# Fundamentals of Biosensors and Electronic Biochips

---

## Bioassay Development and Validation

## - A Medical Device Innovation and Product Development Perspective -

**Fabien Rebeaud, Ph. D.**

November 2024

# About myself…

Former Chief Scientific Officer, Abionic SA (Lausanne)

Now, Biomedical Sciences Director, Liom Health AG (Zurich area)

Non-Executive Director and Advisor, Rea Diagnostic SA (EPFL)

Current Member of two CLSI Working Groups (Allergy assays; Sepsis diagnostics)

fr@liom.com

fabien.rebeaud@gmail.com

**My goals for this lecture are to:**

- Give you a flavour of good practices in in vitro diagnostic (IVD) medical device development
- Provide you with an overview of the state-of-the-art bioassay development and validation practices
- Give examples of how new technologies can change medical diagnosis
- Highlight the challenges and opportunities in the IVD medical device industry

**At the end, I would like you to understand that**:

- The market and your customers know (usually) better than you what is needed – listen to them!
- Planning is key when developing a product ("Do it right first time" mindset)
- Verification and validation aim to ensure the product meets its requirements
- A great Bioassay Developer has deep technical skills, and the capacity to look beyond its activities by understanding market access, regulation, manufacturing…

**Part I (approx. 20 min)**

From an idea to a product – feedback from my 15 years in innovation

**Part II (approx. 40 min)**

Fundamentals in bioassay development and validation

**Part III (approx. 20 min)**

Two practical examples of new technologies solving medical needs

**Q/A, discussion**

# Innovation in medical device

## – From an idea to a concept –

# “Novelty for novelty’s sake is rarely a good idea”

A great technology is no assurance of a successful product – still, it’s a good start

- Listen to the customers, know the market’s needs, grasp the market trend
- Translate these learnings into product requirements
- Design and plan carefully

| Customer says: | Scientist / Engineers must understand: |
|---|---|
| “More accurate than current method” | Sensitivity > 85% and sensitivity > 90% |
| “Affordable” | Selling price US$ < 2’000 |
| “Faster than current methods” | Total turnaround time < 5 minutes |
| “Use a small sample size” | Require <50 ul of blood |

# A product cannot be successful if it doesn't respond to a need

Example of a wrong understanding of customer needs:

**Problem**: *sepsis-causing pathogens are identified too late to start the right treatment (antimicrobials) on time safely*
**Solution**? *Iridica. Combined PCR/ESI-MS for faster pathogen identification*

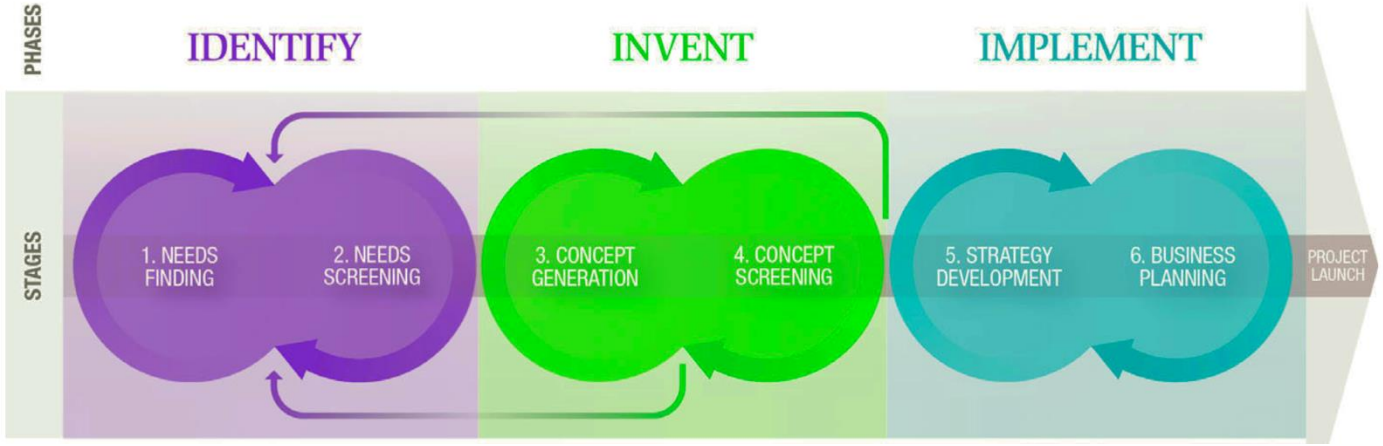
→ Technology acquired for US$ 250m by Abbott Laboratories, commercialised in 2014. Removed from the market in 2017:

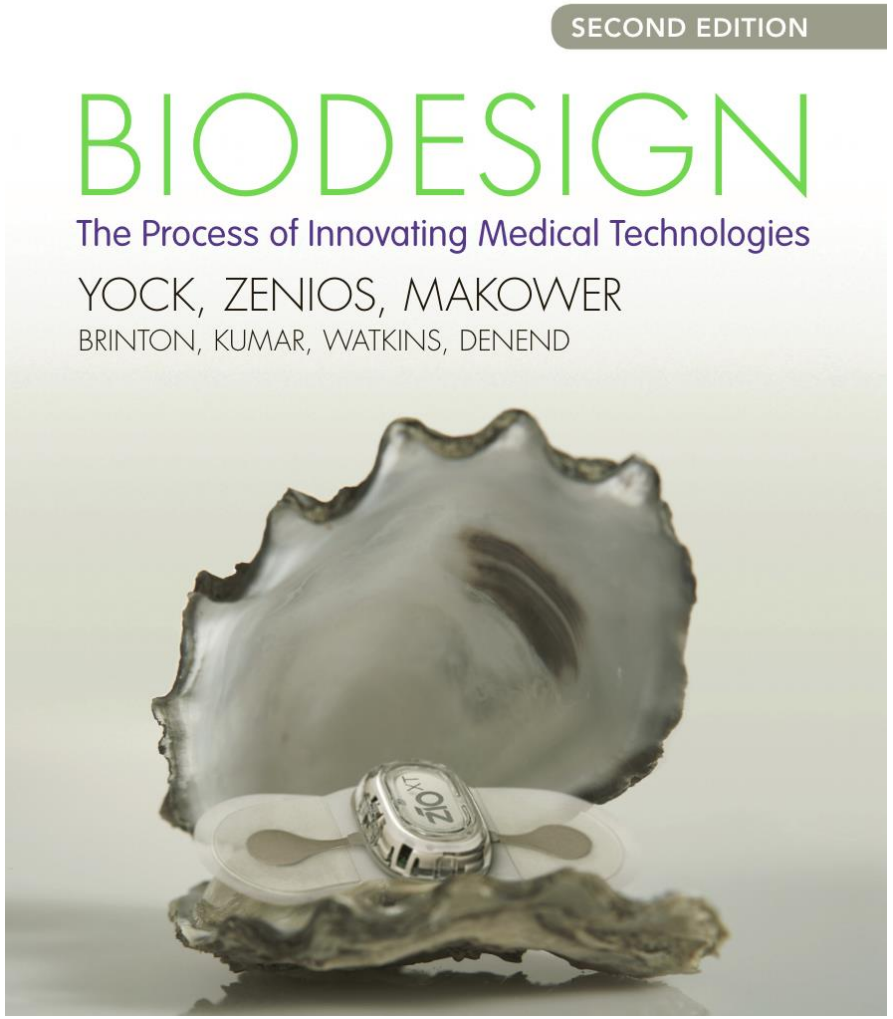
- Too expensive (device, reagents)
- Too low throughput

→ **not meeting customer (hospital) needs**

# The Biodesign framework aims at helping product developers identifying high value needs

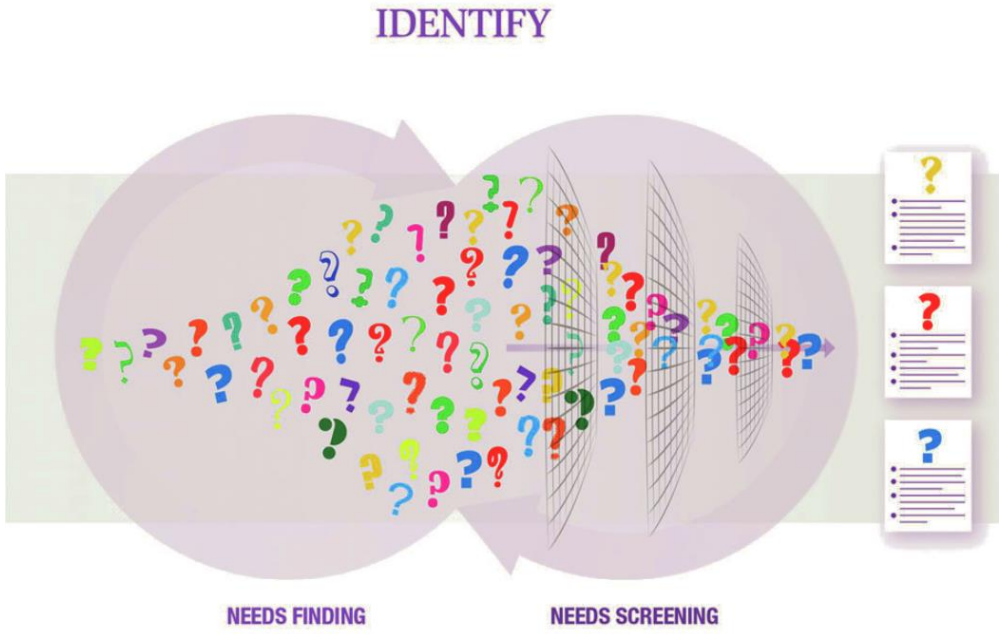
The Biodesign book is a step-by-step guide to medical technology innovation

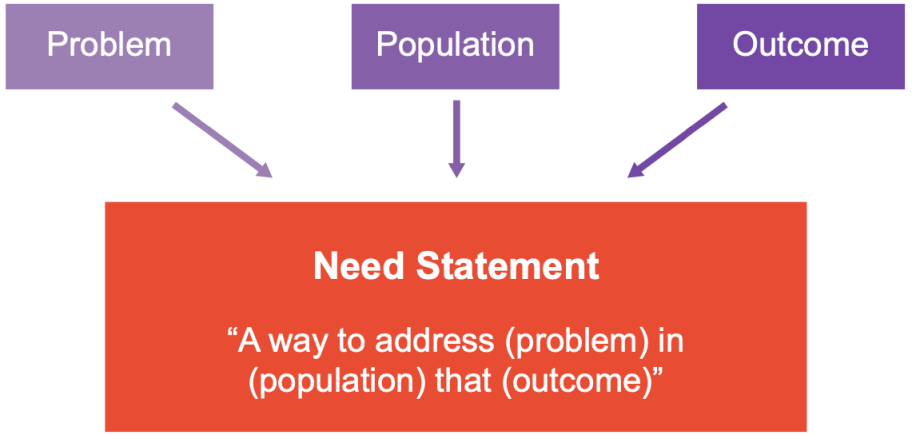


# Start by identifying and formulating “needs”

”Identify” consists of gathering unmet medical needs through observation and then reducing this list to a promising few based on information about the key clinical, stakeholder, and market characteristics



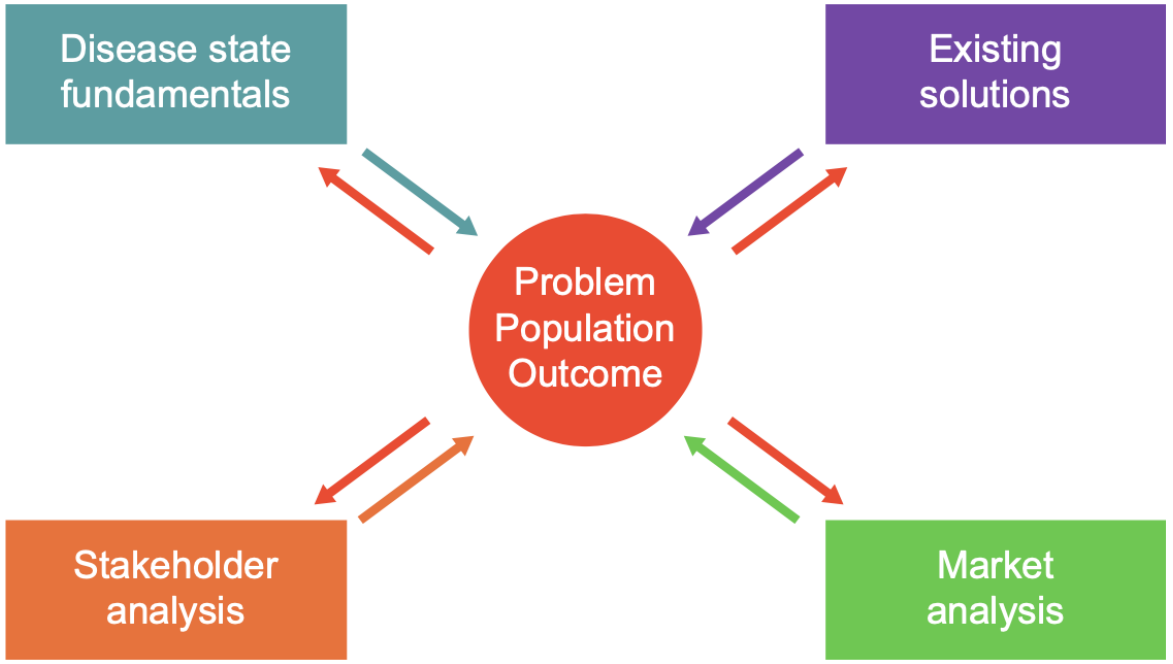

“A way to improve glycemia control in adults leaving with insulin-treated type 2 diabetes mellitus to prevent disease progression associated with lower quality of life and high healthcare expenditure”

# Start by identifying and formulating “needs”

Need screening consist of a quick survey of multiple areas – do not focus only on technology

A lot can be found in textbooks, but also speak with physicians, and patients

Identify their strengths and weakness, also: speaks with users




Who will embrace or resist your new medical technology?

