sciospec scientific instruments

5TH CLABIO LATIN AMERICAN BIOIMPEDANCE FLORIANOPOLIS – BRAZIL - 2024

Workshop:

impedance measurements instruments, sensors & beyond

An introduction on how to choose, design and successfully use setups for electrical impedance spectroscopy

What we will cover today

- Ways and means to measure impedance
  general approaches and what´s on the market
- What to make of those specs
  Typical pitfalls in interpreting datasheets and key specifications of impedance analyzers
- Mind the overall setup
  What other components than the analyzer affect your measurement
- Why calibration won´t magically fix it all
- The last 10% of the requirements are the hardest
- How not to get caught up in it all.

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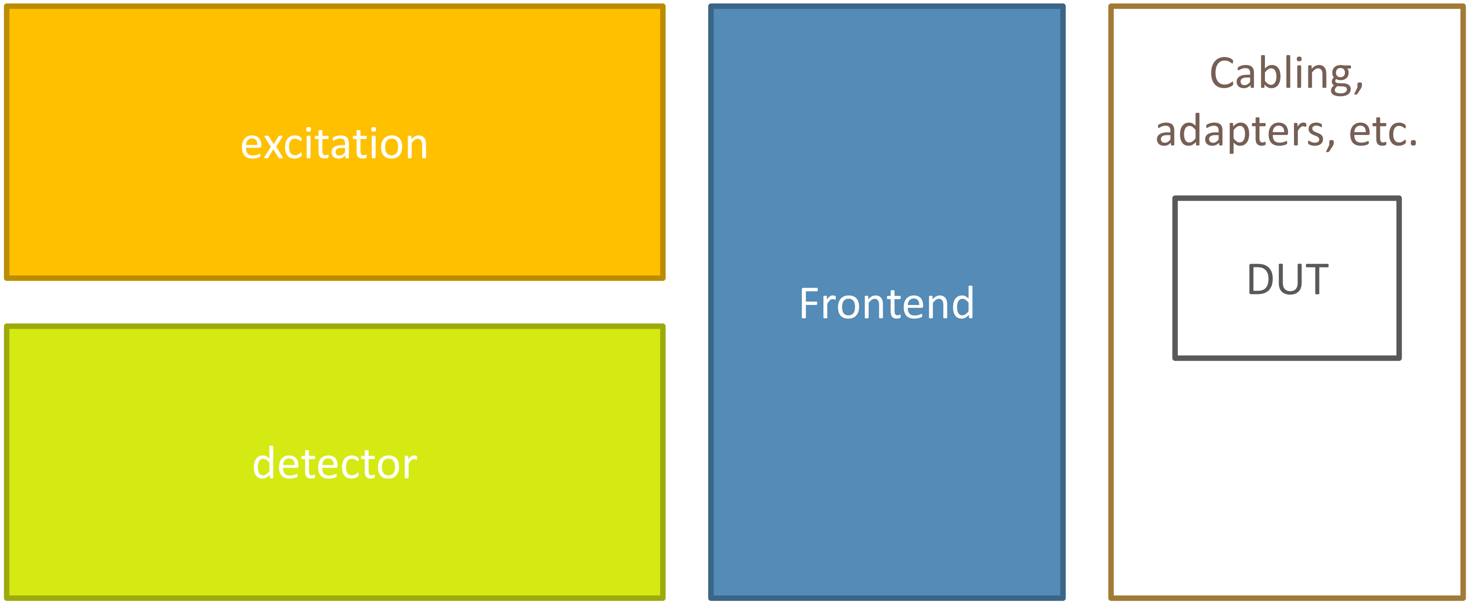
How to measure impedance?

- Core components of any impedance measurement:



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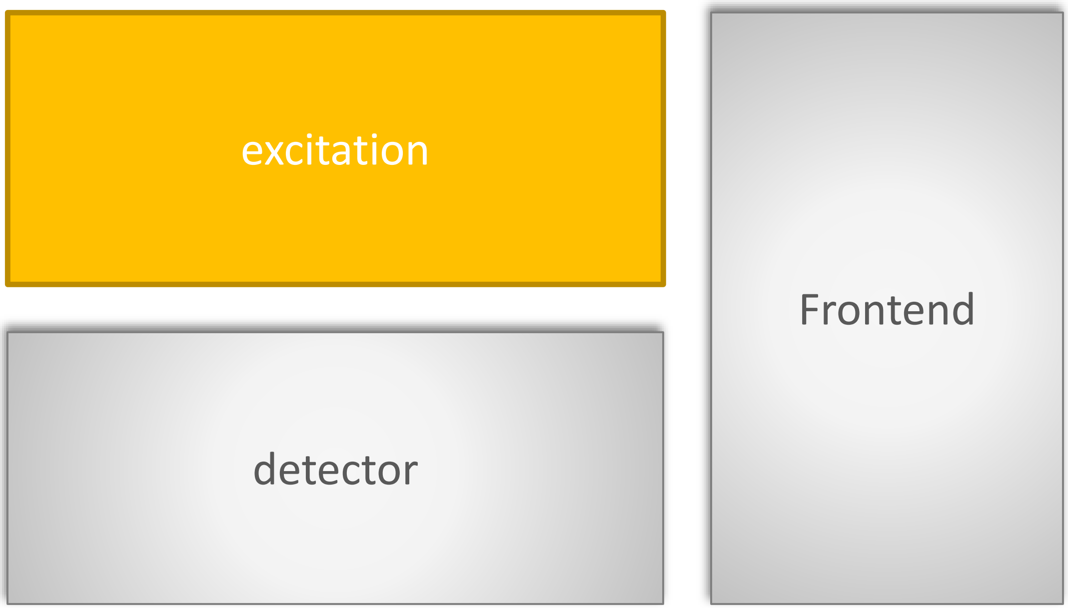

Typical excitation options

- **Type**
  - current
  - voltage
- **Form**
  - Single sine
  - Multi sine
  - Step
  - Complex

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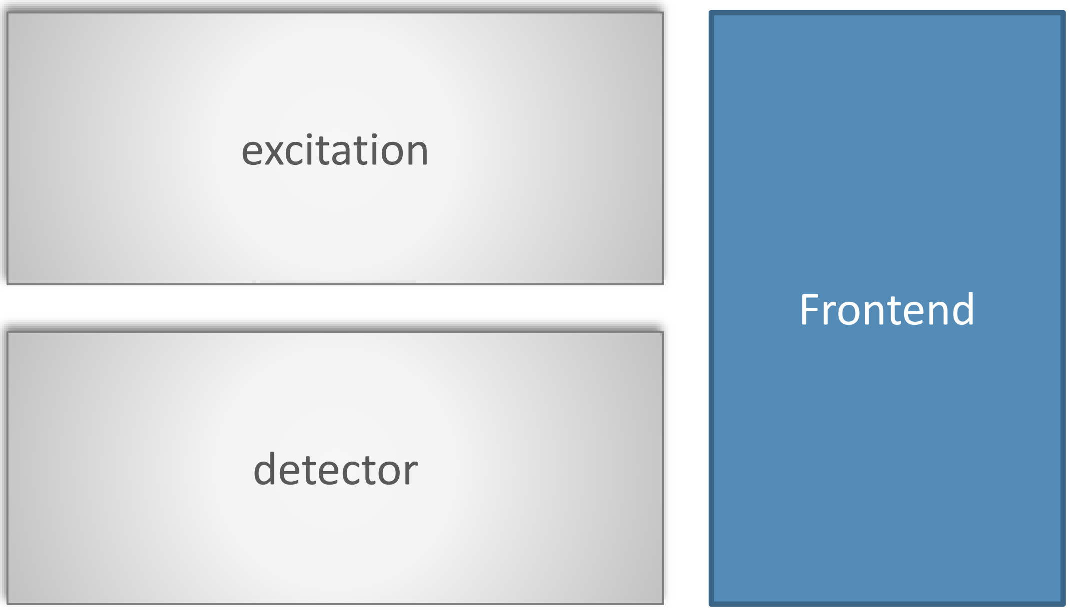

Typical frontend topologies

- **bridges**
  - current nulling
  - resonance
  - Phase (auto balance)
- **Current-voltage (I/V)**
- **directional coupler (VNA/SNA)**

