audio & Video | For Authors | Advertise | About | Help

Archive > Specials and supplements archive > Challenges in irreproducible research

SPECIAL See all specials

CHALLENGES IN IRREPRODUCIBLE RESEARCH



ÖSTERREICHISCHE
AKADEMIE DER
WISSENSCHAFTEN



Reproducibility in science?

NATURE | NEWS FEATURE



The secret war against counterfeit science

China has a lucrative market for fake research reagents. Some scientists are fighting back.

David Cyranoski

10 May 2017

TECHNOLOGY FEATURE CHECK YOUR CHEMISTRY

Chemical probes and screening libraries can easily get mixed up or messed up, causing misleading results for unwary biologists.



Reproducibility in science?

Biometrical J

48 data-driven papers:

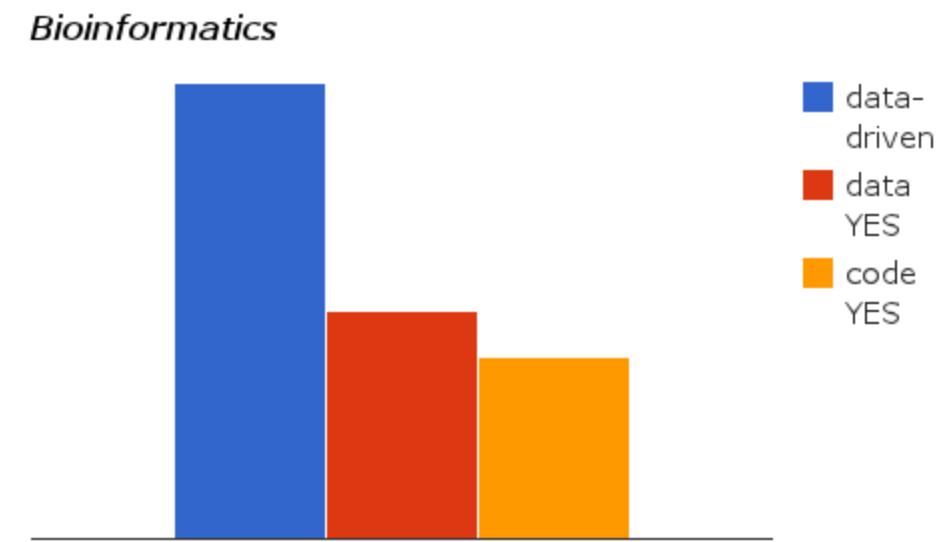
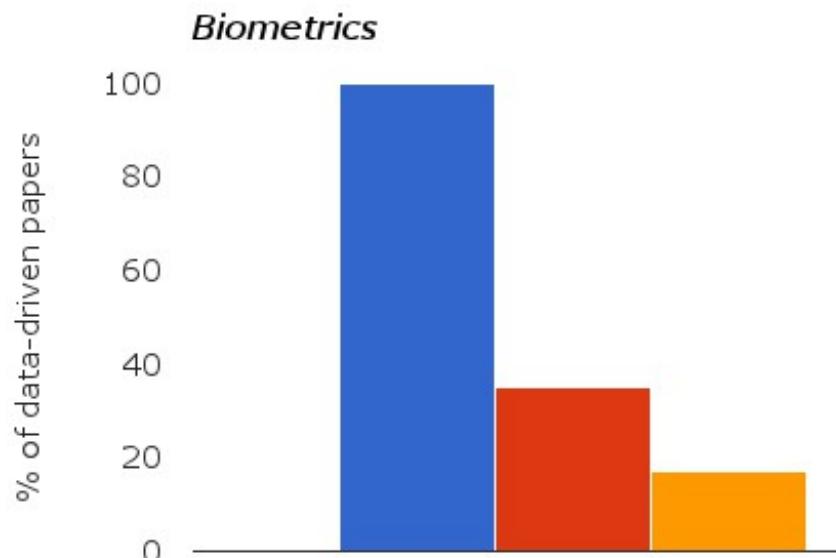
- 35% data
- 17% code

[Hothorn *et al*, 2009; Hothorn & Leisch, 2011]

Bioinformatics J

69 data-driven papers:

- 50% data
- 40% code



Reproducibility in science?

Box 1. Some Research Practices that May Help Increase the Proportion of True Research Findings

- Large-scale collaborative research
- Adoption of replication culture
- Registration (of studies, protocols, analysis codes, datasets, raw data, and results)
- Sharing (of data, protocols, materials, software, and other tools)
- Reproducibility practices
- Containment of conflicted sponsors and authors
- More appropriate statistical methods
- Standardization of definitions and analyses
- More stringent thresholds for claiming discoveries or “successes”
- Improvement of study design standards
- Improvements in peer review, reporting, and dissemination of research
- Better training of scientific workforce in methods and statistical literacy

JPA Ioannidis (2014) How to Make More Published Research True, PLOS Medicine

MAQC-I, MAQC-II, MAQC-III/SEQC

MAQC-IV/SEQC2

ARTICLES

nature
biotechnology

The MicroArray Quality Control (MAQC) project shows inter- and intraplatform reproducibility of gene expression measurements

nature biotechnology

MAQC Consortium*

nature
biotechnology

MAQC-I - 2006

ARTICLES

MAQC-II - 2010

The MicroArray Quality Control (MAQC)-II study of common practices for the development and validation of microarray-based predictive models