Not only the size and growth, but also the segmentation, trends…

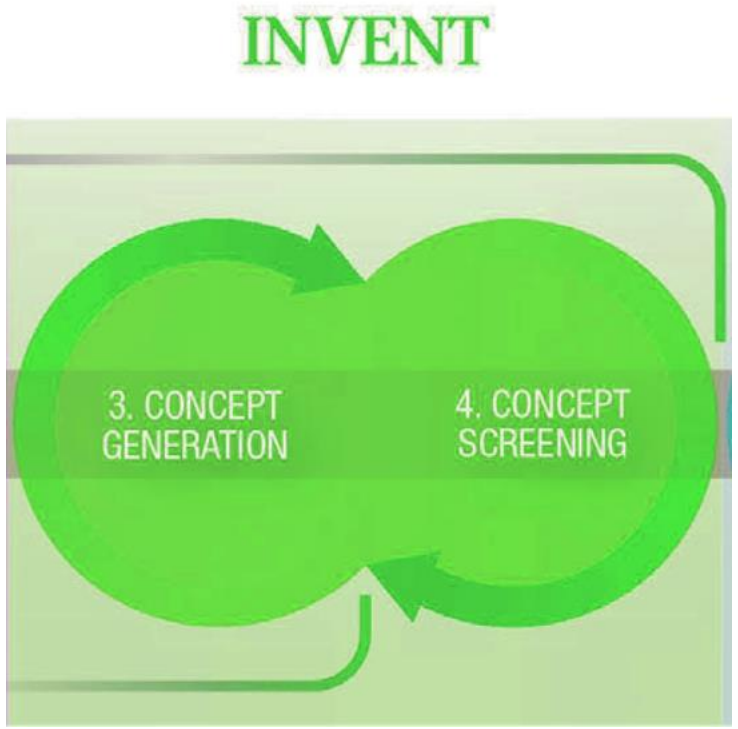
## Typically, apply a semi-quantitative ranking of needs

i.e., the diabetes need is ranked very high because:

- **Size of the problem**: Diabetes affects 800m people Worldwide, and the number is steadily increasing
- **Accessibility and affordability**: Current solutions are invasive, expensive, and have short lifetime (2 weeks)
- **Clinical benefit**: Improving glycemia is proven to prevent disease progression

Be ready to “kill” 90% of your ideas. Be laser-focus while still being agile and ready to change

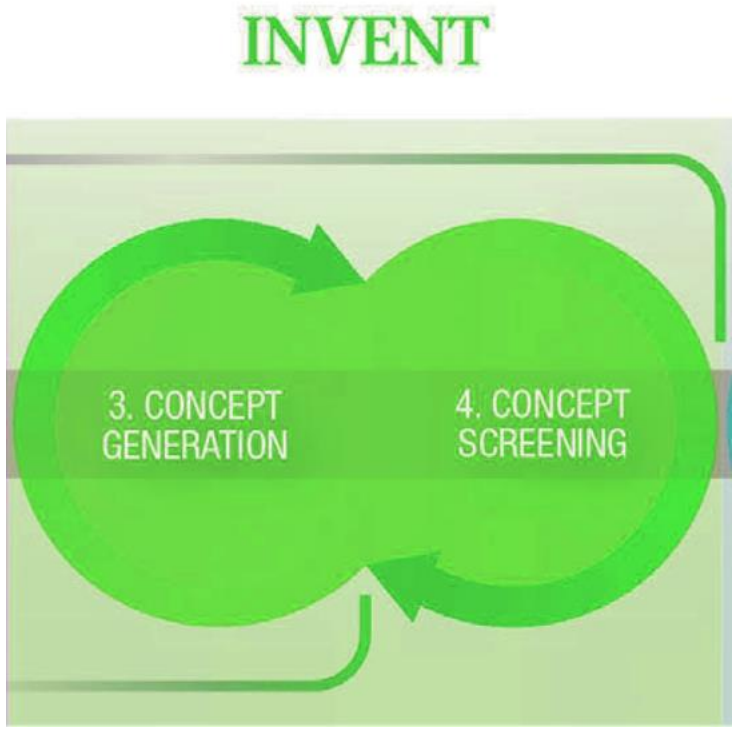
# Now, it’s time to invent




At this stage:

- **Concept generation** is about design ideation and initial concept selection
- Generate as many concepts as possible through brainstorming sessions
- Critically assess each design
    - Technology risk?
    - Development risk?
    - Time and cost?
    - Resources, expertise?

# Now, it's time to invent




Iterative, cross-functional work
The first round is a matter of hours/subject

At this stage:

- **Concept generation** is about design ideation and initial concept selection
- Generate as many concepts as possible through brainstorming sessions
- Critically assess each design
    - Technology risk?
    - Development risk?
    - Time and cost?
    - Resources, expertise?
- **Concept screening** is about performing a series of evaluation (basic at this stage) of:
    - Intellectual property landscape
    - Regulatory landscape
    - Reimbursement models
    - Business models
    - …

# Now, it’s time to invent

The goal of concept exploration is to translate a promising concept from an idea into a rudimentary design, and then into a working form factor to answer important technical questions (”technology de-risking”)

**Prototyping is key: Test fast. Fail fast. Learn. Iterate**

- Define requirements (“must have”, “nice-to-have”…)
  - Based on inputs from the market, the customer, the user
  - But also based on regulations, industry-standards… (“non-spoken requirements”)
- Define a “minimally viable product” that can be tested in simulated or real-world conditions
- Customer / user feedback is key
- Run iteration cycles

- Make sure you clearly scope the goal of your prototype: publication? Tech proof-of-concept? Test the market?

# Part I – wrap-up

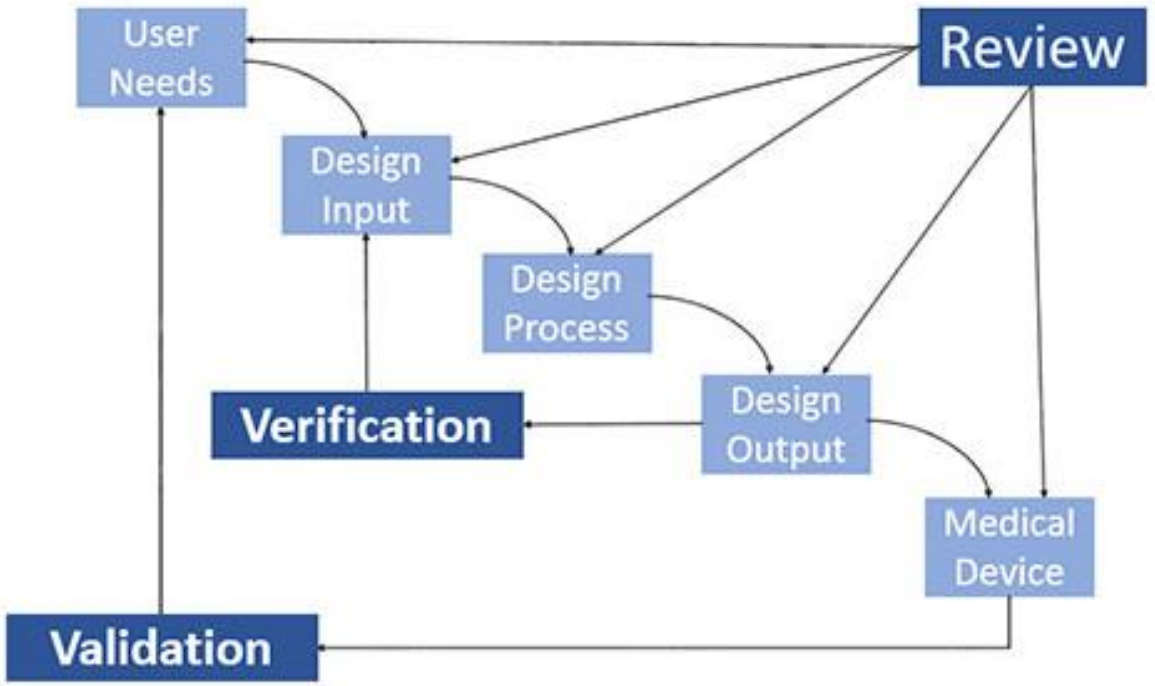
- Spend time looking for a match between market need/opportunities and new solutions addressing this need
  - Iterative process – favour efficiency and value creation over perfection
    - You will learn more along the way – walk the thin line between being laser-focused on your next objective while keeping the agility to make a 90 ° move
    - Accept that 90% of your ideas will not be pursued
- Seek a diversity of opinions
- Clearly define the scope of your next prototype

# Innovation in medical device product

## – Assay development –

# The ISO 13485 provides guidance on how to develop safe and effective medical devices

At the core of the standard: Design Control




**A stepwise process with checkpoints to ensure the final product meets the product you wanted to develop**

**Design input**

- Translation of customer/market needs into (measurable/quantifiable) technical requirements.

**Design Process**

- Develop the product according to plan. Design Outputs describe all the components, parts, and pieces that go into your product.

**Verification**

- Making sure that you have objective evidences that specified requirements (“inputs”) are met (“outputs”). (“you have developed the product right”)

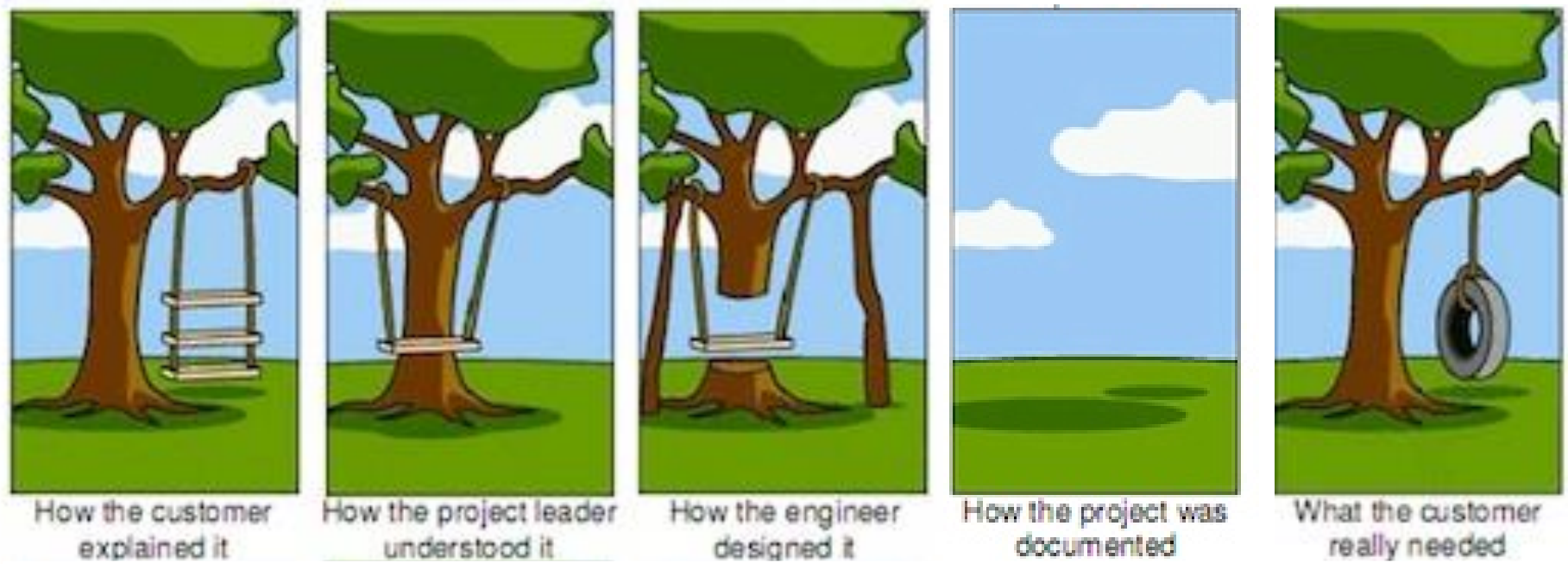
**Validation**

- Makes sure that the product conforms to End User requirements and application. → The product is validated in simulated conditions where its actual performance is tested (e.g., clinical testing of medical devices). (”you have developed the right product”)

Source: www.operonstrategist.com

# The ISO 13485 provides guidance on how to develop safe and effective medical devices

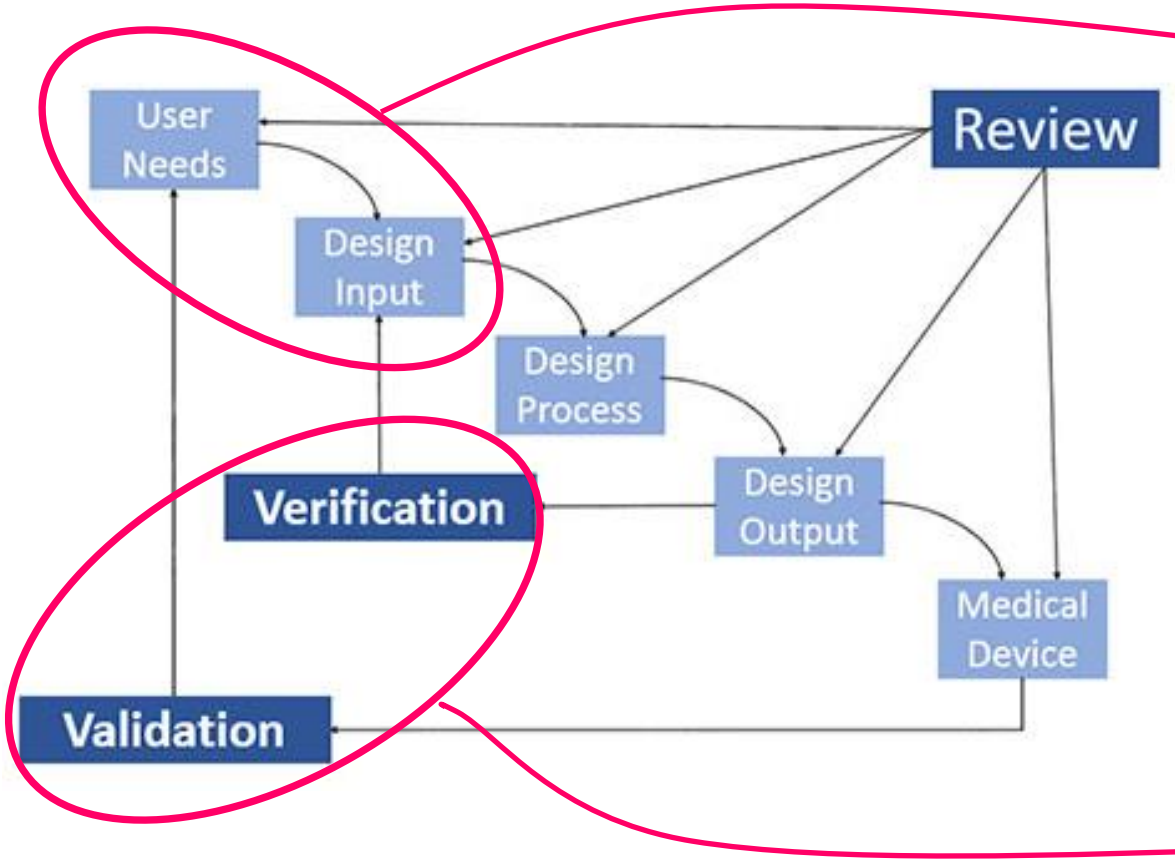
At the core of the standard: Design Control and requirements management




Source: www.operonstrategist.com

# The ISO 13485 provides guidance on how to develop safe and effective medical devices

At the core of the standard: Design Control




You start with understanding what shall be developed
You translate that into requirement specifications that are:

- → Objectives
- → Unambiguous
- → Testable
- → Measurable

You then test the requirements against your specifications and then against the user's needs

Verify that the product measure your biomarker (technical requirement, lab environment, prototype)

Validate that the user can use you product to make a diagnostic (usability, real-life environment, utility)

Source: www.operonstrategist.com

# An assay is characterized by several parameters

Back to biochips and assays: key performance parameters

- Limit of blank / detection / quantification
- Assay reportable range
- Precision (various variance components)
- Analytical accuracy
- Analytical selectivity
- Stability (reagents, final product)
- …

Part of a device's technical requirements

NOTES: 1 – Not only valid for IVD, but for any IUO or RUO assays!