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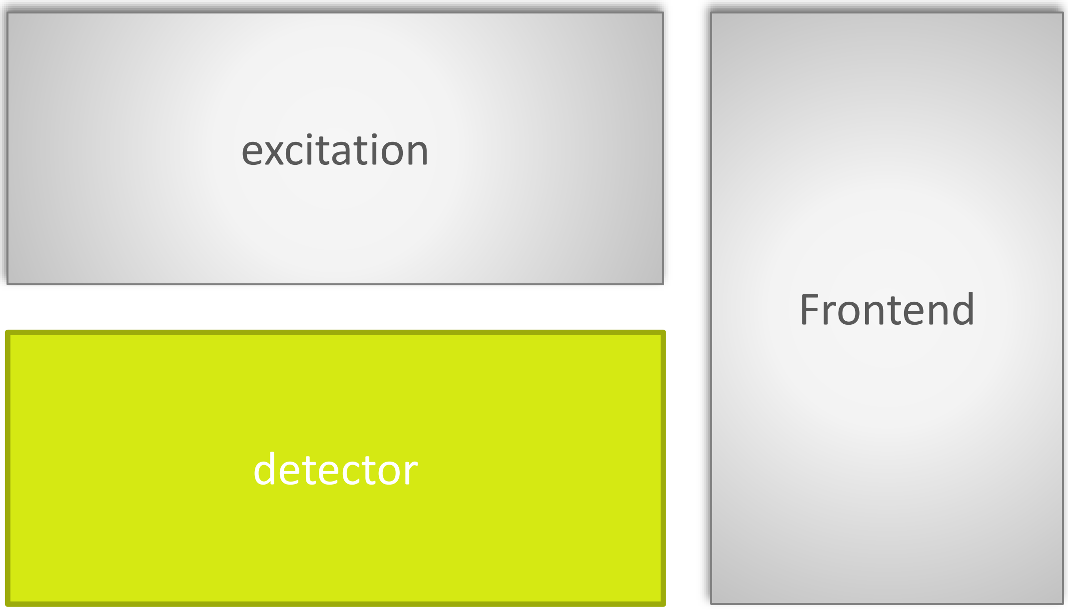

Typical detector approaches

- **lock in**
  analog, digital, phase balancing mixer or dual phase
- **Time domain sampling**
  typ. Spectral transform (e.g. FFT)
- **Power detector**
- **Alternative demodulation**
  (e.g. Sciospec SineFit)

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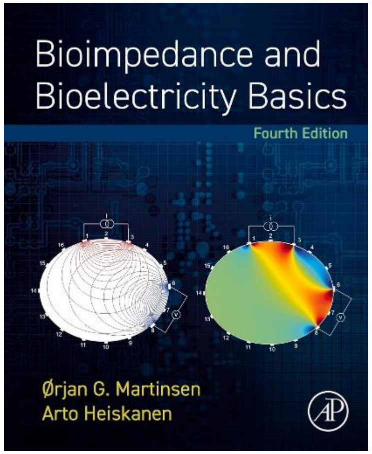
You already think that´s a lot of options?

- to make it even more confusing: many different combinations of these are possible and can be varied through additional modifications like
  - optional down mix/modulation
  - current measurement type (shunt, transimpedance)
  - grounded / floating architecture
  - inverted or noninverted frontend
  - differential or single ended excitation
  - potentiostatic, galvanostatic control or unregulated

- All of these options have implications towards performance and applicability but fortunately some of these are combined into typical analyzer types
  - LCR meters
  - network analyzers
  - electrochemical equipment
  - impedance analyzer
  - Other (time domain analyzers, oscilloscopes, spectrum analyzers, …)

More detailed overview in „Bioimpedance and Bioelectricity Basics“ 2023 (Orjan G. Martinsen & Arto Heiskanen)



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LCR meter

- Very basic approach
  - typically built upon bridge methods
  - Newer and high end tech also uses current-voltage approach
  - manufacturers: IET Labs, Hameg, Sourcetronic, Keysight/Agilent, GW Instek, Wayne Kerr…
  - Typ. Hz… <1MHz (except. RF LCR meters like the Agilent E4982A (25k€) - 1 MHz to 3 GHz)
  - Not intended for EIS, but rather testing electrical components -> low spectral resolution
  - typ. slow acquisition rates

Hameg HM8118 (2.500€)

- 0.05% basic accuracy (0.5% across range)
- 10 mOhm and 10 MOhm for frequencies from 20 Hz to 200 kHz
- up to 84 ms measurement rate
- only one frequency point

Keysight E4980A (13.500€)

- 0.05% basic accuracy (10% across range)
- 10 mOhm to 100 MOhm in the range between 20 Hz to 2 MHz
- list sweep function with up to 201
- down side: still slow: 180 ms per point even at high frequencies

Sciospec LCR-1 (3.500€)

- 0.01% basic accuracy (10% across range)
- 1 mOhm to 1 TOhm in the range between 100mHz Hz to 10 MHz
- Wide Range and high accuracy
- Compatible to multiple different test fixtures

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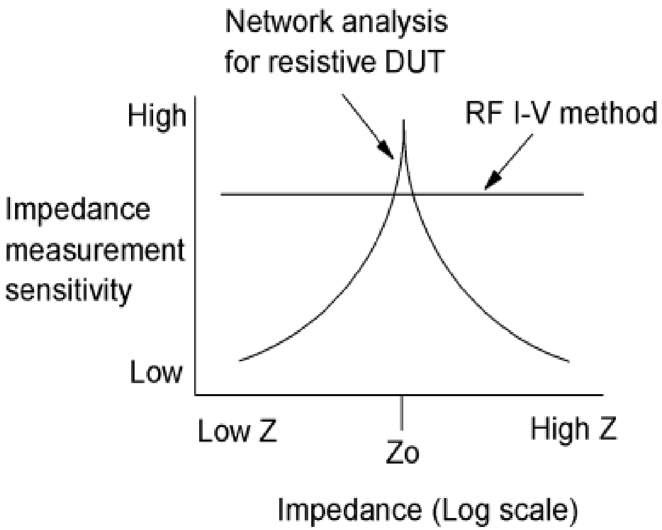
Network analyzer