MAQC Consortium*

ARTICLES

nature
biotechnology

MAQC-III/SEQC - 2014

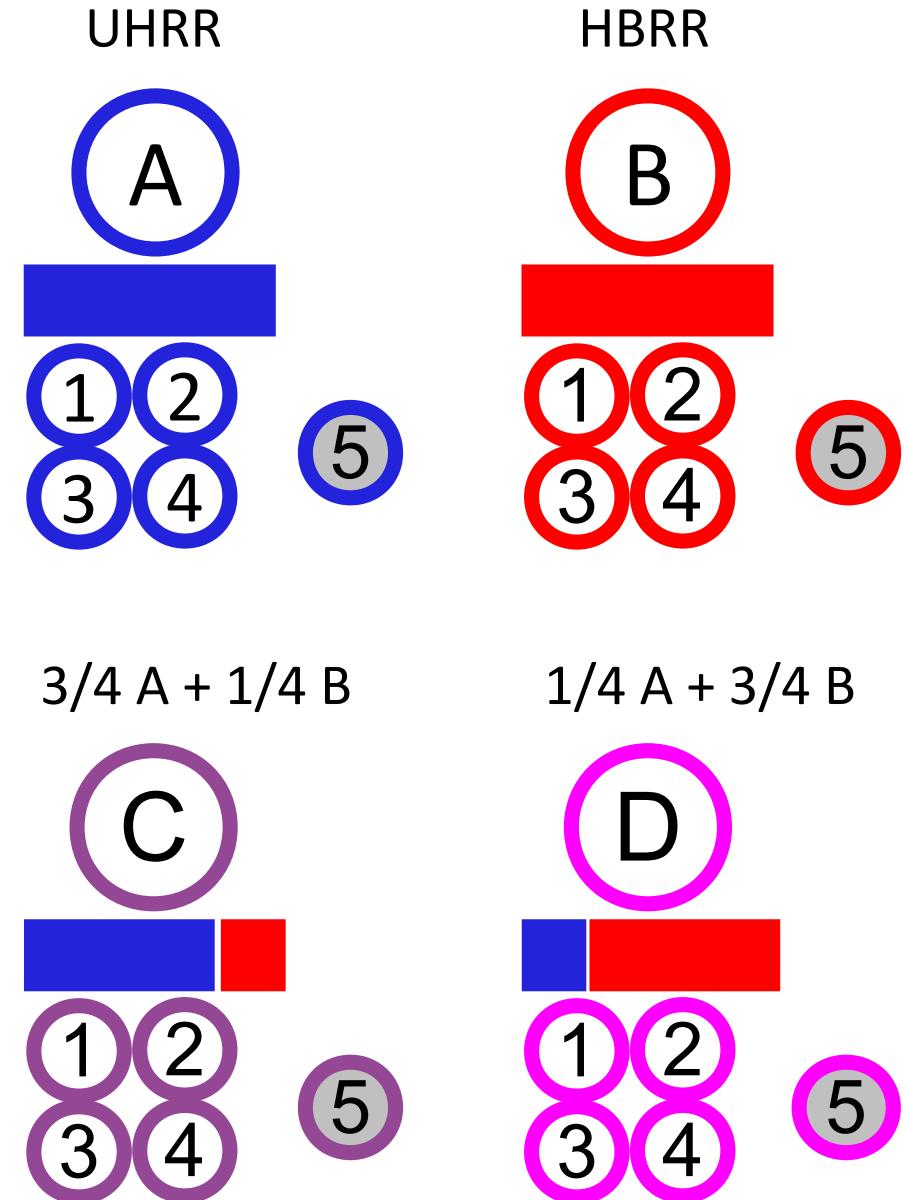
A comprehensive assessment of RNA-seq accuracy, reproducibility and information content by the Sequencing Quality Control Consortium

SEQC/MAQC-III Consortium*

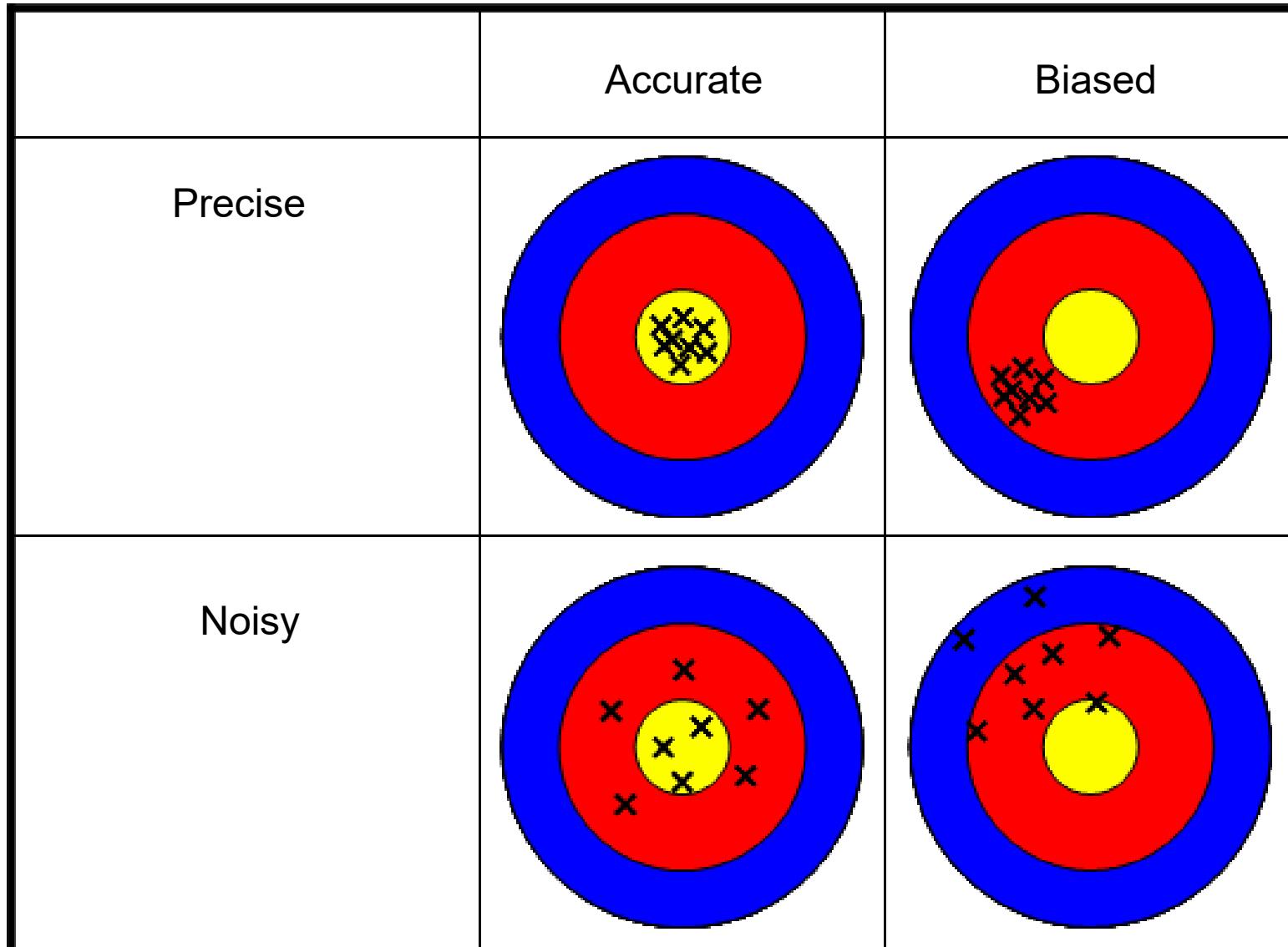
SEquencing Quality Control consortium

A comprehensive synthetic benchmark

- standardized, publicly available benchmark samples
- known mixing ratios
- **multi-site (6 sites)**
- cross-platform
- nested replicates
- ERCC spike-ins