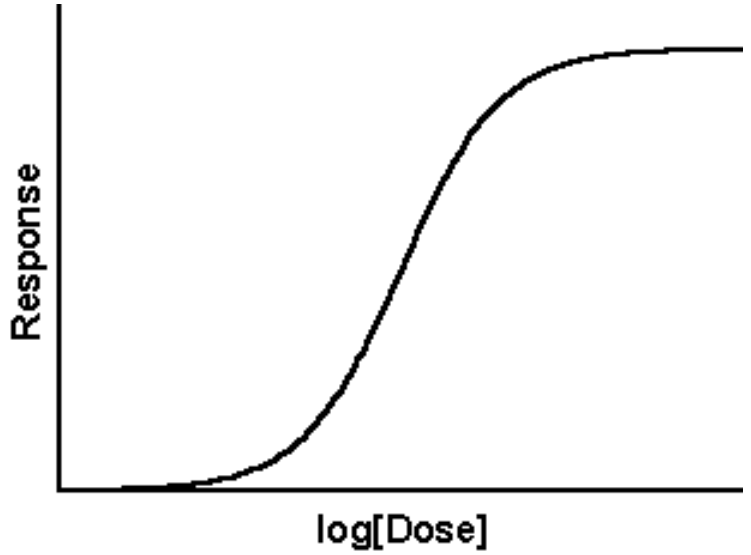
2 – For IVD, diagnostic performances are also key («clinical performance», «clinical benefit»)

3 – Great analytical performances of a diagnostic test are useless without great clinical value

# The calibration curve tells you a lot. Really a lot.

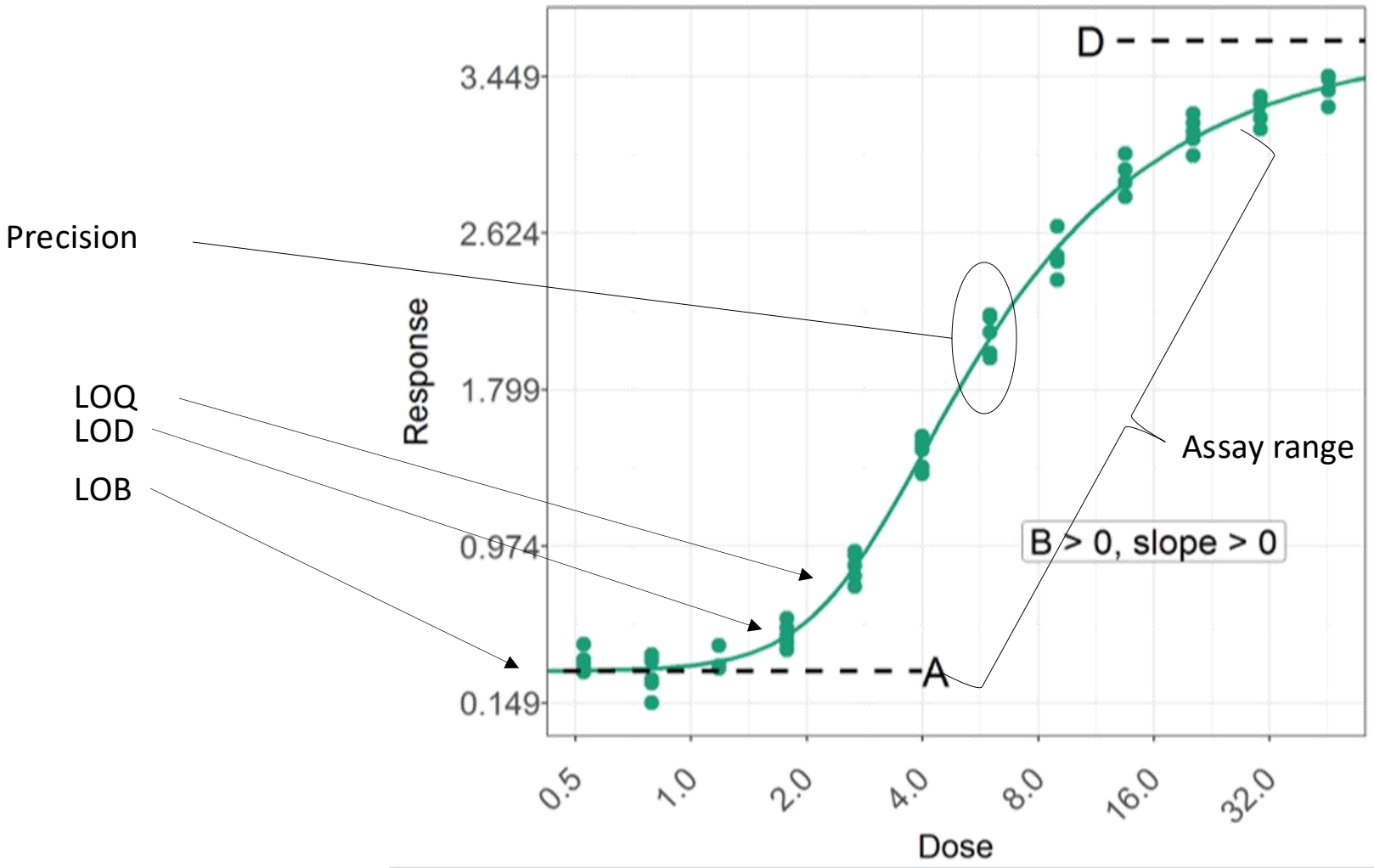
Calibration of ligand binding assay (LBA)

- In LBA, the response results from the complex interaction of the analyte with the binding reagent (i.e., an antibody).
- A nonlinear relationship between the mean response and the analyte concentration generally characterizes calibration curves of LBA with complex biomolecular interactions (i.e., protein-protein).
    - Here, the typical calibration curve is sigmoidal, with a lower boundary (asymptote) near the background response (nonspecific binding, system noise…) and an upper asymptote near the maximum response (biological and/or system plateau).



# The calibration curve tells you a lot. Really a lot.

You can estimate several key assay characteristics from a calibration curve




- Calibration curves of LBA are generally characterized by a nonlinear relationship between the mean response and the analyte concentration.

Source: www.quantics.co.uk

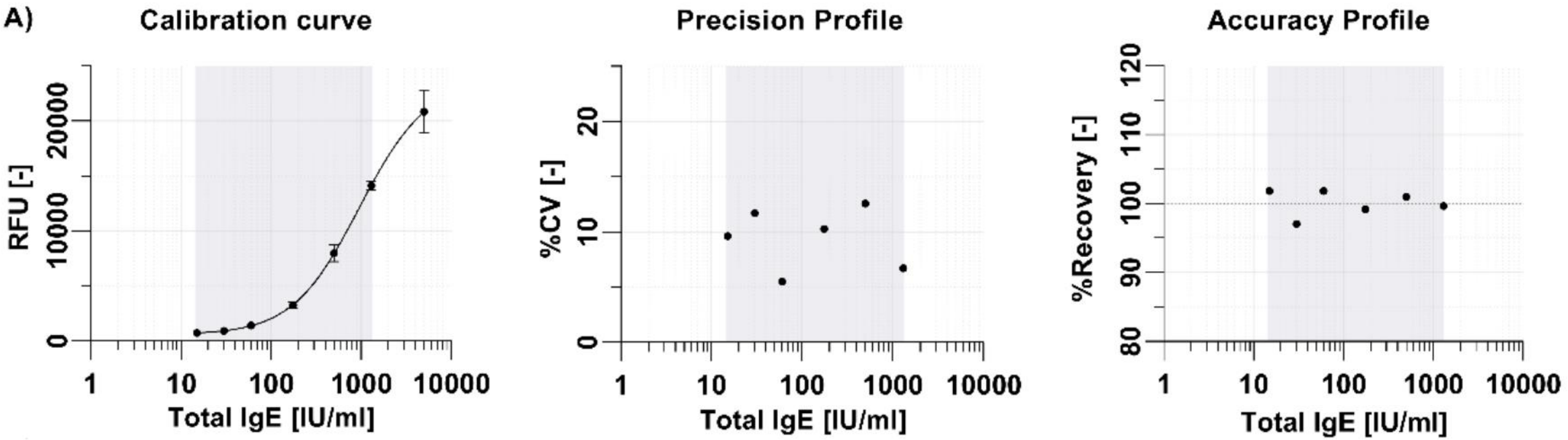
# Most development work is around dose-response curve

## Calibration of ligand binding assay (LBA)

- The goal of a calibration strategy is to obtain accuracy and precision within an established acceptable range.
- The key metric is the agreement of nominal calibrator concentrations with back-fitted concentrations read off the fitted calibration curve as if they were unknown samples.
    - **Recovery** [%] = 100 x ([back-calculated]/[nominal])
    - **Relative error** (%RE) = 100 x (([back-calculated] - [nominal]) / [normal])
- First, look at your data! Then select a fit-for-purpose model, taking into consideration your objectives and the (bio)chemical reaction taking place in your system.

# Most development work is around dose-response curve

Calibration of ligand binding assay (LBA)




- Fitting strategy is also about selecting right doses, number of replicates, applying weighting strategy, anchor dose, forcing the fit through a specific dose…
- Validate your fitting strategy's performance over a sufficiently large number of independent data set
- Keep the biochemical mechanisms and mathematical logic in the loop!

Source: Putallaz et al., 2019

# Without “good” calibration, no chance to have a “good” assay

## Calibration of ligand binding assay (LBA)

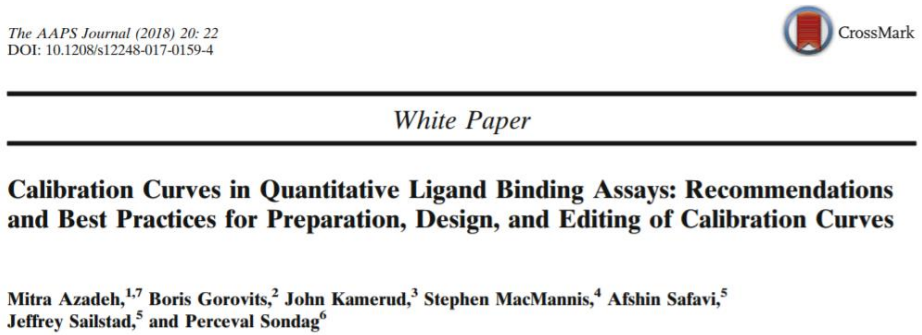
Practically speaking:

- First of all: start by looking at your data and think about your need, your system, your biomolecule before running into complex analyses!
- Quickly screen key assay parameters by running calibration curves (reagents selection, sample dilution, capture / detection reagent concentration…)
- Run high-density calibration curves (including doses above and below anticipated upper and lower detection limits), until an apparently acceptable assay range is obtained.
    - Typically, end-up with 5 to 8 doses (for 4- or 5-PL model)
    - Perform calibration with each dose in duplicate or triplicate (depending on your repeatability)
- Choose the best fit and calibrator doses, based on established precision and accuracy goals.
    - Typically, 4-PL or 5-PL models should be the most appropriate ones
    - Apply weighting and anchor points if (and where) necessary
    - Optimise accuracy (%RE) and precision (%CV) where it makes the most sense (i.e., around medical decision points)

# Recommended reading to go further:

Calibration of ligand binding assay (LBA)

Recommended “guides” to calibration (freely available on the web):



*The AAPS Journal (2018) 20: 22*
DOI: 10.1208/s12248-017-0159-4

CrossMark

*White Paper*

**Calibration Curves in Quantitative Ligand Binding Assays: Recommendations and Best Practices for Preparation, Design, and Editing of Calibration Curves**

**Mitra Azadeh,[1,7] Boris Gorovits,[2] John Kamerud,[3] Stephen MacMannis,[4] Afshin Safavi,[5] Jeffrey Sailstad,[5] and Perceval Sondag[6]**

***The AAPS Journal* 2007; 9 (2) Article 29 (http://www.aapsj.org).**

*Themed Issue: Bioanalytical Method Validation and Implementation: Best Practices for Chromatographic and Ligand Binding Assays*
*Guest Editors - Mario L. Rocci Jr., Vinod P. Shah, Mark J. Rose, and Jeffrey M. Sailstad*

**Appropriate Calibration Curve Fitting in Ligand Binding Assays**

*Submitted: February 21, 2007; Accepted: June 8, 2007; Published: June 29, 2007*

John W. A. Findlay[1,2] and Robert F. Dillard[3]

[1]Pharmacokinetics, Dynamics, and Metabolism, Pfizer Global Research and Development, Groton, CT
[2]Current address: Gilead Sciences Inc, 4 University Place, 4611 University Drive, Durham, NC 27707-3458
[3]BioStatistics and Data Management, Takeda Pharmaceuticals North America, Inc, Deerfield, IL

# Most components in biofluids are present in low to very low concentration (nM, pM)

## Limit of blank (LoB) and of detection (LoD)

- **LoB:** the highest measurement result that is likely to be observed (with a stated probability) for a blank sample
- **LoD**: Lowest amount of analyte in a sample that can be detected with (stated) probability (although perhaps not quantified as an exact value)

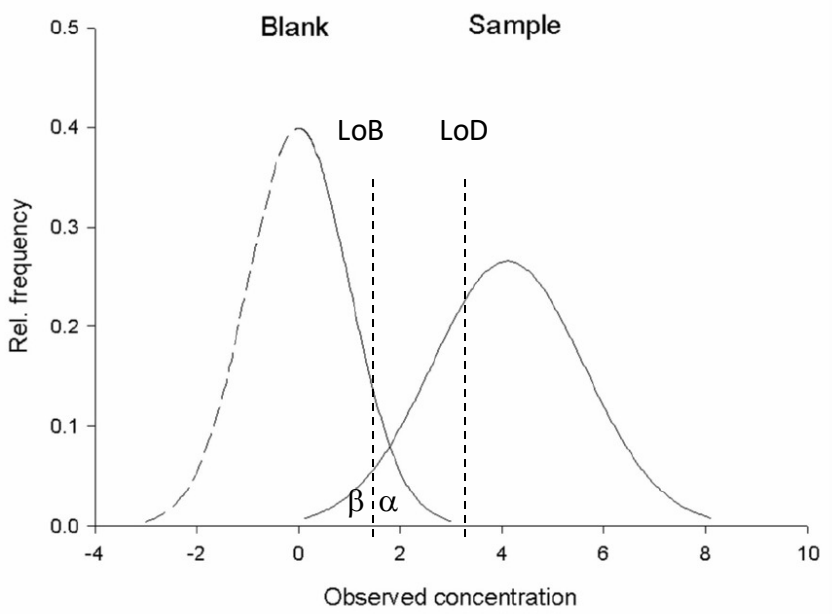



**Figure 1. Distributions of Observed Concentrations for the Blank and a Sample With a Low Amount of Analyte.** The dashed line corresponding to concentration less than zero indicates that some instruments do not report values less than zero.