- THE solution for high frequency
  - up to 110 GHz
  - reflection measurements: determine ratios of inserted to reflected power
  - very fast acquisition
  - SNA will not give phase information – this needs VNA
  - manufcaturers: Rohde & Schwarz, Agilent or Anritsu
  - cheap solutions (1000…5000€) – very low precision and dynamic range!
  - directional couplers limit lower frequency (typ. > kHz)
  - only small impedance ranges (typ. 1 Ohm ... few kOhm)
  - Very pricy: from around 25 k€ up to well over 100 k€



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Electrochemical equipment

- For apps where electrochemistry is the focus
  - Potentio/galvanostats can be extended with ac impedance analysis through FRAs
  - Very good bias control and large current/voltage coverage available
  - Prices vary from 3k…80k€
  - manufacturers: Solartron, Ivium, Gamry, Sciospec or PalmSens
  - typ. slow acquisition rates
  - most only have very basic impedance analysis capability (ranges, precision, etc.)

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Impedance analyzers

- Best overall solution for impedance spectroscopy
  - Either current-voltage or auto-balancing bridge method
  - large impedance ranges at high precision
  - Frequencies from DC to several MHz
  - manufacturers: Keysight, Solartron, Sciospec, Zurich Instruments

	Keysight E4990A	Sciospec ISX-3	Zürich Instruments MFIA
			
Frequ	20 Hz ... 120 MHz	100 µHz ... 100 MHz	1 mHz ... 5 MHz
Imp	25 mΩ ... 40 MΩ	1 mΩ ... 1 TΩ	1 mΩ ... 1 TΩ
Accuracy	0.08 %	0.01 %	0.05 %
Speed	>3.5 ms/point	>0.3ms/point	>20 ms/point
Price	20 k€ (10 MHz) 45 k€ (120 MHz)	6.5 k€ (10 MHz) 15 k€ (100 MHz)	11 k€ (500 kHz) 13 k€ (5 MHz)
misc	• large (40 V) DC Bias range • stand alone operation through frontpanel controls and display	• multiplexing options • extension port • isoIO • EIT mode • medical research version	• lock-in amplifier mode • PID/PLL control mode • additional demodulators • digitizer mode

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What an instrument spec will and won´t tell you (rtfm!)

- Key specs
  - precision, speed, compliance and excitation ranges, etc.
  - careful: key specs are generalized specs, that hide underlying dependencies
  - excitation amplitude, range selection, speed have huge impact
  - Precision & speed both are at least dependant on frequency and absolute impedance!
- Good starting point: the precision-range-plot
  - Plot accuracy of measured impedance over frequency and absolute impedance value
  - Can reveal significant differences to the spec summary!

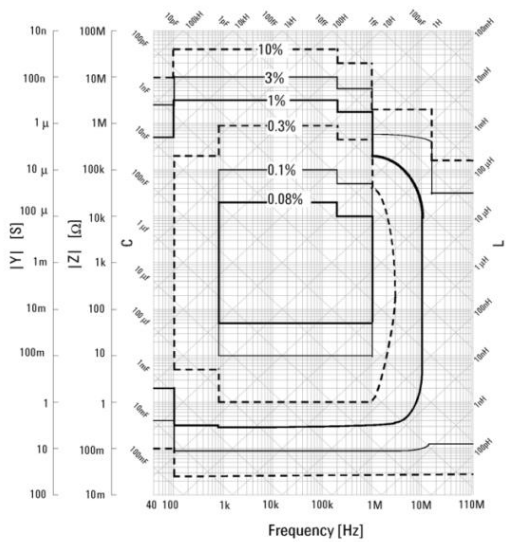
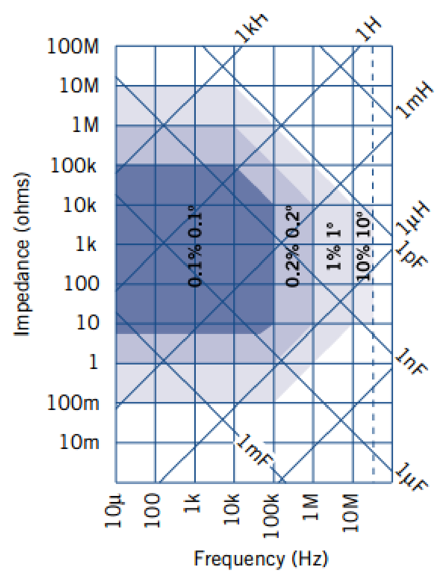