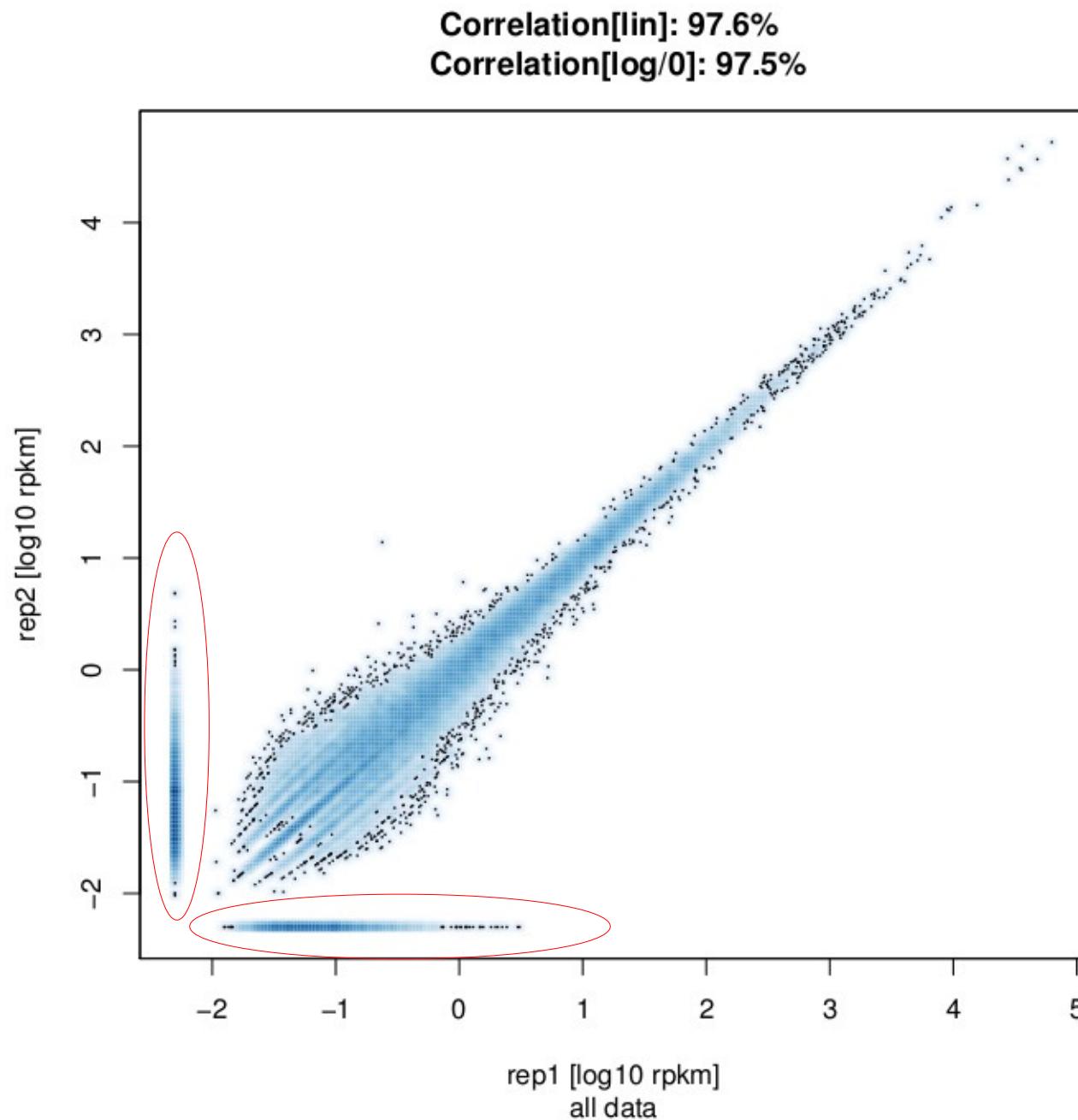
Bias and noise



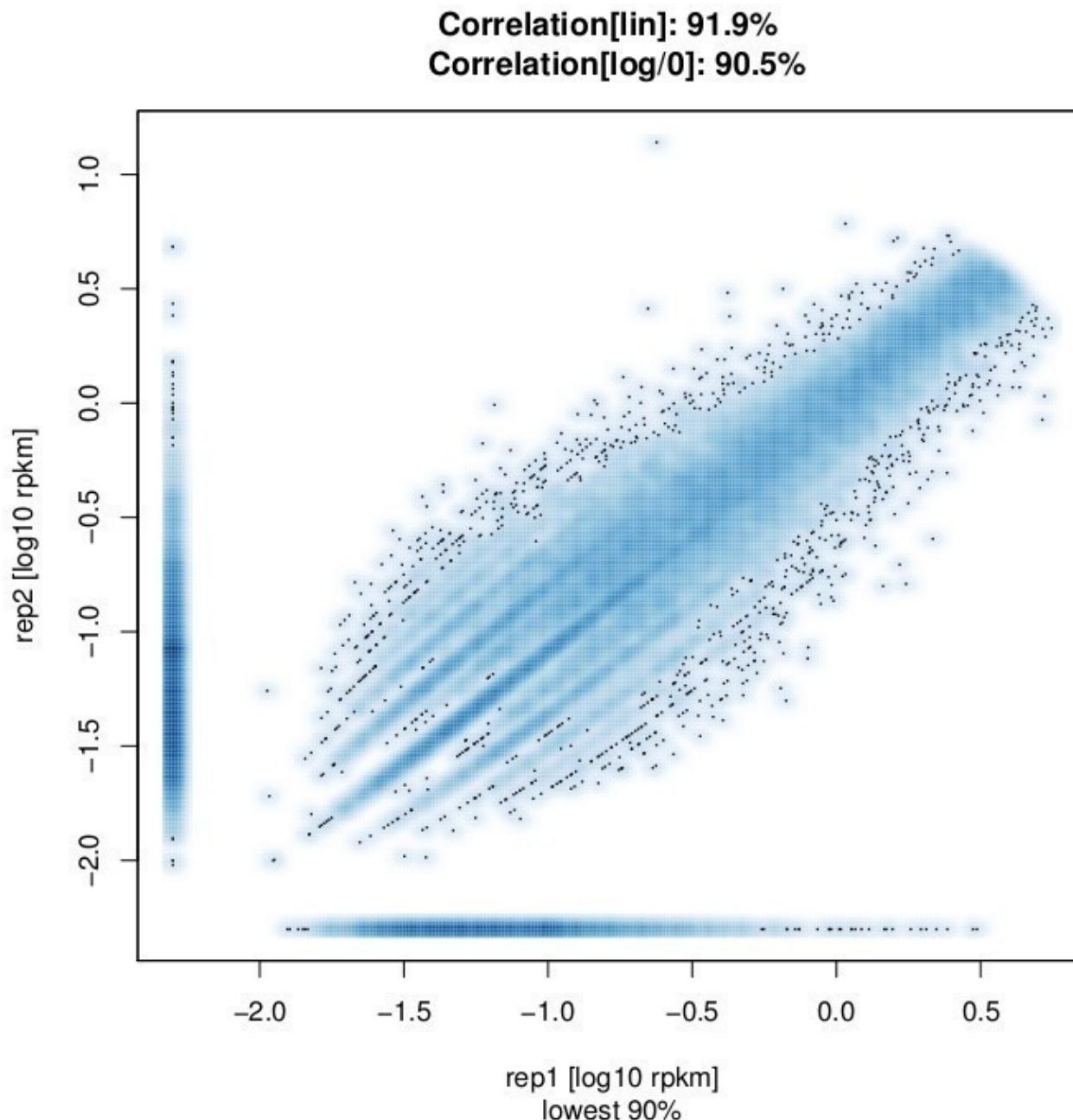
Sources of variation

- Measurements process / lab
- Random sampling by NGS

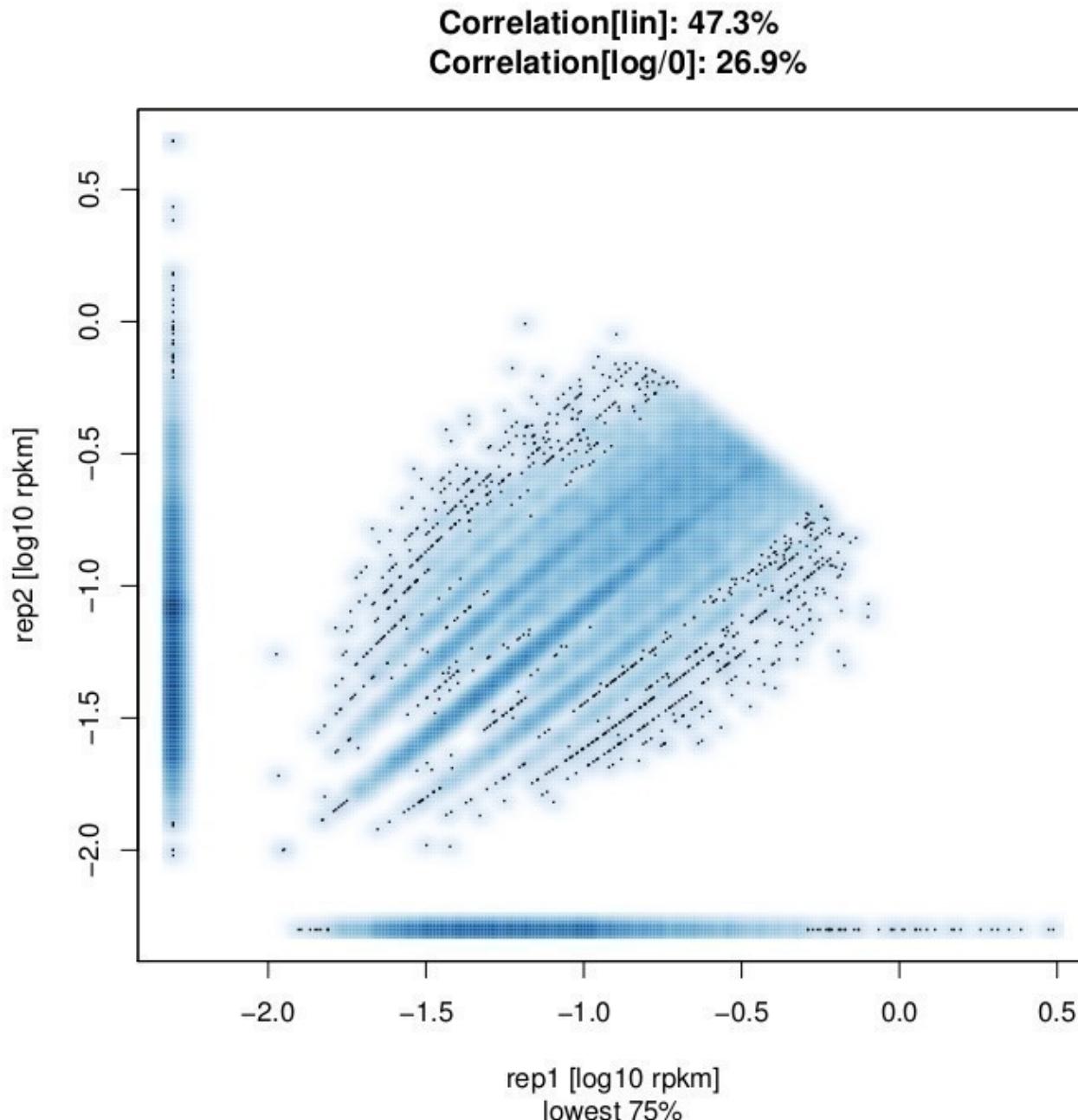