Source: CLSI EP-17A

# Limit of blank

## Limit of blank and of detection

- Assuming a Gaussian distribution of blank values:
- $LoB = \mu_B + 1.645\ \sigma_B$ (where $\mu_B$ and $\sigma_B$ are the mean and standard deviation of blanks, respectively)

- Practically speaking:
  - To determine the LoB, perform 120 measurements of blank sample(s). Check data normality
    - Early-stage development, estimate with fewer replicates – be resourceful and efficient
  - To capture variability, use at least two days, two products lots and two Operators
  - Blank samples can be naturally occurring, diseased subjects or stripped samples
  - In the case of non-Gaussian distribution (quite common), then LoB is the 95$^{th}$-ranked value of the dataset

CLSI: EP17-A

# Limit of detection

## Limit of detection

- Assuming a Gaussian distribution of low positive values:

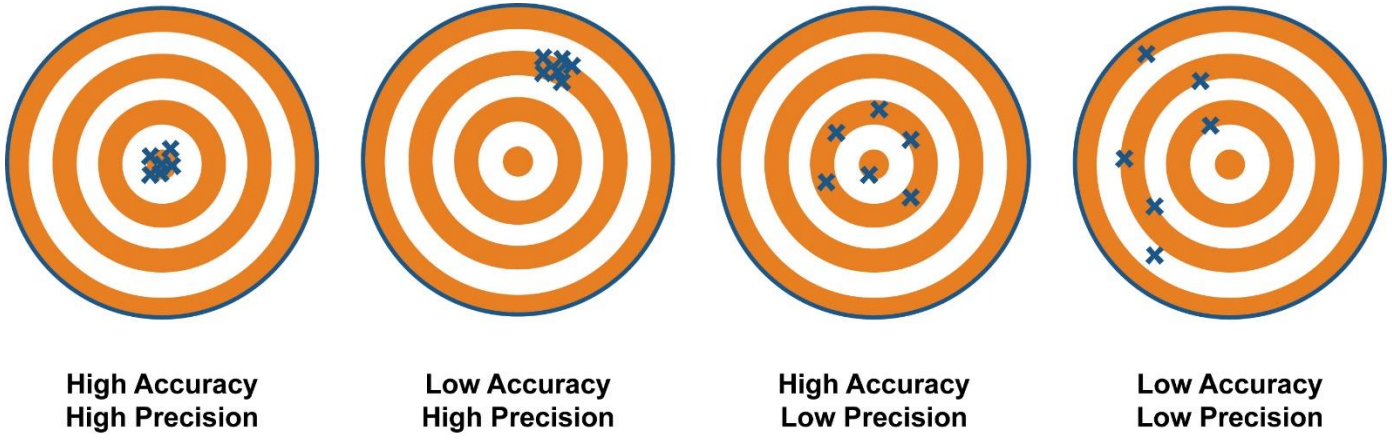
- $\text{LoD} = \overbrace{\mu_B + 1.645\,\sigma_B}^{\text{LoB}} + 1.645\,\sigma_s$ (where $\sigma_s$ is the standard deviation of low-positive samples)

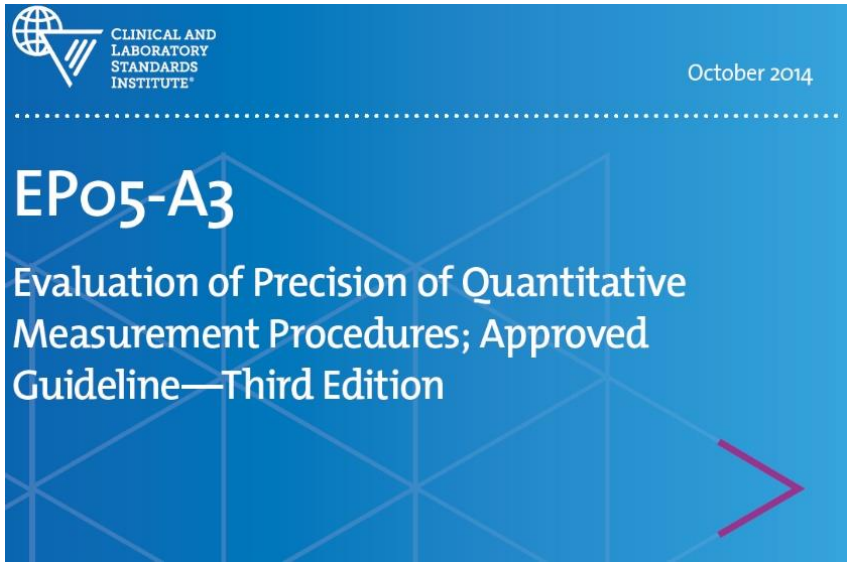
- Practically speaking:
  - Determine the LoD with 120 measurements of low-positive samples (pooled estimated of SD)
  - To capture variability, use at least two days, two product lots and two Operators
  - In case of non-Gaussian distribution (despite log-transformation), then refer to CLSI EP17-A2
  - In the early development stage, you may get an estimate of LoB with less than 120 data points – resourcefulness is key!

# Precision and accuracy are not the same!

Precision and accuracy

Imprecision: random distribution of a set of replicate measurements, expressed quantitatively (SD, %CV)



# Imprecision comes from many sources (“variance components”)

Precision and accuracy

**Source of imprecision:**

- Within-run (not applicable to singleplex assays)
- Between-run
- Lot-to-lot, device-to-device…
- Day-to-days, Operators-to-Operators, site-to-site…

The goal of between-run precision (immunoassay): the lower, the best

- FDA usually requires <15% (20% at LOQ)
- POCT usually targets 10-15%
- Clinical laboratories are often < 10%
- But, in the end, it is all about the clinical need

# The design of precision studies is often complex quite resource-demanding

## Precision and accuracy

### The experimental design

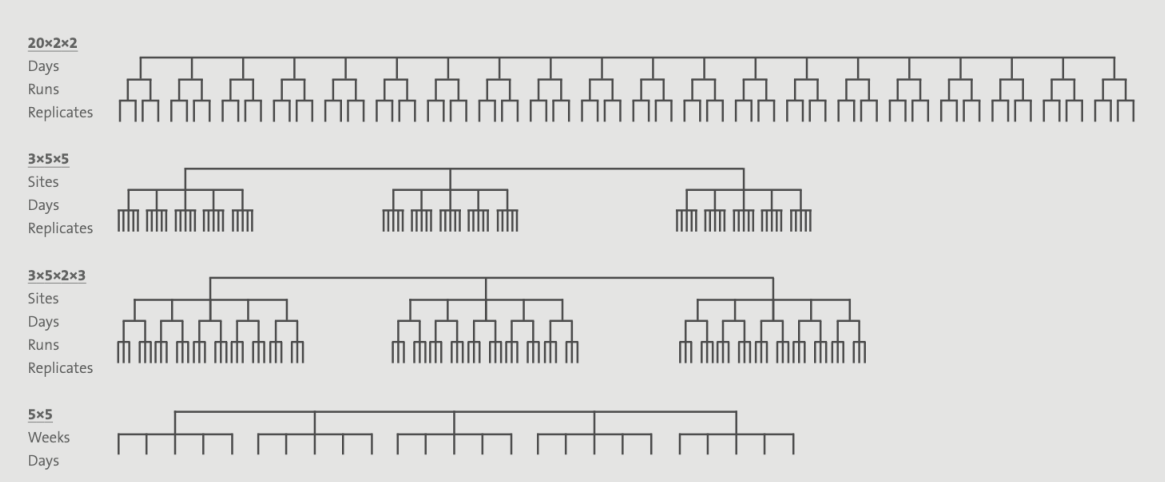



**Figure 3. "Comb" Diagrams.** These represent the standardized single-site 20 × 2 × 2 experimental design, the standardized multisite 3 × 5 × 5 and alternate 3 × 5 × 2 × 3 designs, and (see Figure 2) the QC-like 5 × 5 design used by way of illustration. All are nested (or hierarchical) structures; eg, in the 20×2×2, replicates are nested within runs, and runs within days. And all are balanced designs. The first and second designs each involve two factors—days and runs for the 20×2×2, sites and days for the 3×5×5—hence both designs are amenable to analysis by two-way nested ANOVA. The last two designs involve three factors and one factor, respectively, corresponding to three-way nested and one-way analyses.

### Outcome presentation

| PSP Dose [ng/ml] | N [-] | Mean [ng/ml] | SD [-] | CV [%] |
|---|---|---|---|---|
| **Low** | 10 | 49.5 | 2.3 | 7.2 |
| **Intermediate** | 10 | 110.8 | 10.8 | 8.0 |
| **High** | 10 | 176.8 | 25.4 | 11.5 |
| **Average imprecision** | | | | 8.9 |

**Table 1 l Between-run imprecision of the PSP assay on the abioSCOPE device.** The average between-run imprecision, calculated as the mean coefficient of variation issued from 10 replicates obtained on a same device with a same lot, was 7.2% for a low dose sample, 8.0% for an intermediate dose sample and 11.5% for a high dose sample. PSP: Pancreatic stone protein, N: Number of replicates, SD: Standard deviation, CV: Coefficient of variation.

Sources: CLSI EP05-A3 and Abionic PSP White paper (2019)

# In new technologies, precision is often a challenge…

… because it's new. Because now it's often low concentration. Because you do not have time to optimize

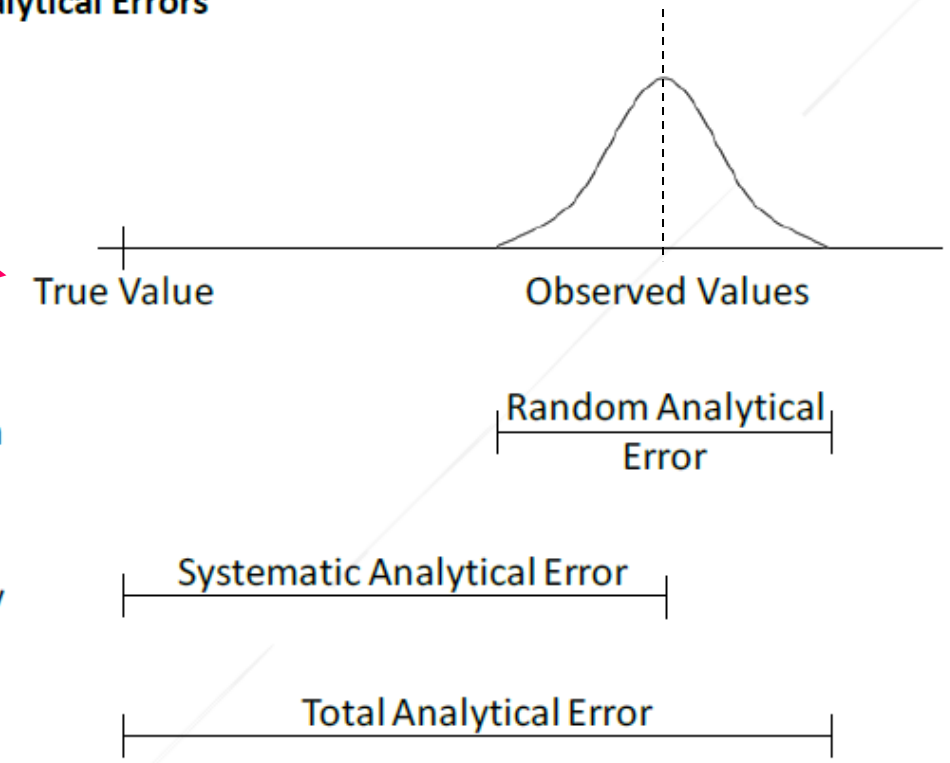
Practically speaking (*my advices*):

- During early development, focus on multiple replicates over a couple of days to quickly get a first estimate of precision
- Brainstorm and test hypotheses regarding the presumed sources of imprecision (also consider pre-analytical steps – particularly relevant for near-patient testing (think about the challenge of nasopharyngeal swab in SARS-CoV-2 testing)) and manufacturing
- If acceptable and need to go through extensive verification study: dig into CLSI EP05-A3 and/or seek help of specialists
- When speaking of assay parameters, precision values usually come in first or second place (with assay reportable range). It highlights how important it is to reach the goal for precision

# Combining precision and accuracy = total error

## Precision and accuracy: total analytical error

**Figure 1: Definitions of Precision and Accuracy in terms of Random, Systematic and Total Analytical Errors**




Note: for new biomarkers, the "true" value cannot always be easily determined!

# Bioassays can be influenced by the presence of non-target molecules

## Analytical Selectivity ("Interference testing")

- Interfering substances can be a significant source of error in clinical measurements. Such errors may, in some cases, represent a hazard to the patient

- Endogenous interference originates from substances present in the patient's own specimen.
  - Hemoglobin, bilirubin, biotin, rheumatoid factor, human anti-mouse antibodies…

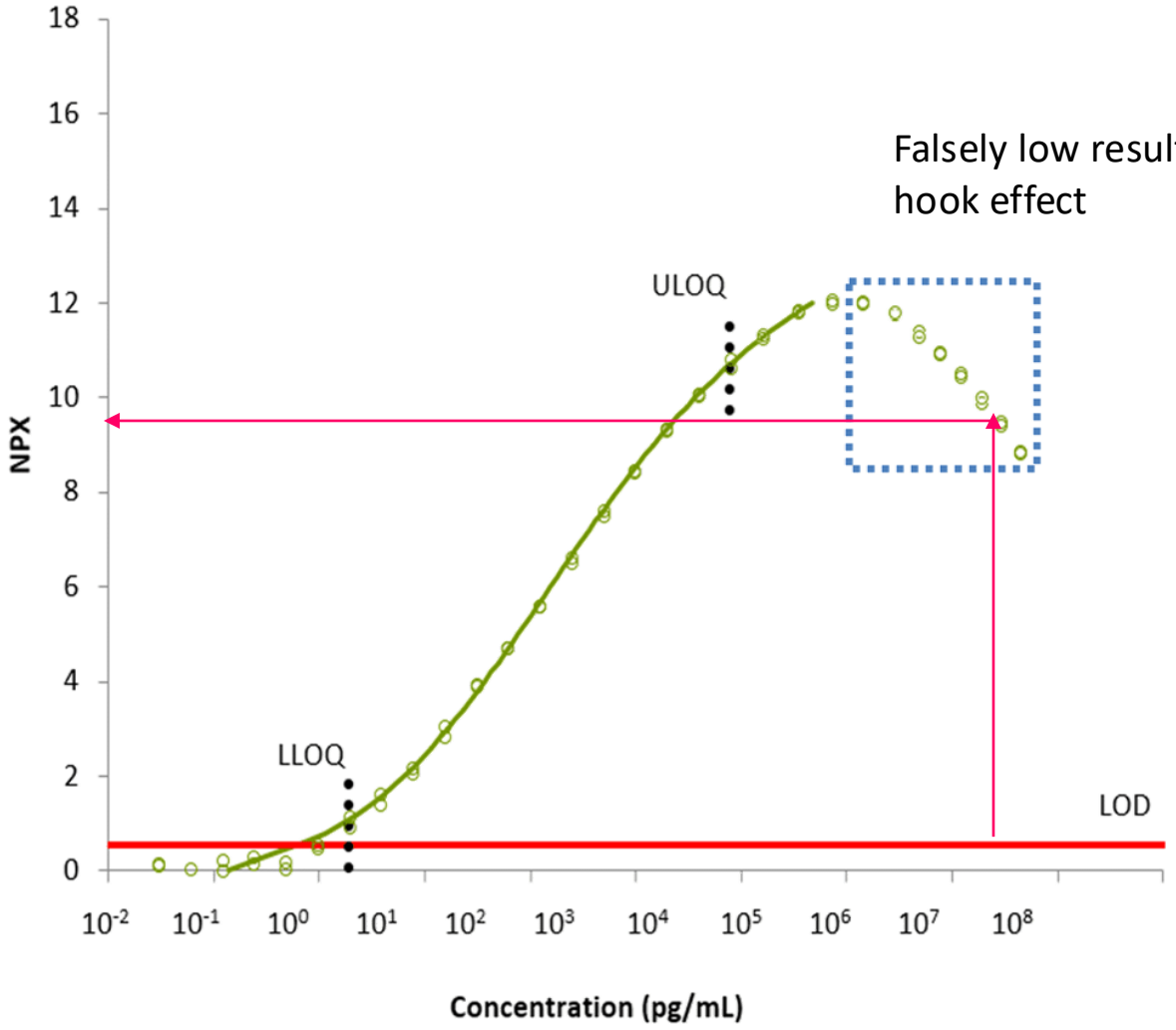
- Exogenous interferences are substances introduced into the patient's specimen
  - Drugs, nutritional products
  - Substances from collection tube
  - Test sample additives such as preservatives
  - Carryover contamination