Figure 4. Examples of Calculated Impedance Measurement Accuracy at Four-Terminal Pair Port of the Agilent 4294A's Front Panel (Oscillator Level = 0.5 Vrms)



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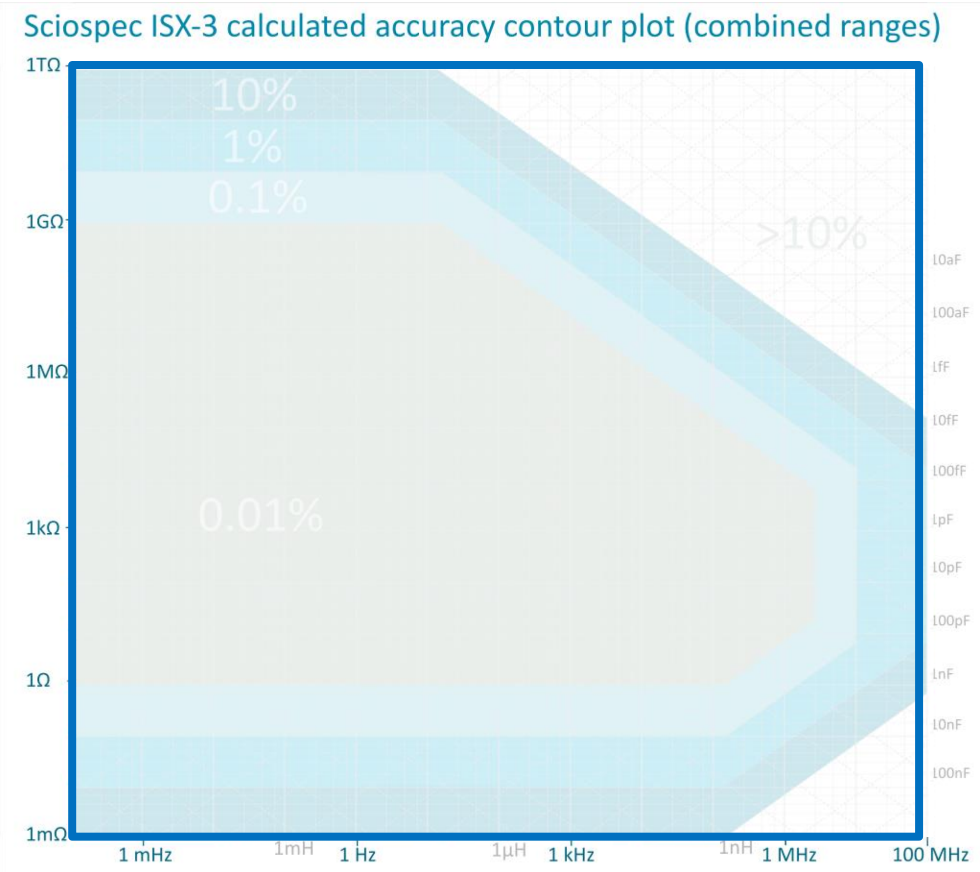
Accuracy range plots vs. spec summary