Reproducibility of expression level estimates



Reproducibility of expression level estimates

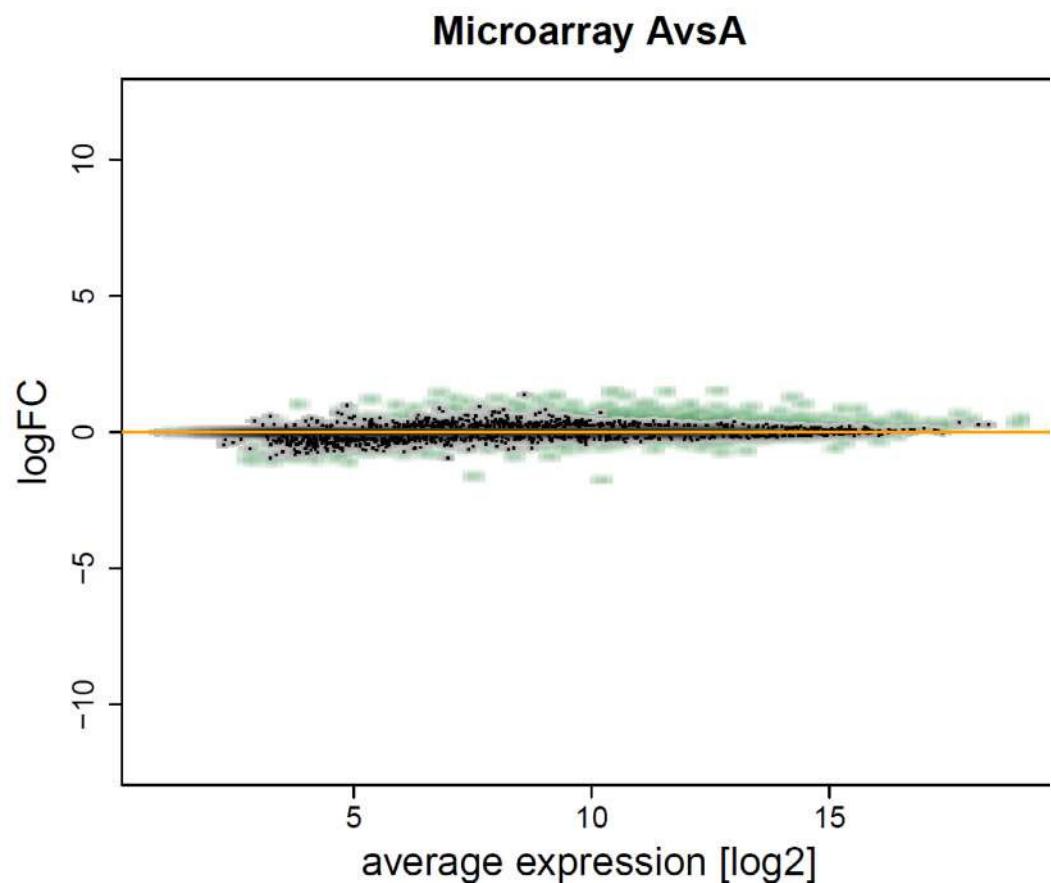
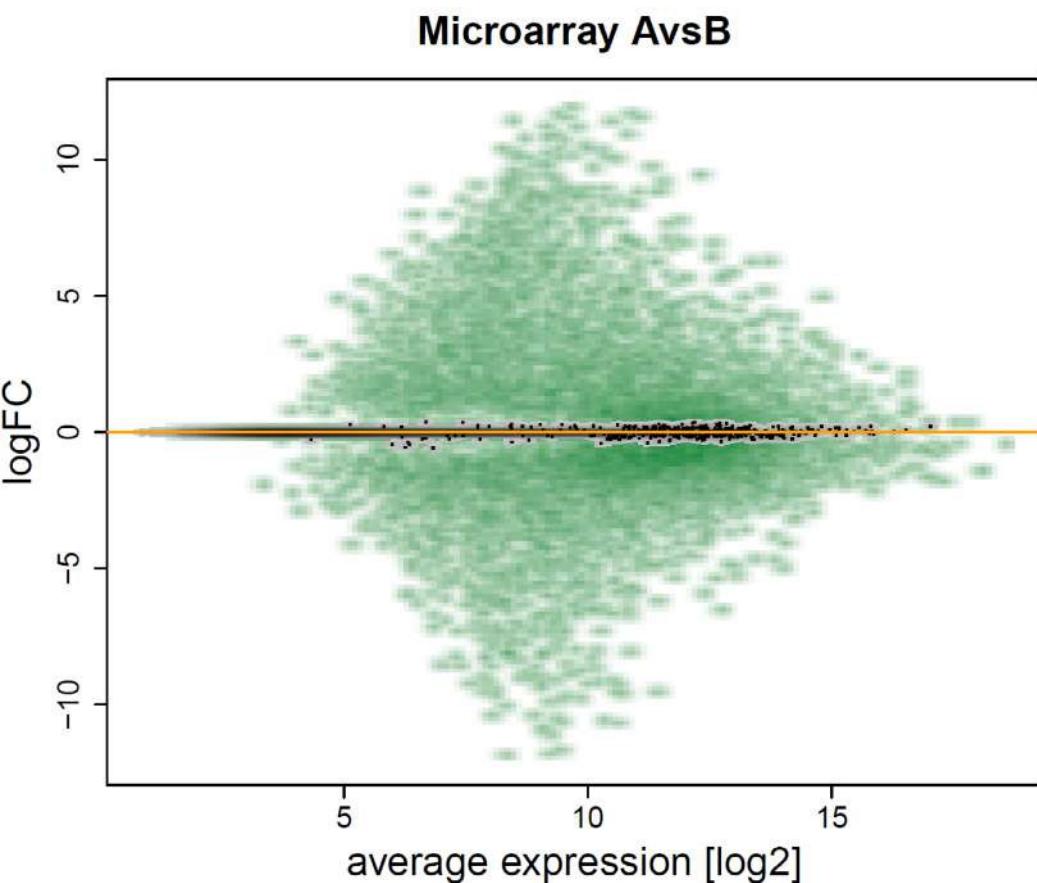