# Also, extreme target analyte concentration can lead to undesired effects

## Interferences

- Hook Effect (analyte excess) caused by a depletion of the capture molecules

Reported concentration

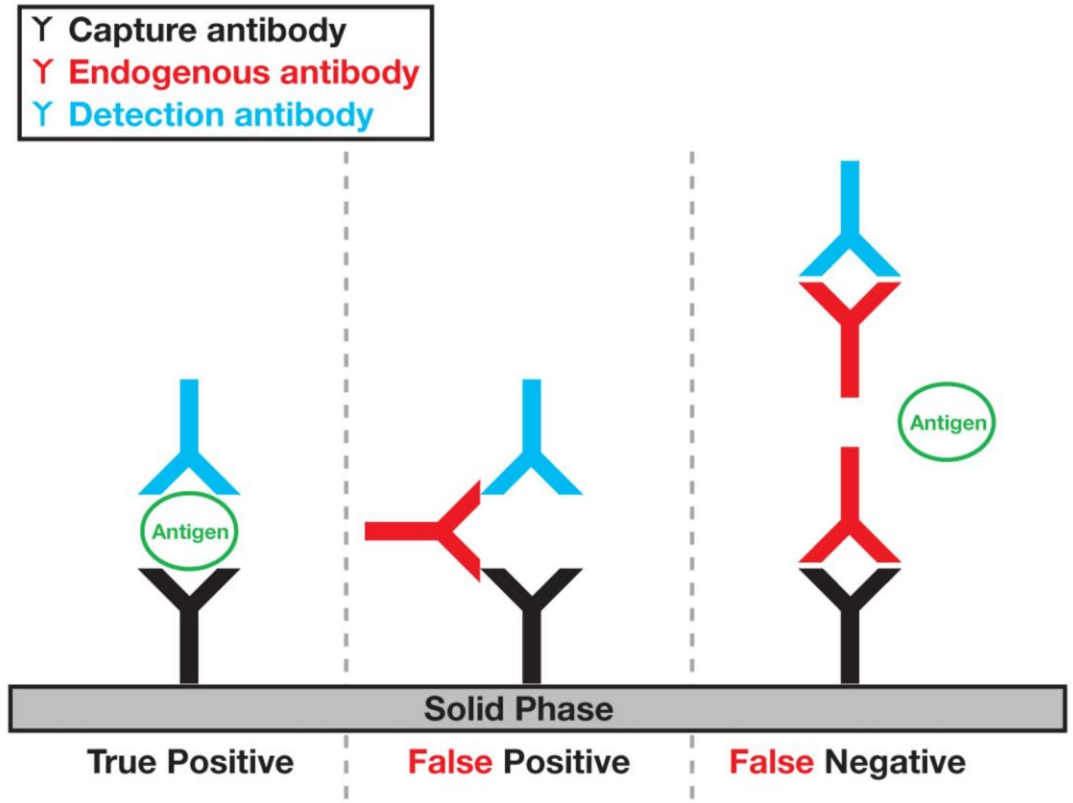


# Endogenous antibodies may also interfere with a test

Interferences

Endogenous antibody interferences:

- Heterophilic antibody (*antibodies to external antigen, cross-reacting with self-antigen.)*
- Anti-animal antibodies (*typically anti-mouse antibodies*)
- Autoantibodies



# An assay development perspective

## Interferences

- Defining the presence of an interference:
    - Generally, a change of X% (usually 10%) from original results confirms interference
    - Sample difference is assessed by paired t-test, and if $p<0.05$ it is considered statistically significant, and interference is occurring
    - An interference is not necessarily a killer.

Practically speaking:

- Define a list of substances and their concentration to be evaluated (talk to regulation agencies)
- Analyze multiple time samples with / without the potential interfering substance at several concentration, including clinically elevated
- Blot the bias (absolute and/or relative) versus the analyte concentration for test samples and control samples

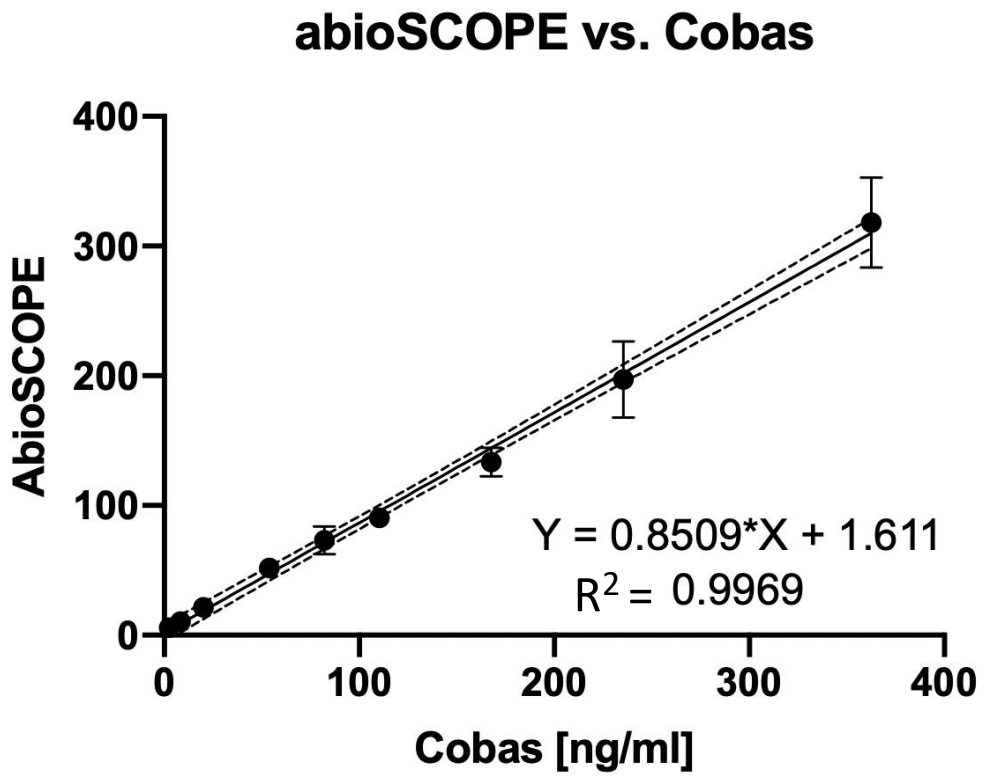
# An assay development perspective

Method Comparability (also sample type comparability)

There are several ways to evaluate the comparability of two measurements systems. Linear regression statistics and difference plots (Bland Altman analysis) have both advantages and limitations.

Standard PLS assumes that you know the X values perfectly, and all the uncertainty is in Y.
But: usally both X and Y variables are subject to error → fit linear regression using a method known as Deming.
(*Deming is the method of choice in many situations where no "true values" are available with one measurement system)*.

(Deming regression statistics can easily be done using basic assay development software, such as Excel Analyze-it or Graph Pad Prism)



# An assay development perspective

Method Comparability (also sample type comparability)

Describes a linear relationship between two sets of data, but not their agreement. High correlation does not necessarily mean high agreement!

Difference plots allow observing local bias better than scatter plots visually and quantifying agreement between two quantitative measurement procedures.

Take care of the ”mean bias”, which can mask unacceptable local bias.

Link the bias to your assay performances goals. Is a local bias acceptable? If yes, how much?

Want to read about difference plot ? >> Biochemia Medica 2015;25(2):141–51


Lessons in biostatistics

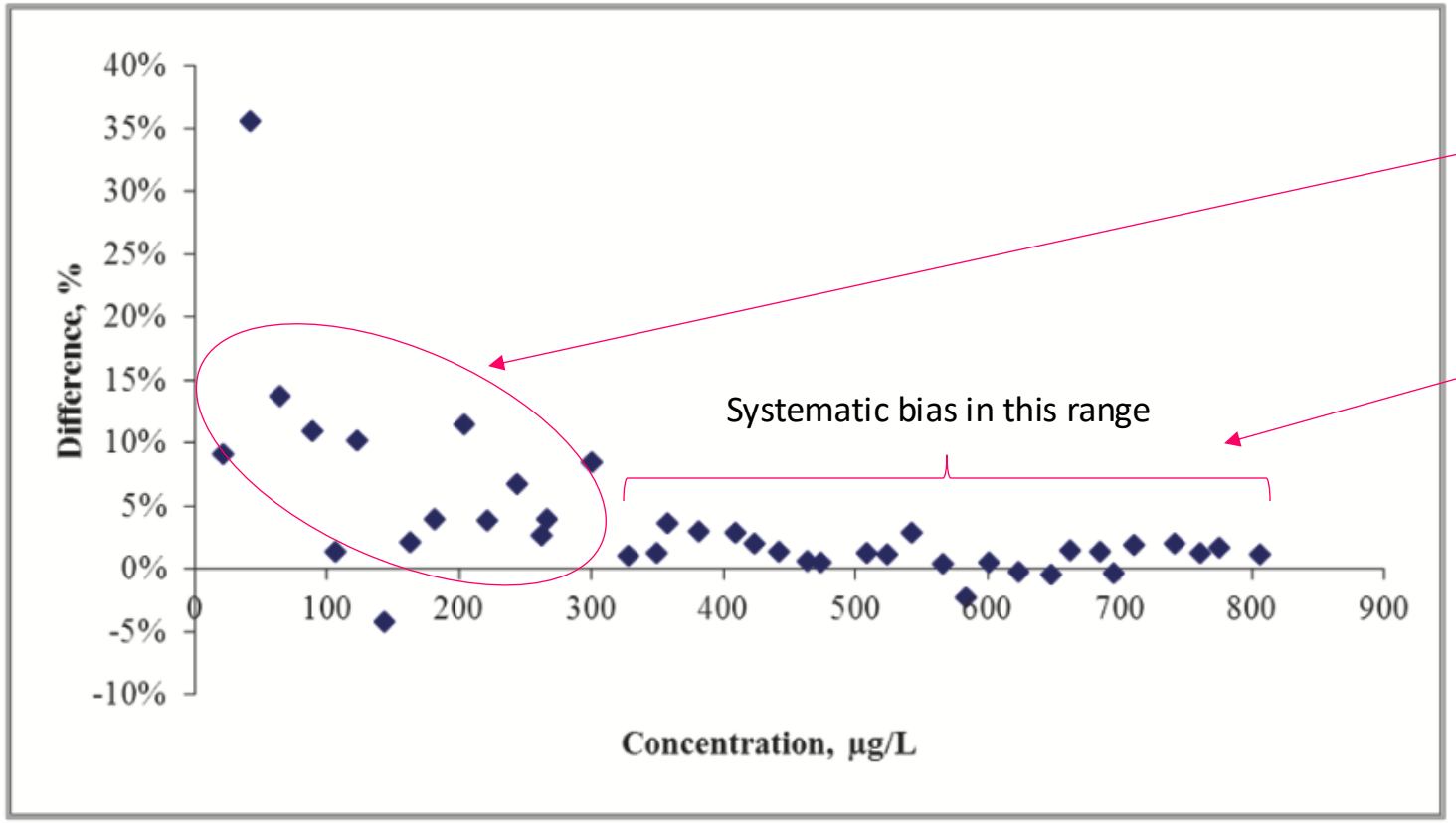
Understanding Bland Altman analysis

Davide Giavarina

Clinical Chemistry and Hematology Laboratory, San Bortolo Hospital, Vicenza, Italy

# Examples of bias plot

Method Comparability (also sample type comparability)




Bias becomes high as concentration decreases, with large differences between datapoint, suggesting an imprecision problem at low concentration

Working on the calibration may correct this bias

# Innovation in medical device product

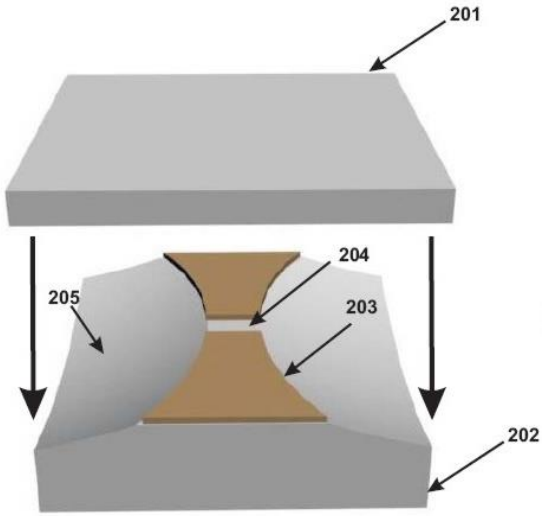
# Practical examples:

(i) **Nanofludic-based immunoassay (Abionic SA)**

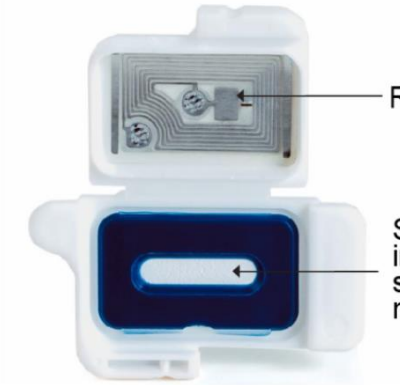
(ii) **Non-invasive glucose sensing (Liom Health AG)**

# Nanofluidic is the study of the behavior, manipulation, and control of fluids that are confined to structures of nanometer

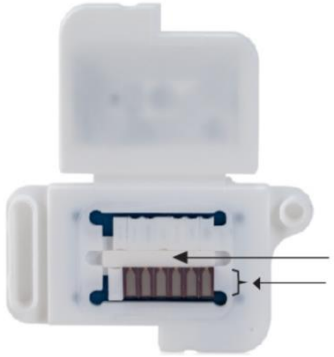
Nanofluidic-based point-of-care platform for immediate, actionable test results