Global summary specs suggest large rectangular window

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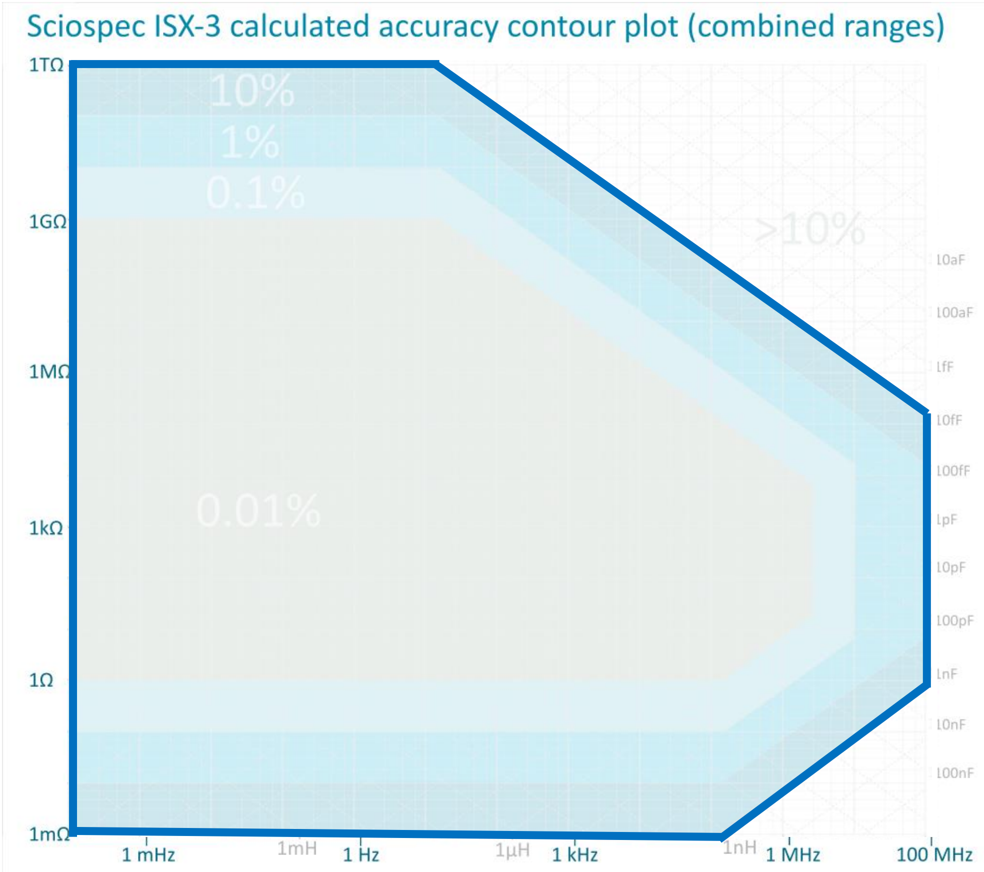
Accuracy range plots vs. spec summary



Typical P-R-plot limit 10% accuracy already greatly reduces the window

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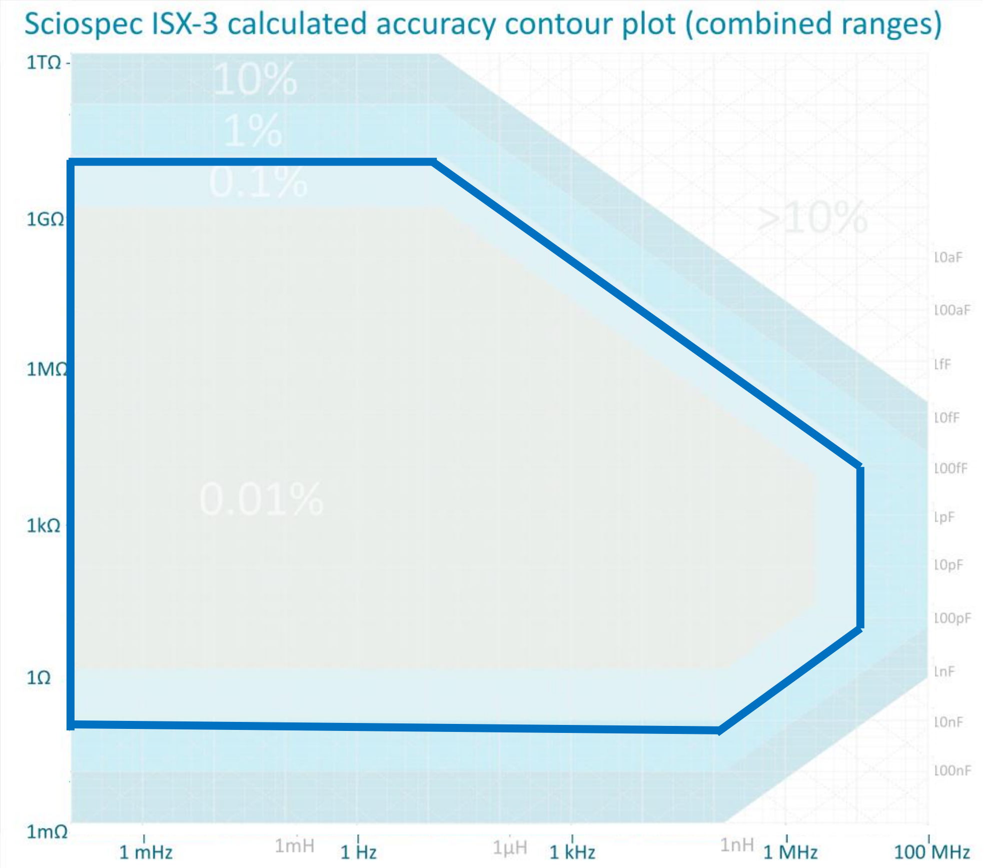
Accuracy range plots vs. spec summary