Reproducibility of expression level estimates



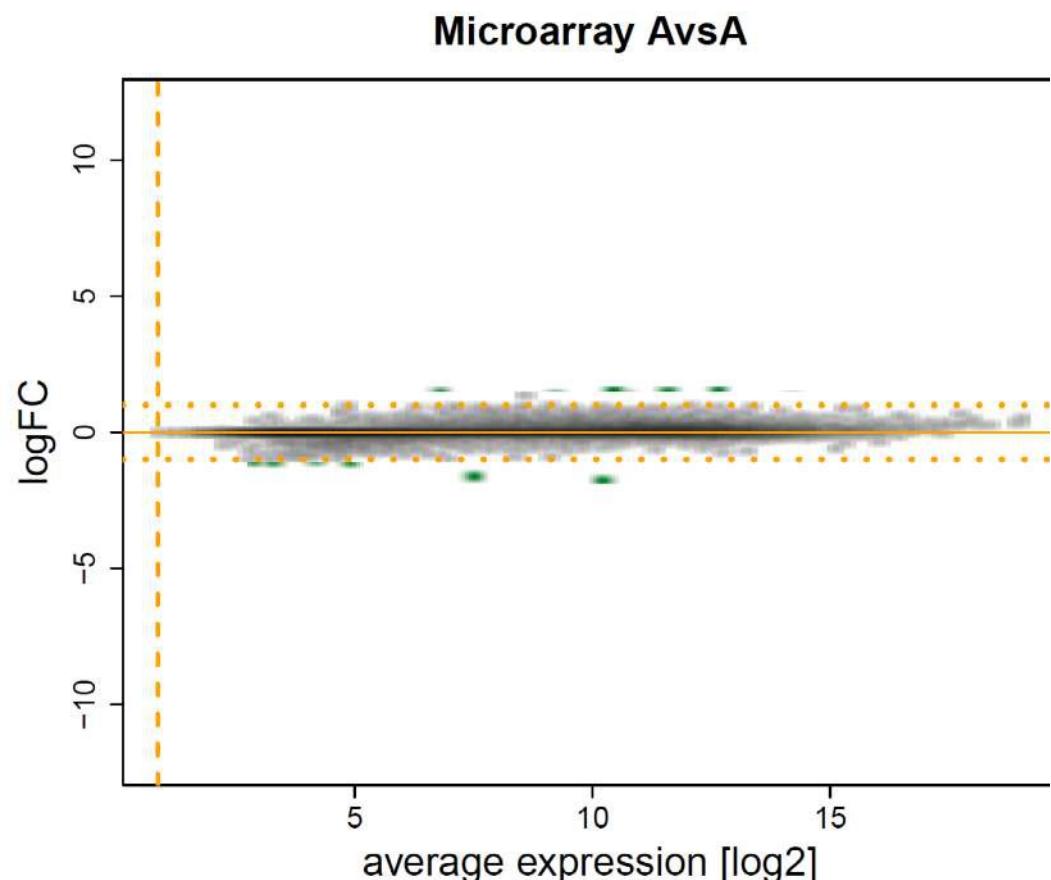
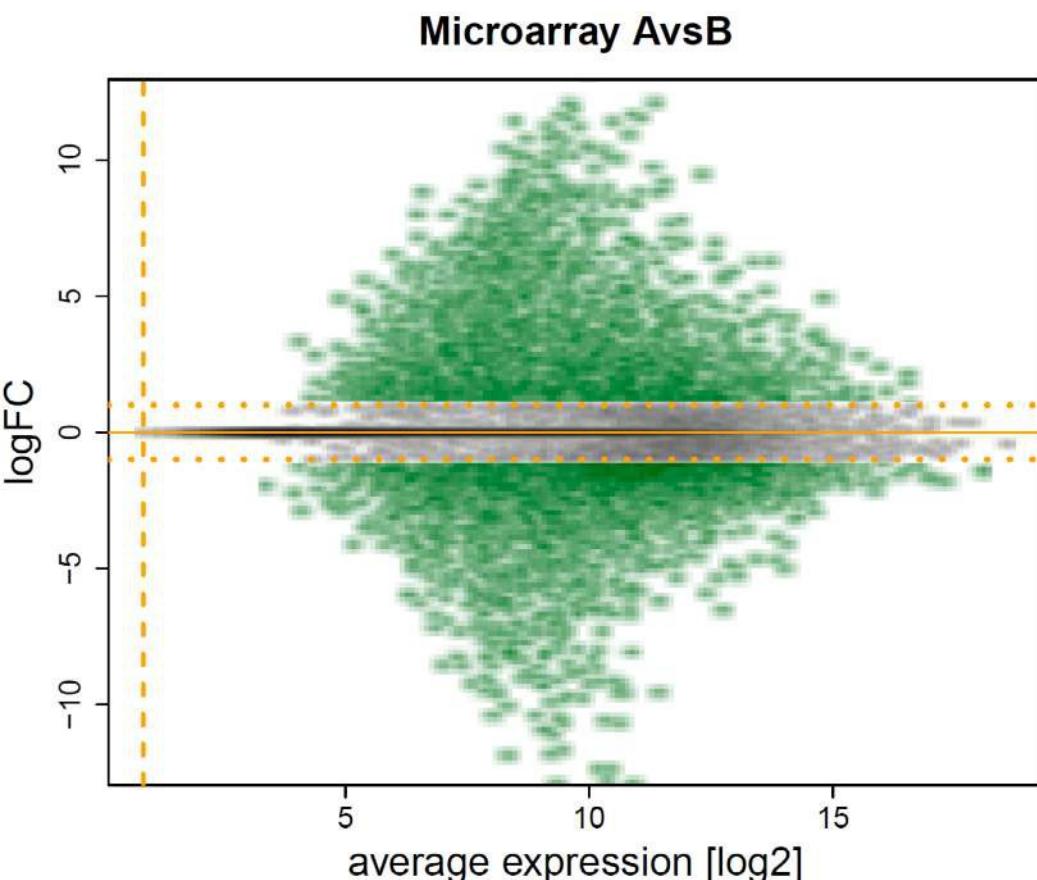
MAQC - III / SEQC