Nanofludic biosensor




Top view



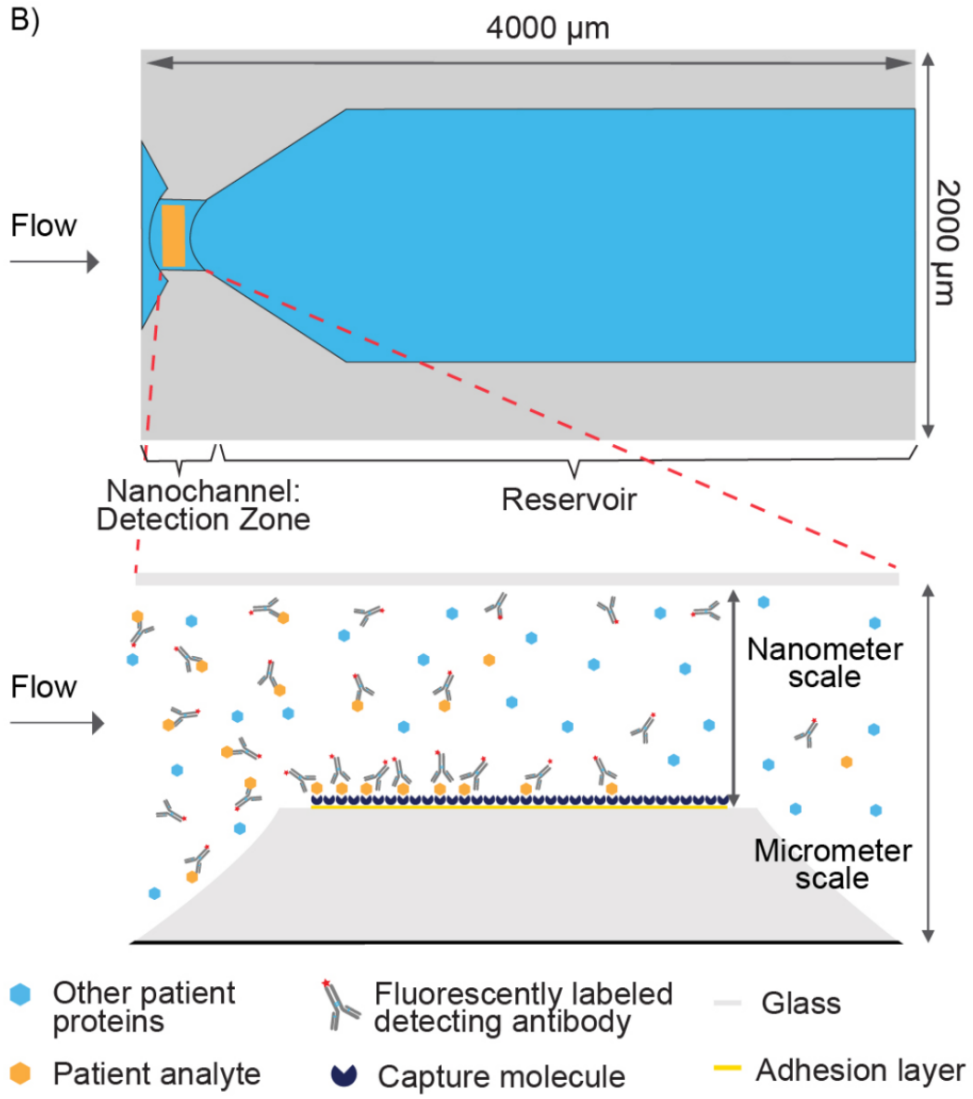

Bottom view

Source: Abionic SA

# Nanofluidic is the study of the behavior, manipulation, and control of fluids that are confined to structures of nanometer

Rapid binding kinetics due to increased surface area over volume ratio

As the capture chamber volume is several thousands of times smaller than a microtiter well: any non-specific background signal is negligible and therefore a washing step is not required.



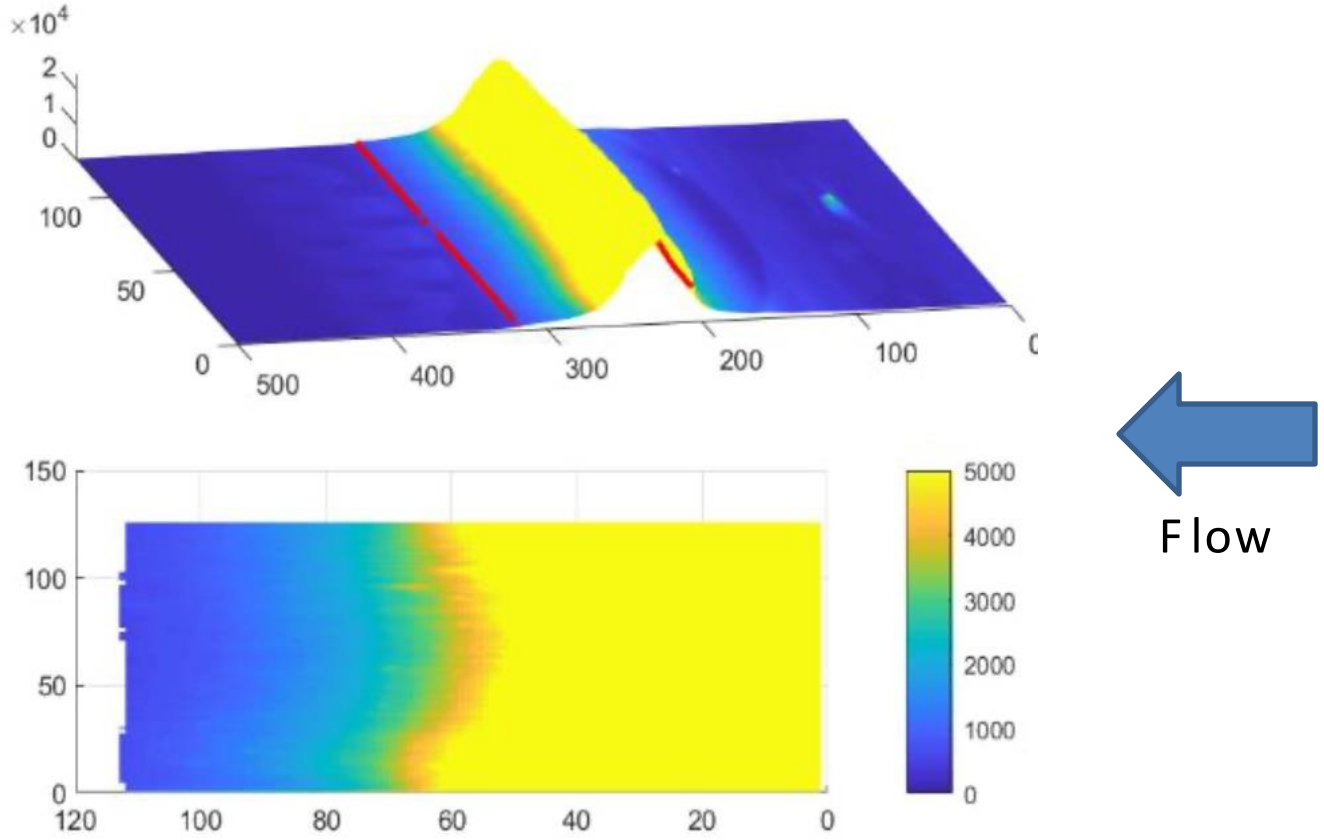

Source: Abionic SA

# Nanofluidic is the study of the behavior and manipulation of fluids that are confined to structures of nanometer

The technology proof of concept (Putallaz et al., 2019)

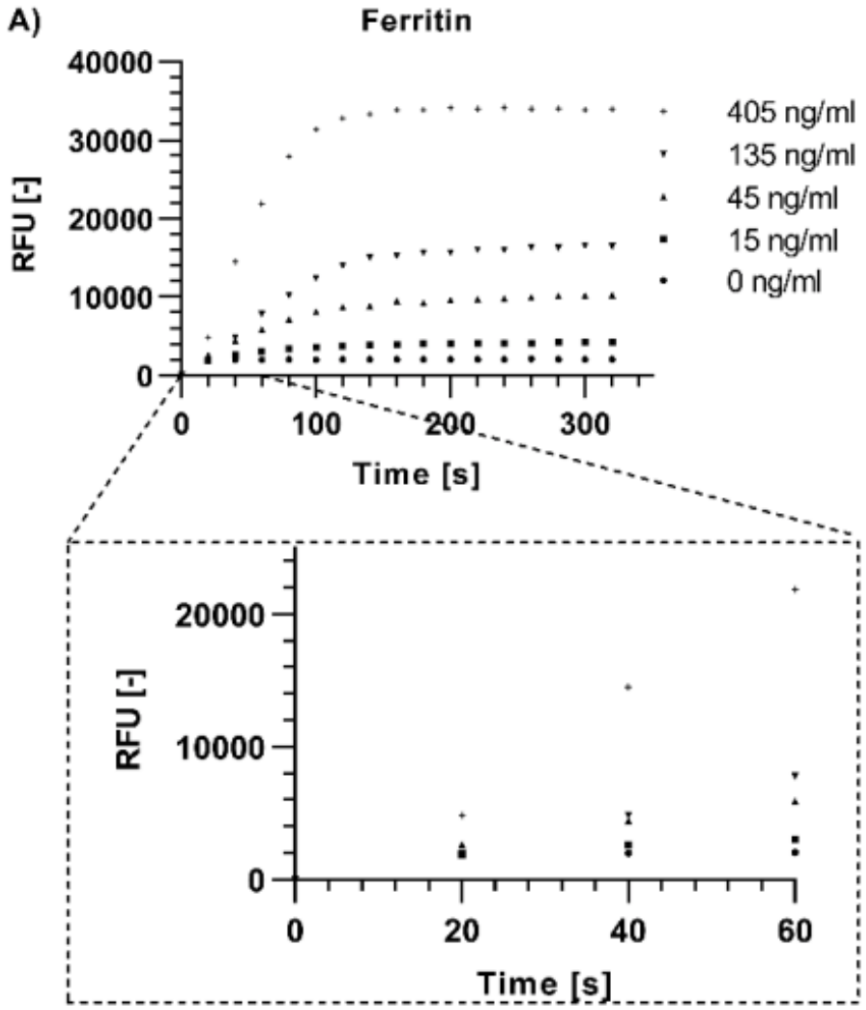
Rapid binding kinetics and near-100% capture efficiency thanks to increased surface area over volume ratio and selection of high avidity antibodies.

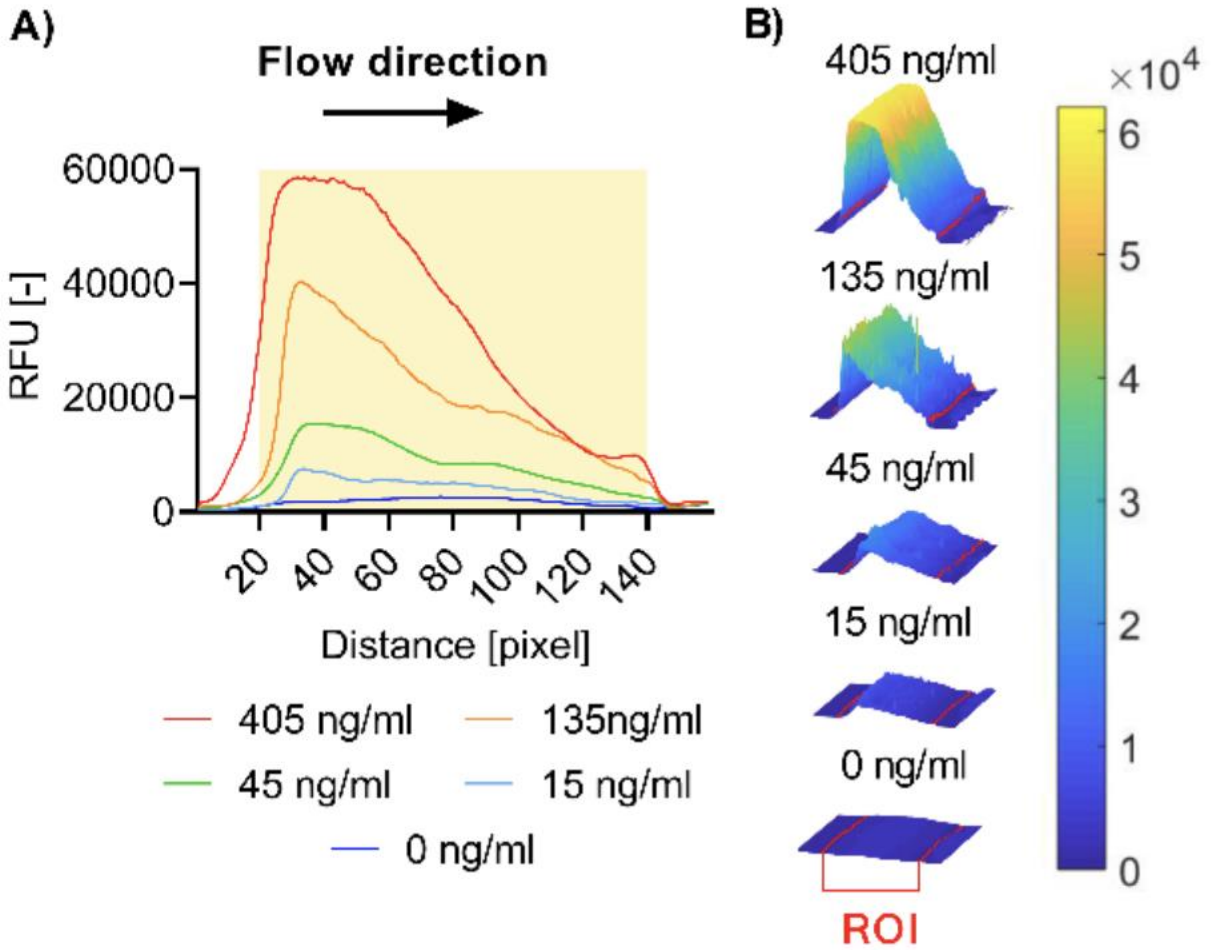
As the capture chamber volume is several thousands of times smaller than a microtiter well: any non-specific background signal is negligible and therefore a washing step is not required.




Source: Puttalaz et al., 2019

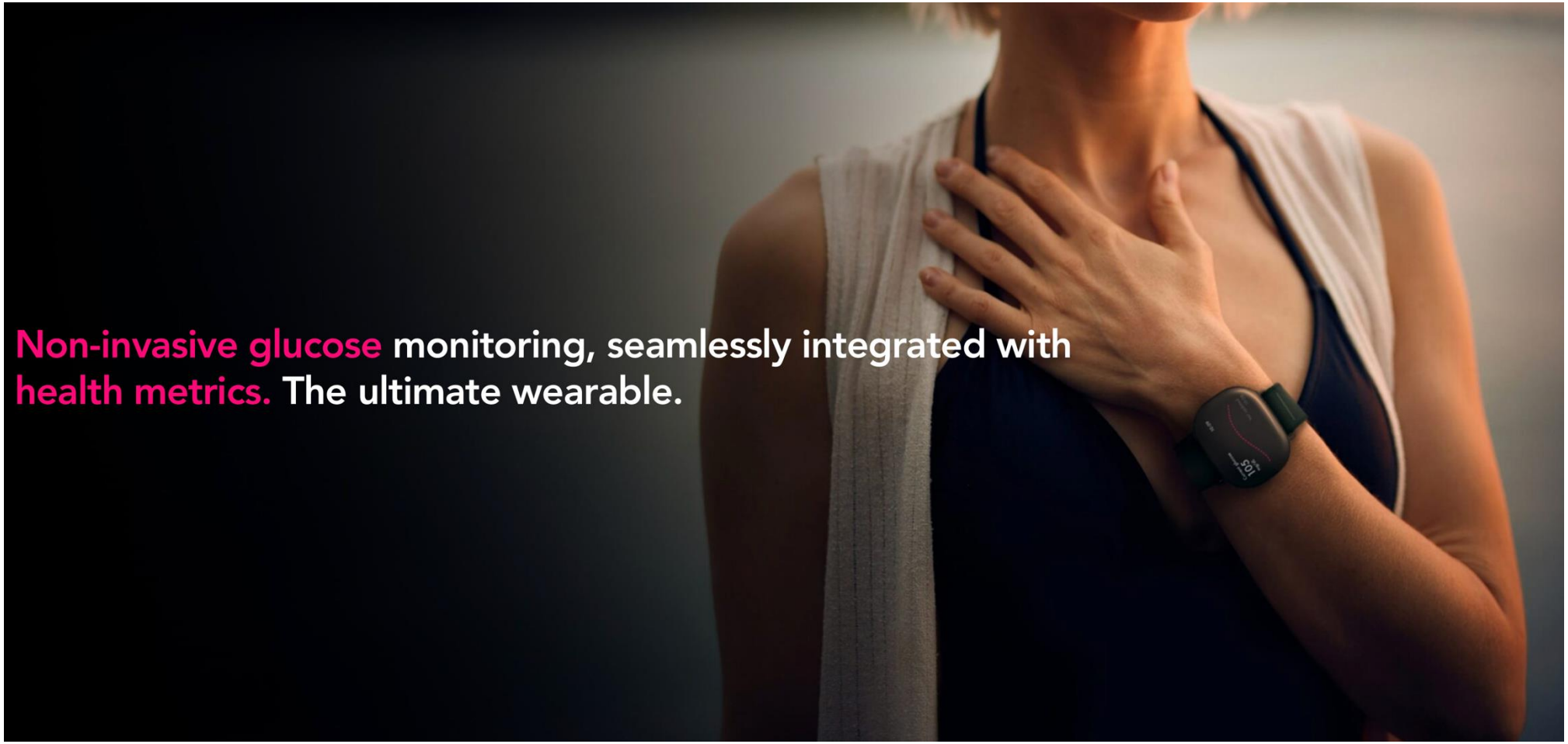
# Nanofluidic is the study of the behavior, manipulation, and control of fluids that are confined to structures of nanometer