Typical P-R-plot limit 0.1% accuracy has drastic impact

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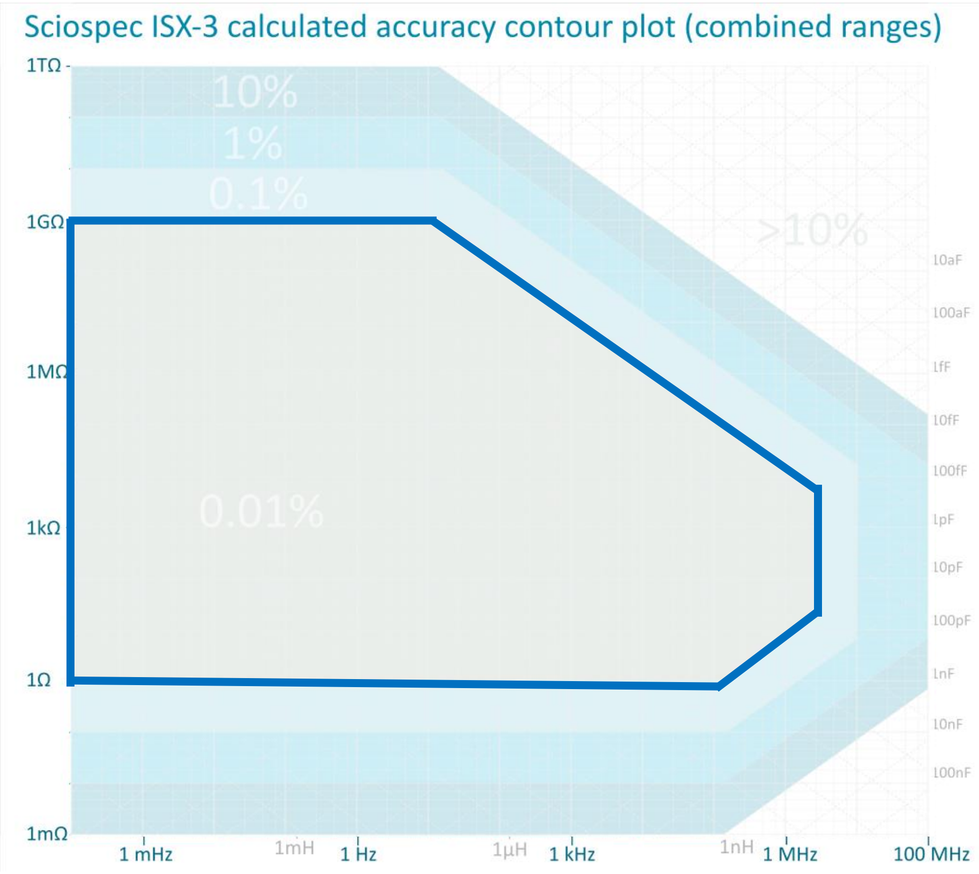
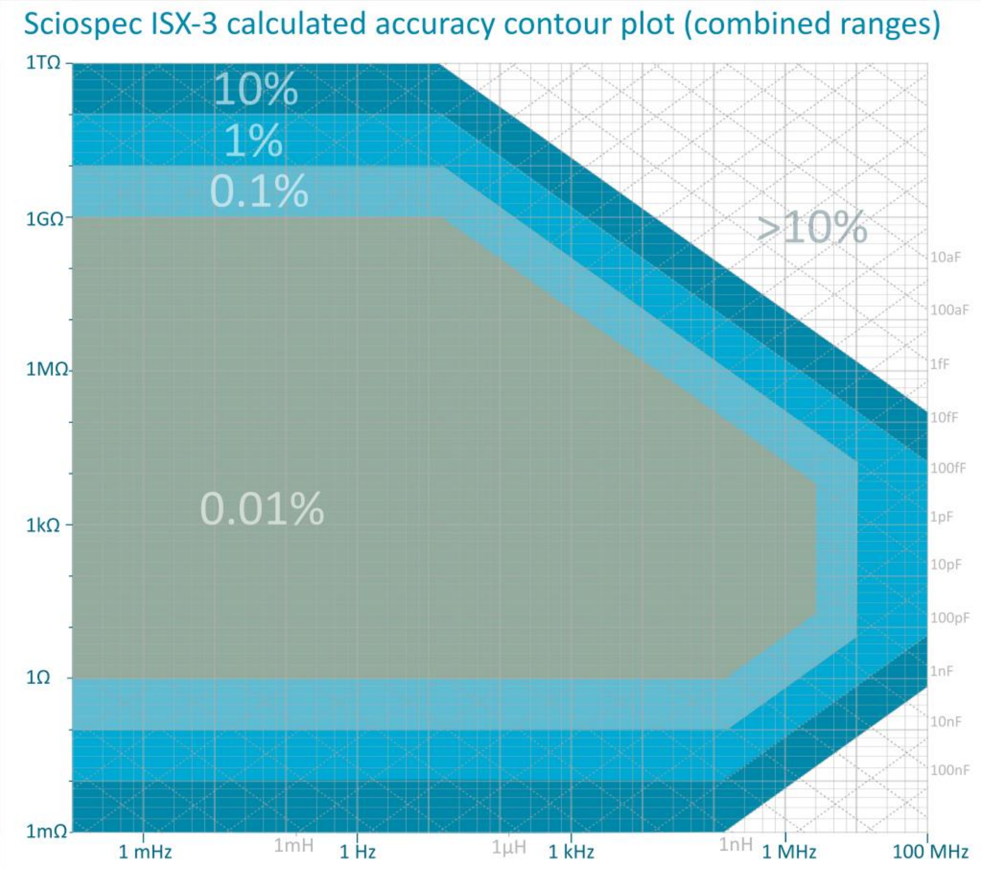
Accuracy range plots vs. spec summary