Cross-site reproducibility



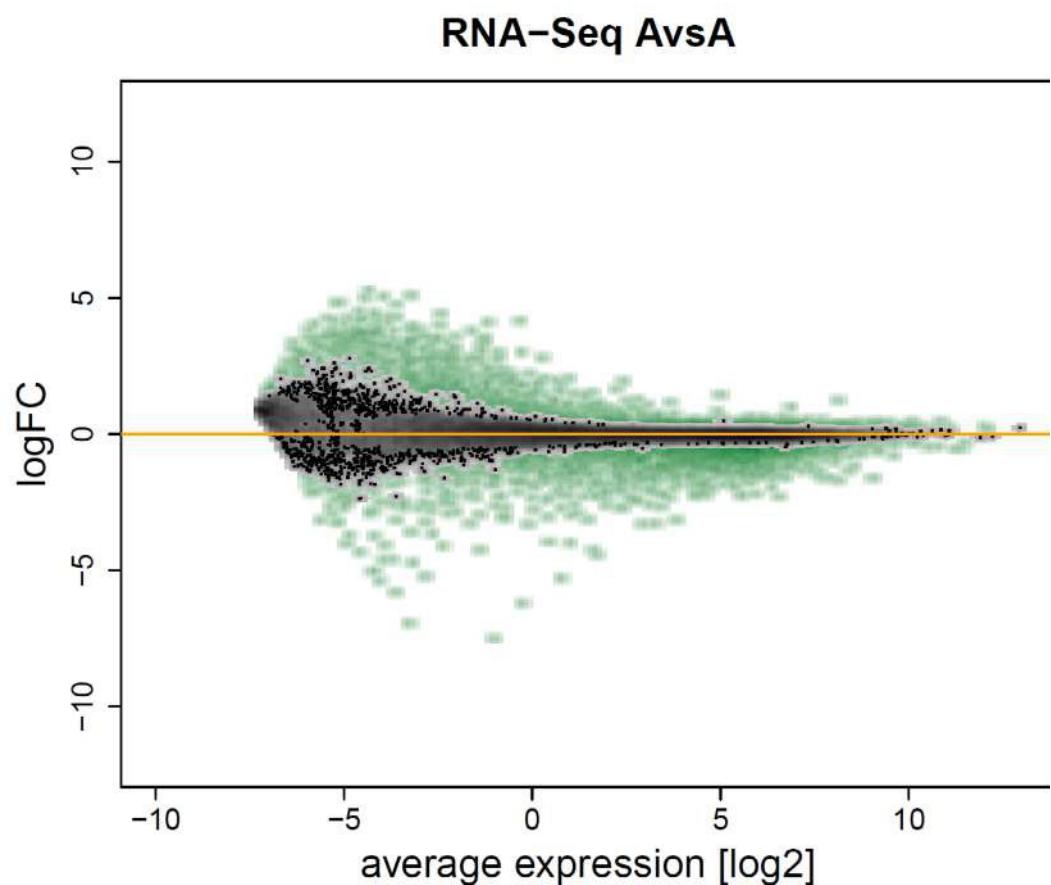
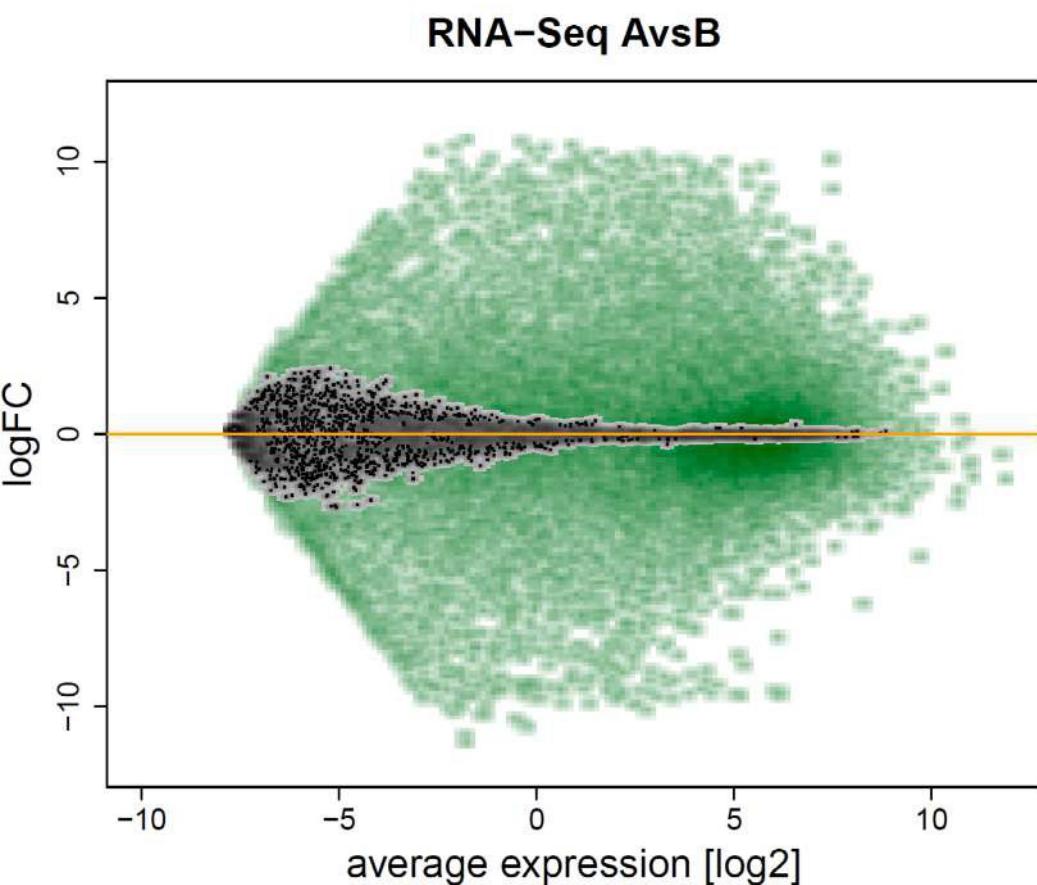
MAQC - III / SEQC