Source: Putallaz et al., 2019

# The quest to non-invasive, continuous monitoring




LIOM

# The quest to non-invasive, continuous monitoring

## LIOM'S OPEN-ENDED GROWTH OPPORTUNITY

- Calibration-free and non-invasive means precision without having to pierce the skin unlocking universal appeal
- Proven form factor + rich biochemical information + convenience = open-ended growth opportunity

Constrained by limited biophysical information

### WEARABLES

**ESTABLISHED WEARABLES**
USD 30bn, 8% CAGR

fitbit GARMIN Google WATCH

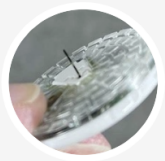
**EMERGING HEALTH WEARABLES**
USD 300m

WHOOP ŌURA

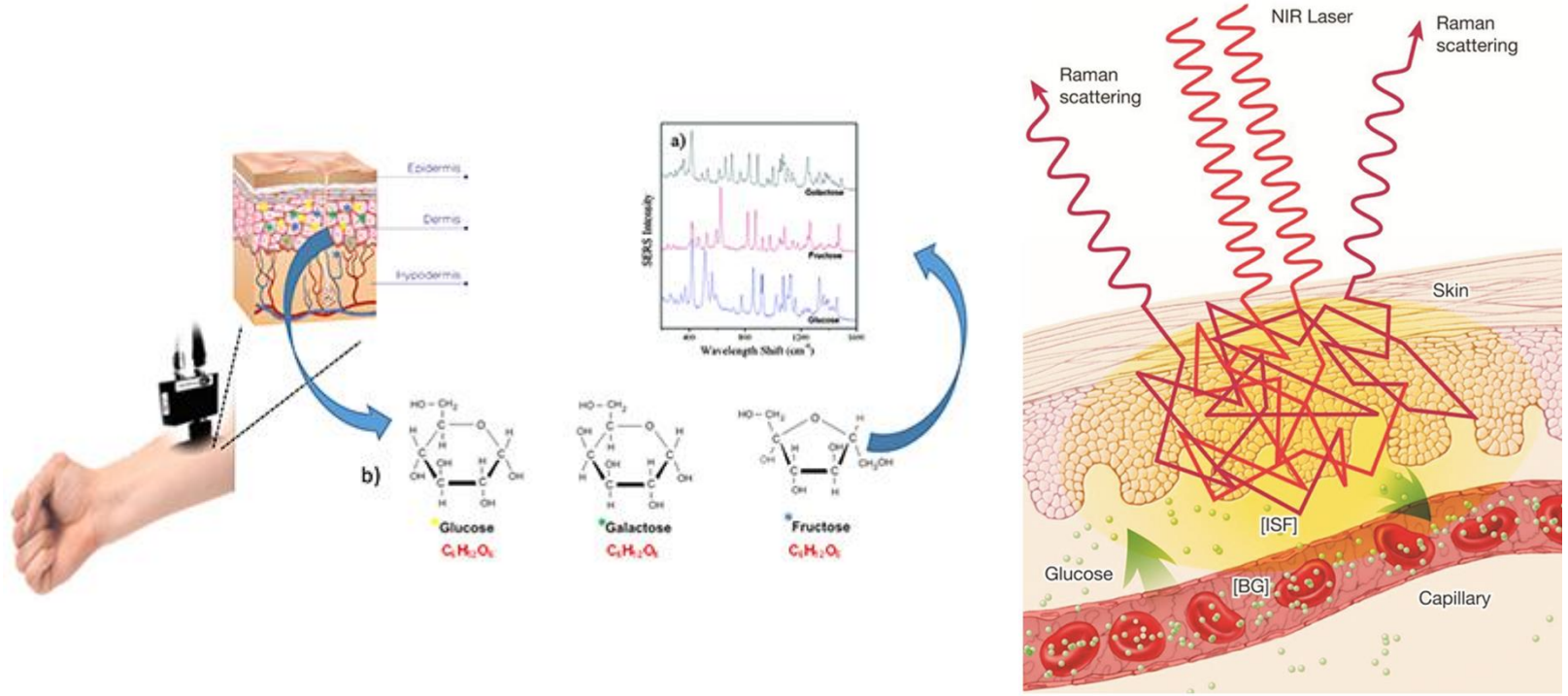
Constrained by invasive needles

**CONTINUOUS GLUCOSE MONITORING (CGM)**
USD 10bn, 13% CAGR

Abbott
dexcom
Medtronic



# The future will be miniaturized wearable enabling fully non-invasive, continuous sensing of glucose

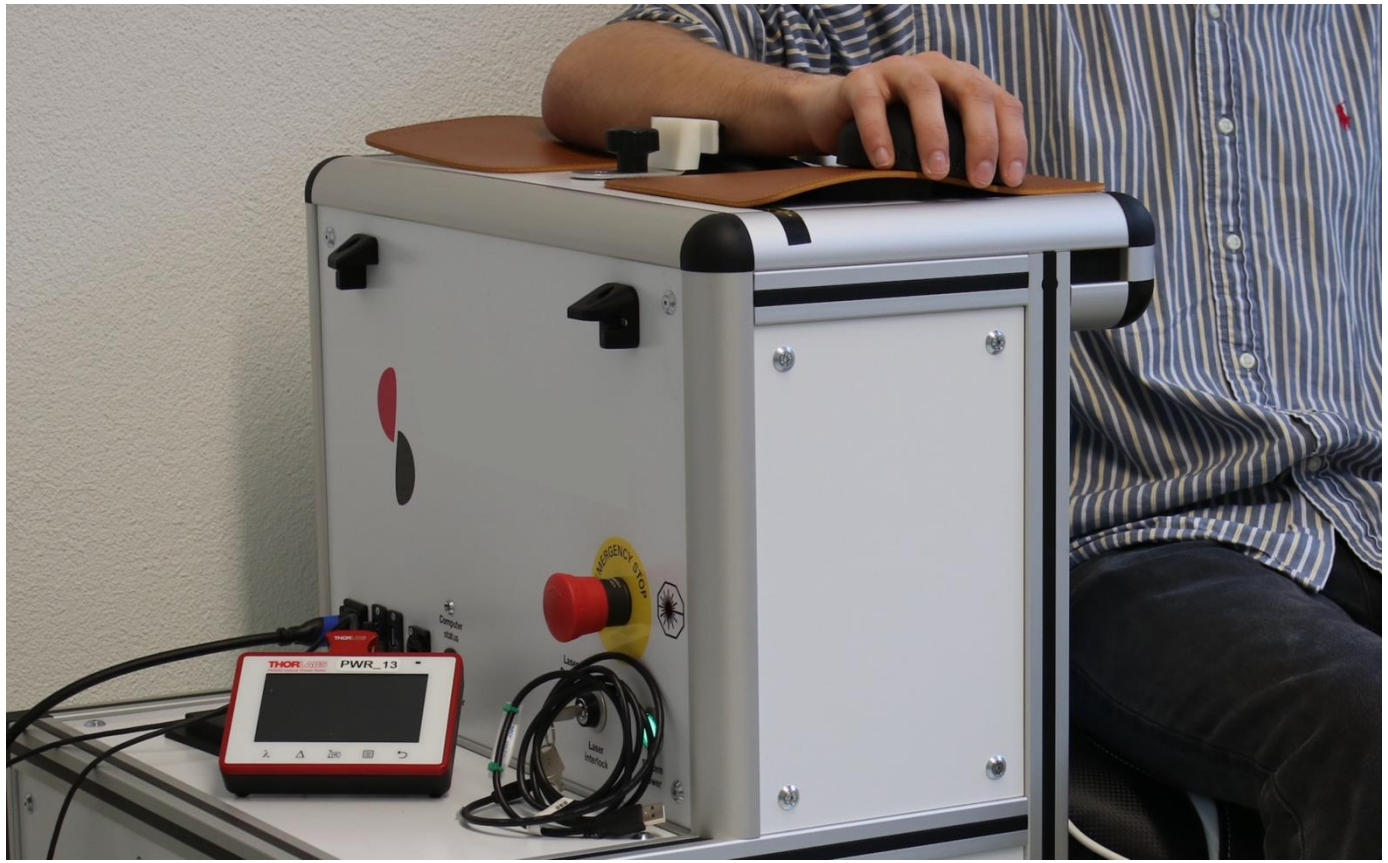



Some challenges explaining why most attempts have failed so far:

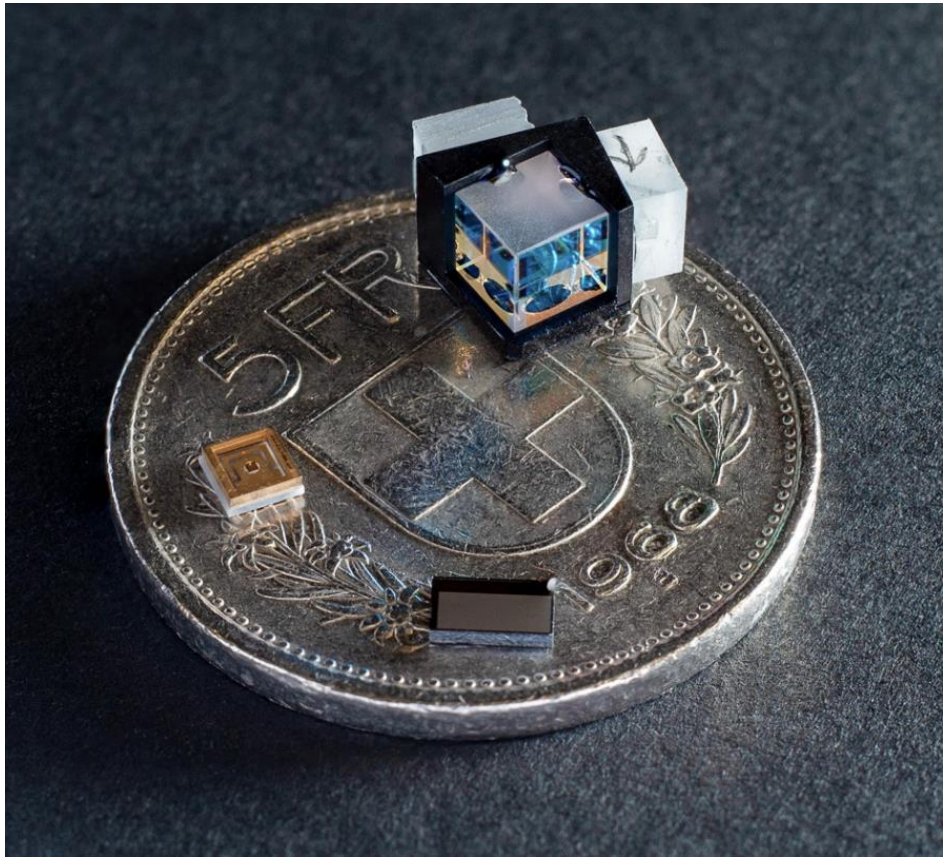
- Robust patient-to-patients consistency, independent of skin properties (colour, thickness, hydration, skin diseases or tattoo…)
- Precision and accuracy maintained over time (no calibration shift or drift)
- Analytic specificity: glucose is not isolated, so multiple cofounding signals are possible
- Miniaturization, cost, connectivity…

# The quest to non-invasive, continuous monitoring

**2024** – The first prototype for technology proof-point
« *Our tech (HW + AI/ML) can detect and track glucose non-invasively* » (Submitted to JDST)




**2025** - The second prototype for form factor and real-life environment proof-point



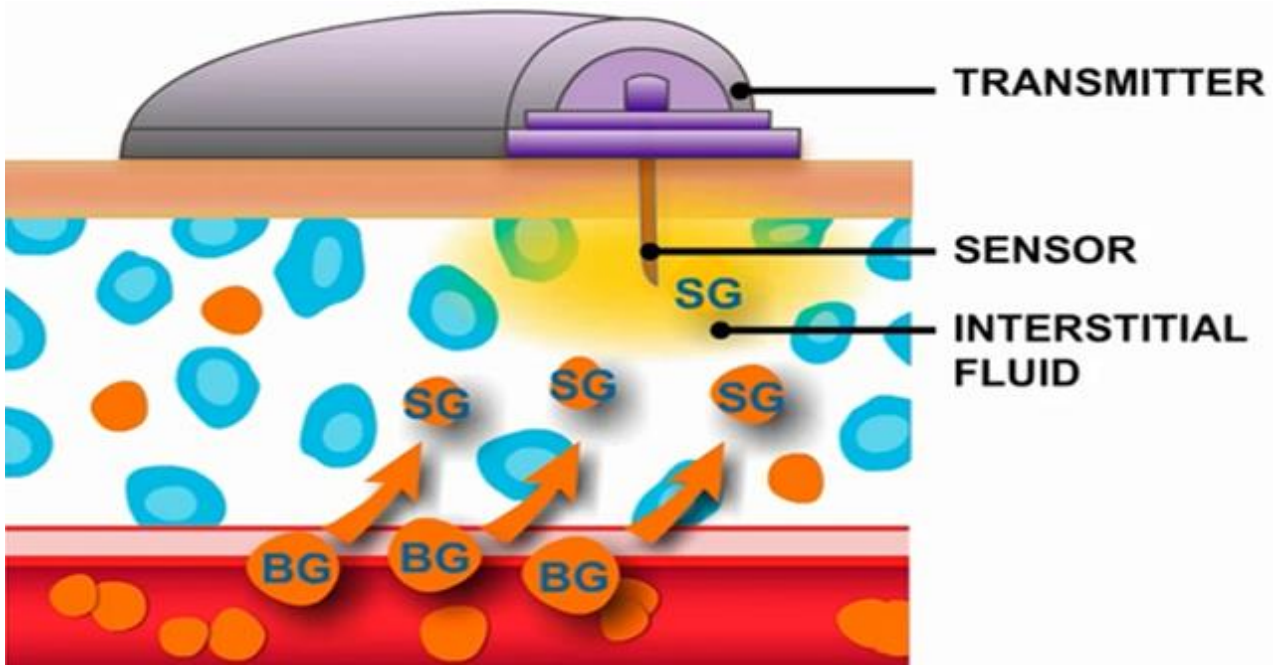
# Current technologies of existing continuous glucose monitoring (CGM) rely on glucose sensing in the interstitial fluids (ISF)

**Dexcom G6**

**Abbott Freestyle**

**Medtronic Guardian**

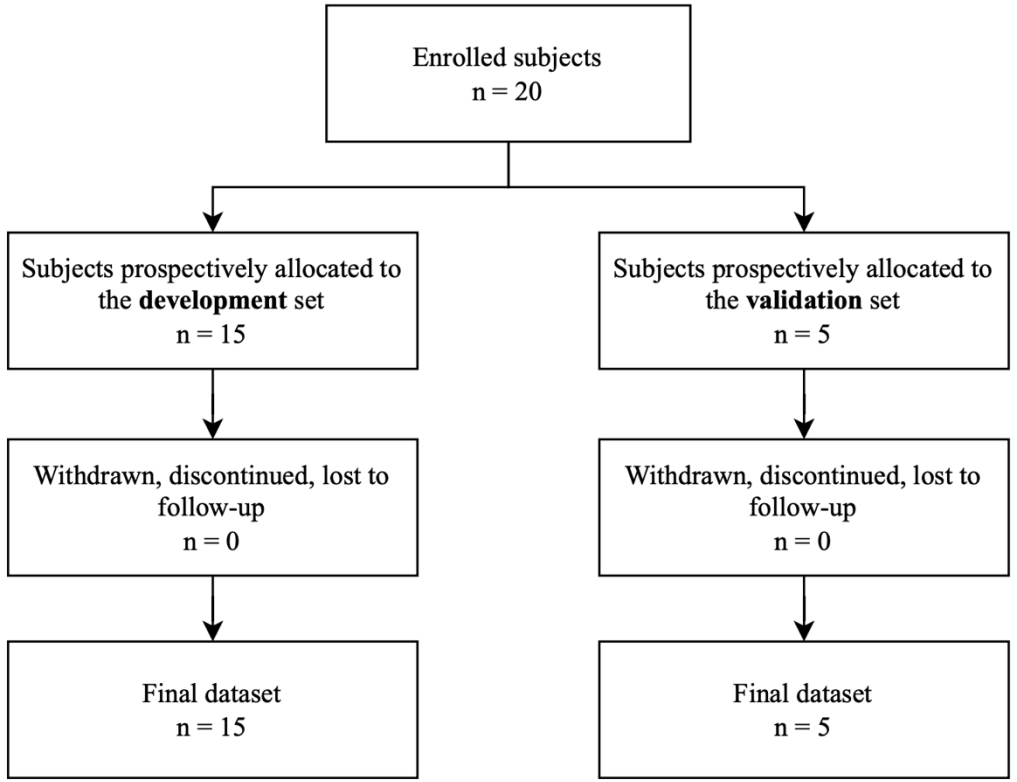
**Medtrum TouchCare Nano CGM**

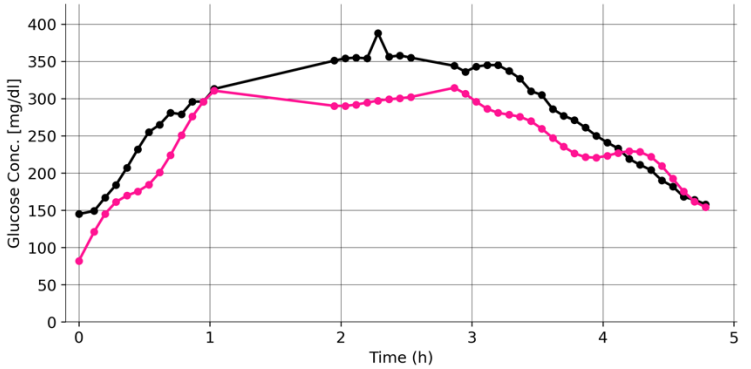


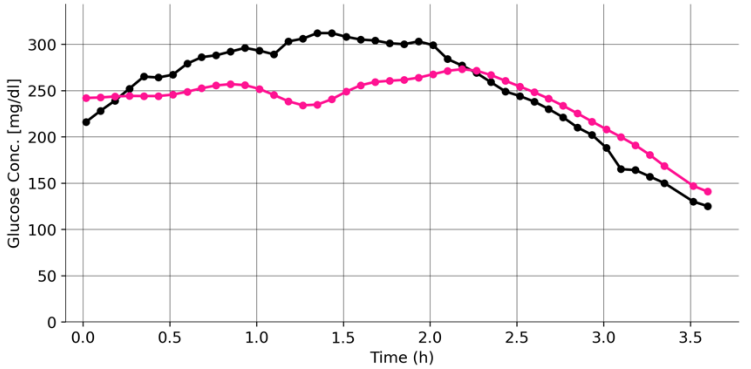
# The quest to non-invasive, continuous monitoring

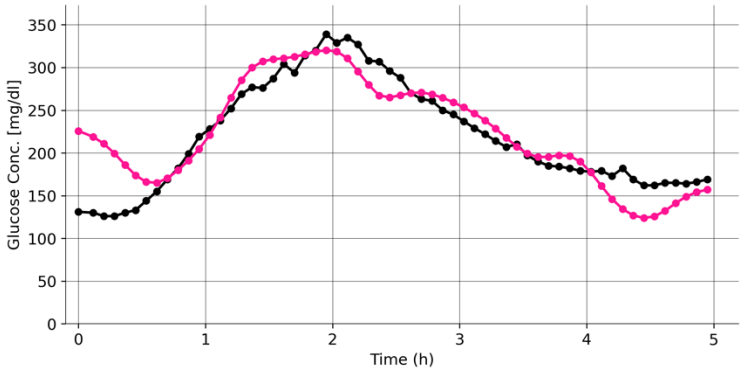
## A prospective pilot study demonstrating non-invasive calibration-free glucose measurement

Martina Rothenbühler, Aritz Lizoain, Fabien Rebeaud, Adler Perotte, Marc Stoffel, J. Hans DeVries



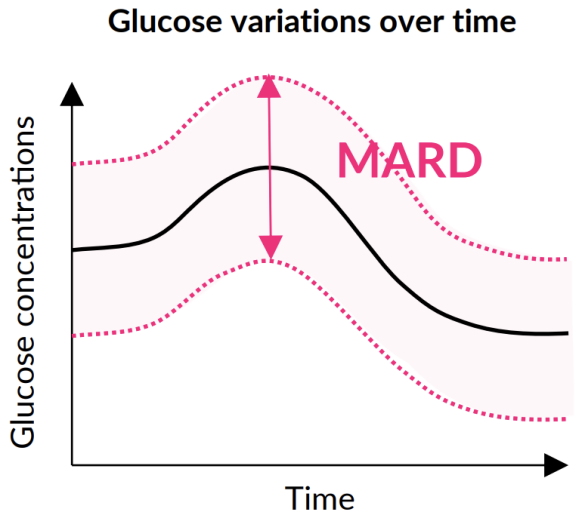



# The quest to non-invasive, continuous monitoring

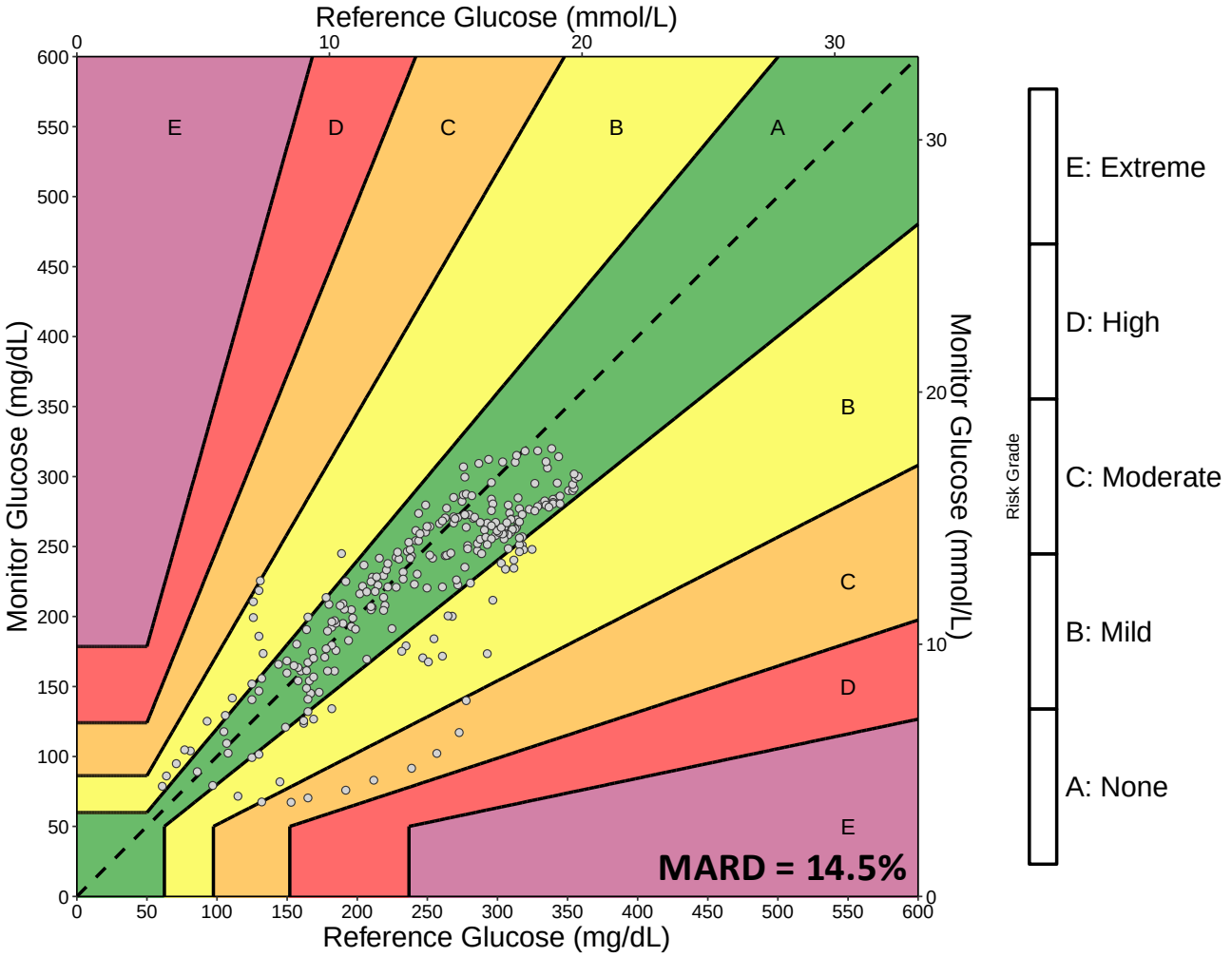
## A prospective pilot study demonstrating non-invasive calibration-free glucose measurement

Martina Rothenbühler, Aritz Lizoain, Fabien Rebeaud, Adler Perotte, Marc Stoffel, J. Hans DeVries

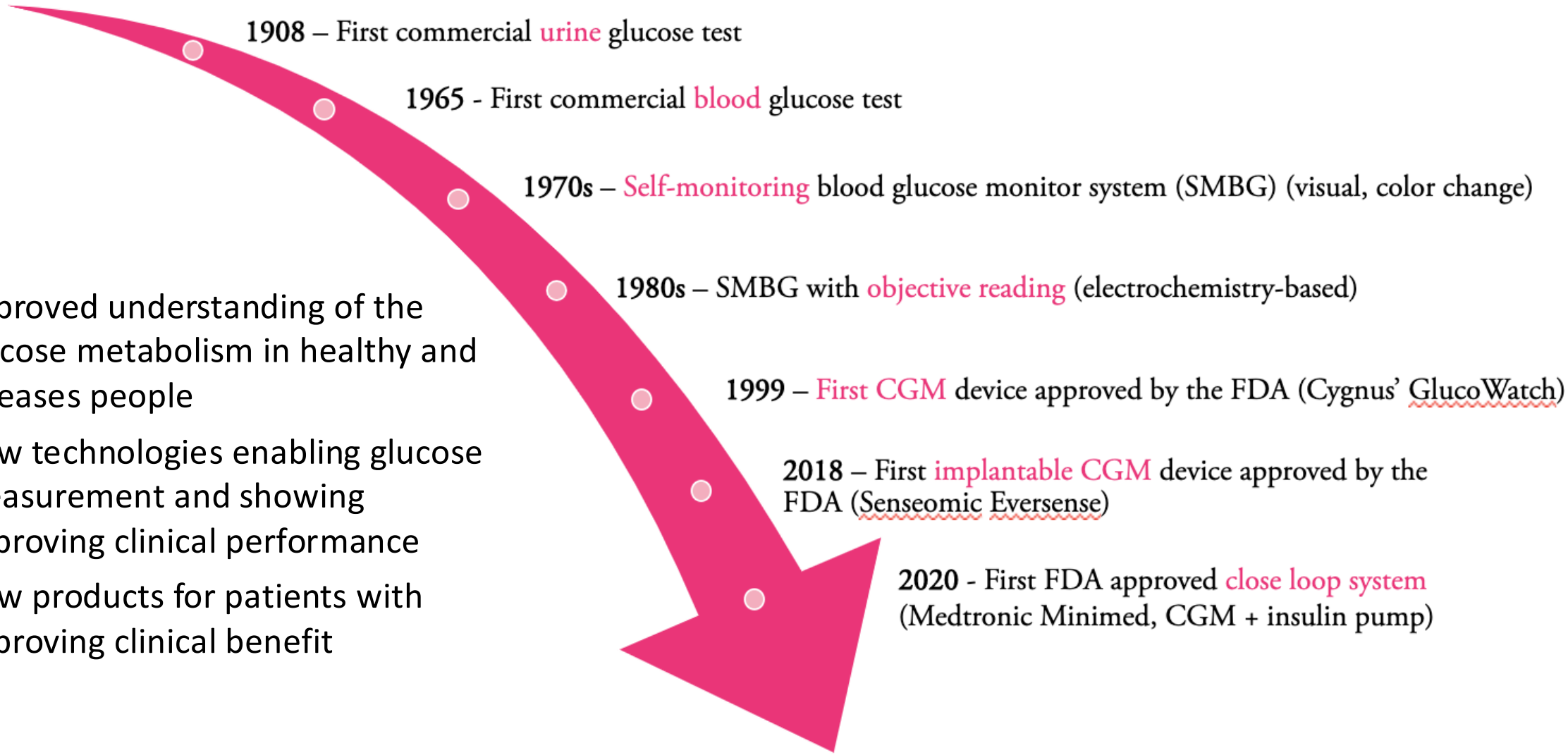



Mean Absolute Relative Difference

$$MARD = \frac{1}{n}\sum_{i=1}^{n} 100\frac{|Test_i - Refi|}{Ref_i}$$



# The history of glucose measurement is tightly bound to technology advancement




- Improved understanding of the glucose metabolism in healthy and diseases people
- New technologies enabling glucose measurement and showing improving clinical performance
- New products for patients with improving clinical benefit

# In Conclusion

- Key message:
  - Identify high-value ideas that will make a genuine difference

    → A novelty for novelty's sake is rarely a good idea

  - Define the intended purpose of what you are developing, as well as the specifications you must reach

    → True, both in academic settings and in the industry!

  - Verify and validate that your assay/product meets what you intended to meet

  - Develop thorough technical skills and open your mind to the business, regulatory and marketing aspects of your activities

# Thank you!

fr@liom.com
fabien.rebeaud@gmail.com