Cross-site reproducibility



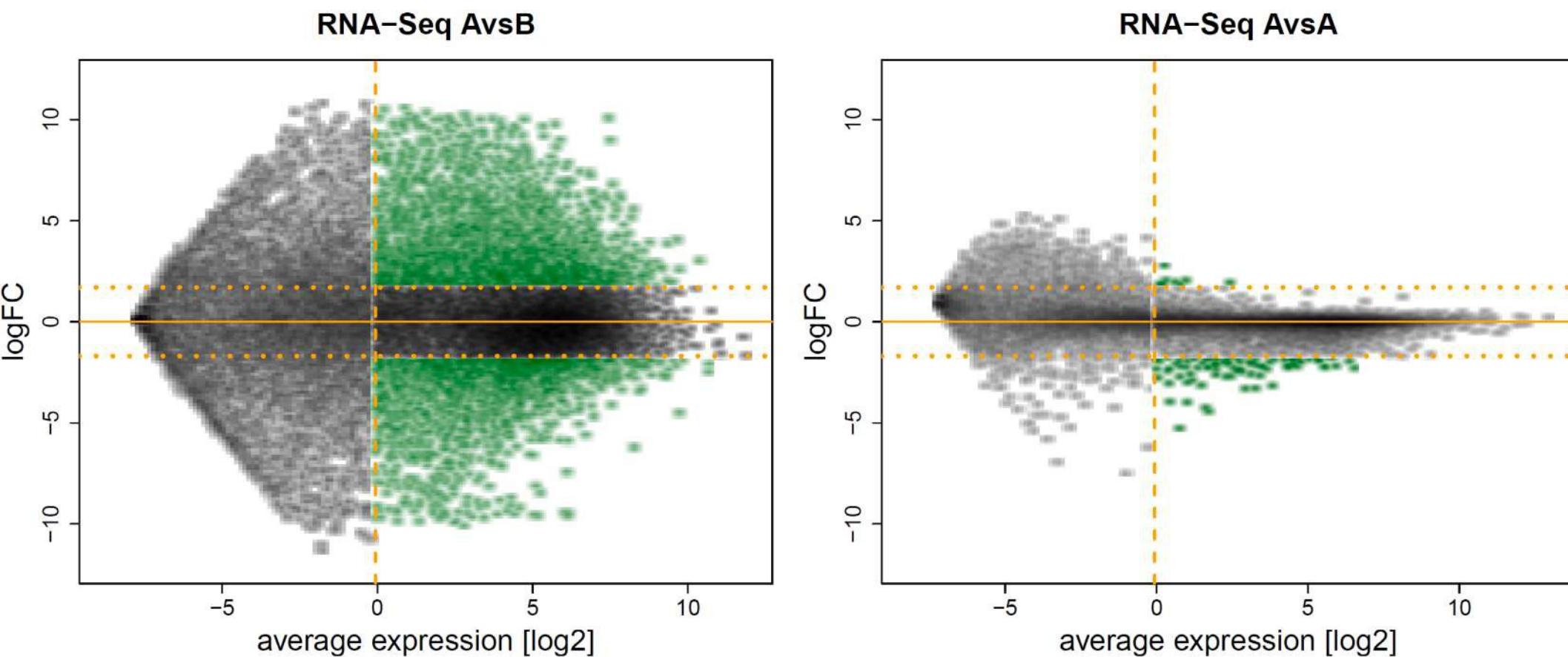
MAQC - III / SEQC

Cross-site reproducibility



MAQC - III / SEQC

Cross-site reproducibility



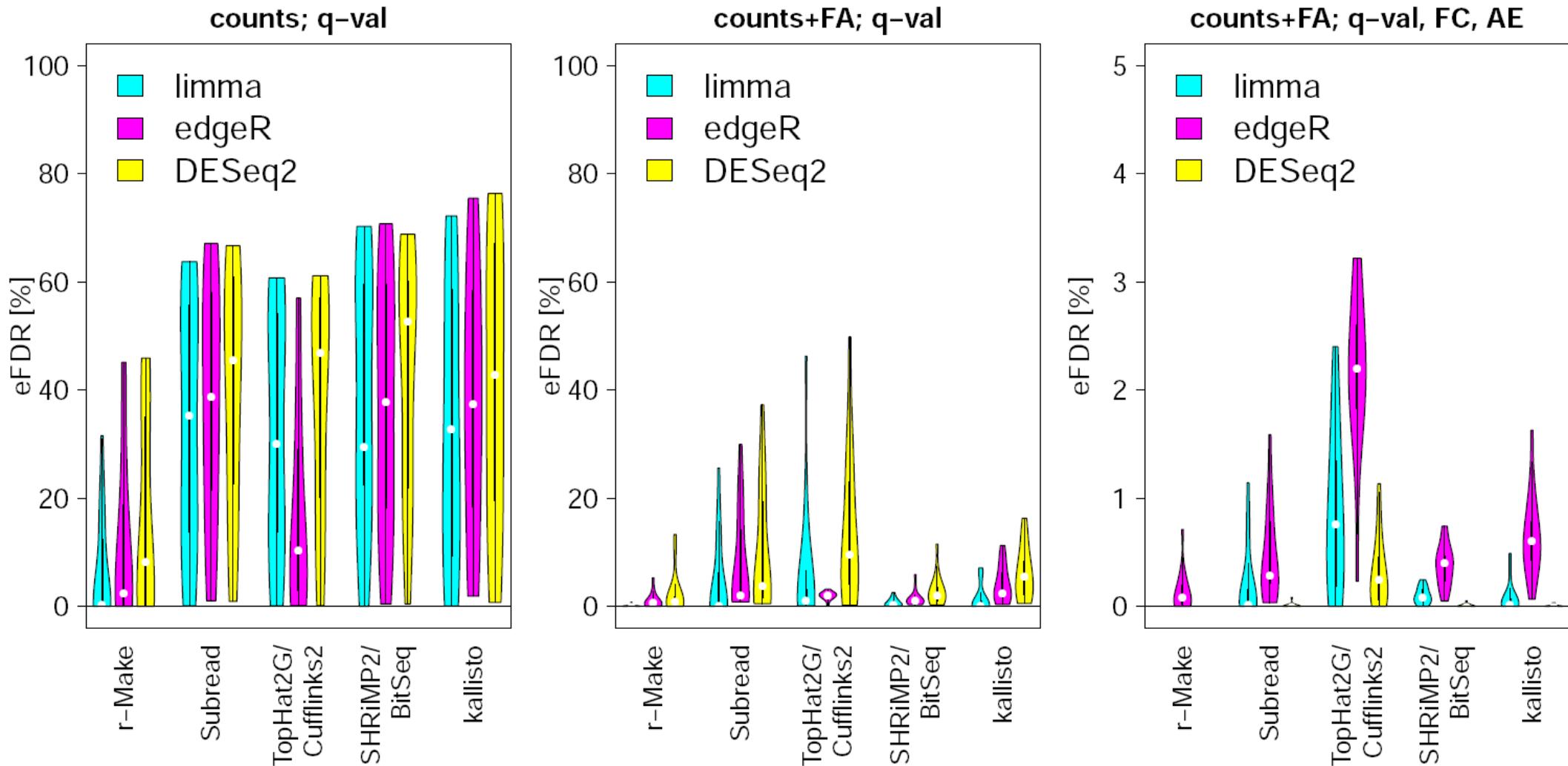
MAQC – III / SEQC

Table 1 Major sources of variation for quality metrics determined using fifth replicates

Quality metrics	Description	Major source of variation
GC content	Percentage of bases for each GC bin (1–100) for all aligned reads	Library preparation (including RNA isolation)
Gene body coverage evenness	Accumulative statistics for the read coverage of exonic regions from 5' UTR to 3' UTR for all genes Each gene is divided into 100 bins to calculate the gene body coverage	Library preparation (including RNA isolation)
Base error rate	The average base error rate for all aligned reads	Sequencing (inclusive of cluster generation)
Nucleotide composition	Nucleotide frequency versus position for aligned reads	Library preparation (including RNA isolation)

Removal of Confounding Factors

Reducing false positives across sites



Are we ready for personalized medicine?





17TH ANNUAL INTERNATIONAL CONFERENCE ON
CRITICAL ASSESSMENT OF MASSIVE DATA ANALYSIS
CHICAGO, U.S.A. | JULY 07-08, 2018

@ ISMB
2018

The MetaSUB Forensics Challenge

Hundreds of novel city microbiome profiles

Construct urban microbiome fingerprints and identify the geographical origin of mystery samples.

The CMap Drug Safety Challenge

Clinical toxicity results and gene expression responses to hundreds of drugs.

Compare or integrate responses of multiple cell lines, predict DILI.

Opt into an FDA meta-analysis.

The Cancer Data Integration Challenge

Clinical data, RNA-seq and microarray gene expression, CNV from aCGH

Demonstrate a robust analysis approach improving the state of the art for both Breast Cancer and Neuroblastoma.

... plus leading keynotes!



MAQC/SEQC Consortium

Leming Shi and Weida Tong, NCTR, FDA



Chris Mason, Cornell University



Wei Shi, WEHI Australia



Wenzhong Xiao, Stanford & Massachusetts General Hospital



Danielle and Jean Thierry-Mieg, NCBI,
NIH



David P Kreil, BOKU University Vienna



David P Kreil



Nancy Stralis-Pavesi



Peter Sykacek



Smriti Shridhar



Maciej Kańduła

MetaSUB in Vienna:

FH-Prof Dr Alexandra Graf
FH Campus Vienna



Dr Paweł Łabaj
OeAW APART Fellow
Boku University Vienna



Thinking beyond ...

The Mason laboratory is working on **a ten-phase, 500-year plan** for the survival of the human species on Earth, in space, and on other planets.

Phase 5 (2051 - 2060) - Test protected human genomes in space environments

Phase 6 (2060 - 2100) - Begin settlement of other planets and genesis of synthetic genomes

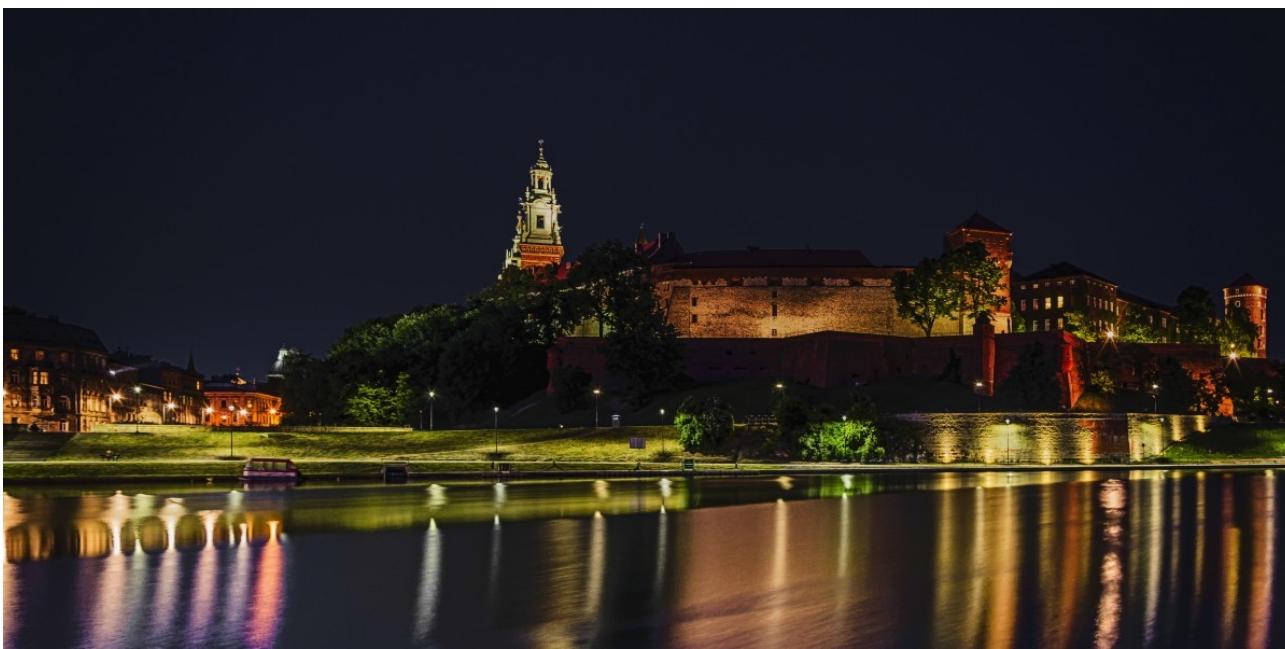
Phase 7 (2101 - 2150) - Expand new genomes to tolerate extremely cold/hot and acidic/basic environments

Phase 8 (2151 - 2300) - Send new genomes (panspermia) to begin seeding of Earth-like planets

Phase 9 (2301 - 2400) - Begin shipment of humans to these new worlds

Phase 10 (2401 - 2500) - Human settlement of new solar system, used as a model for future systems

Phase N (End of universe) - The hardest question - Determine if we should prevent the implosions/entropy death of the universe, or allow self-destruction in the expectation that life will arise again.



Visit us at

www.metasub.org
www.mcb.uj.edu.pl
www.bioinf.boku.ac.at