Typical P-R-plot limit 0.01% accuracy has drastic impact

Full detailed Accuracy Range Plot



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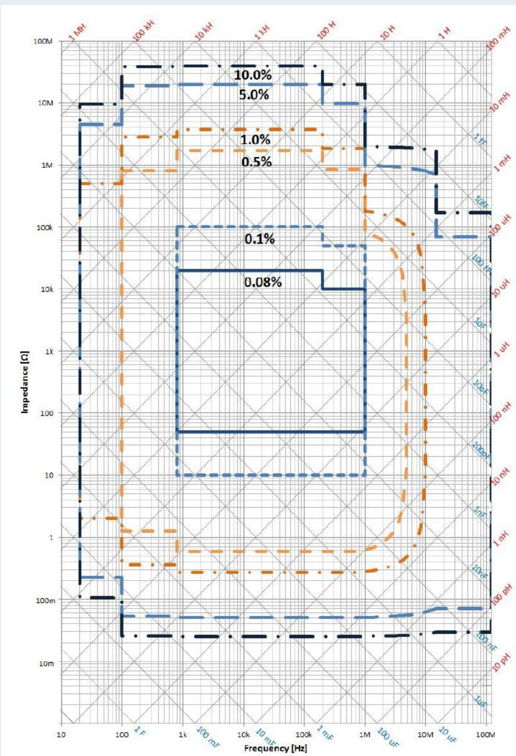
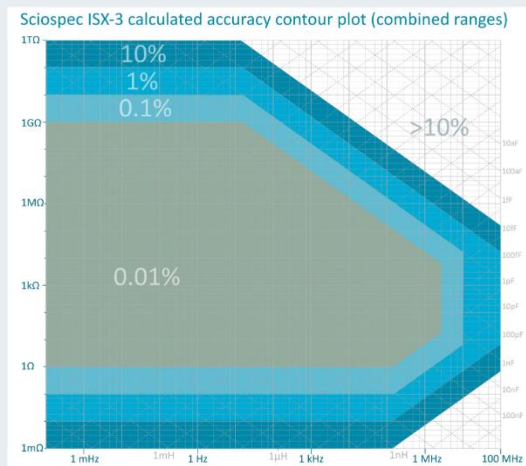
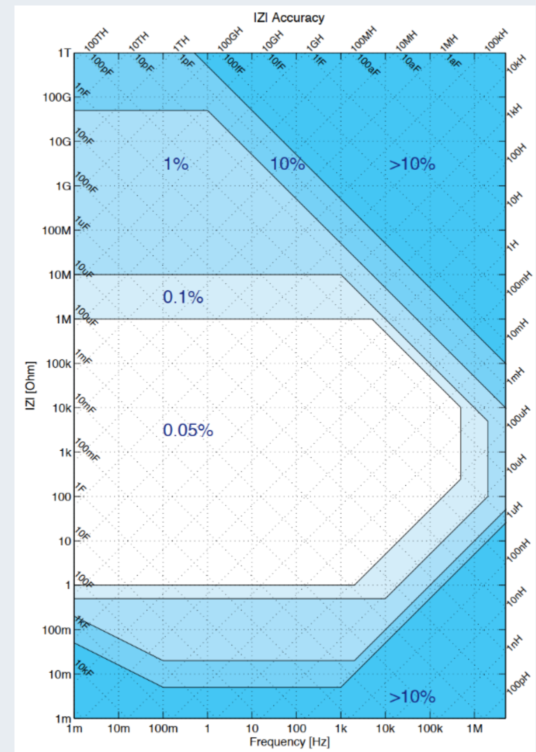
Keysight E4990A	Sciospec ISX-3	Zürich Instruments MFIA
		
		

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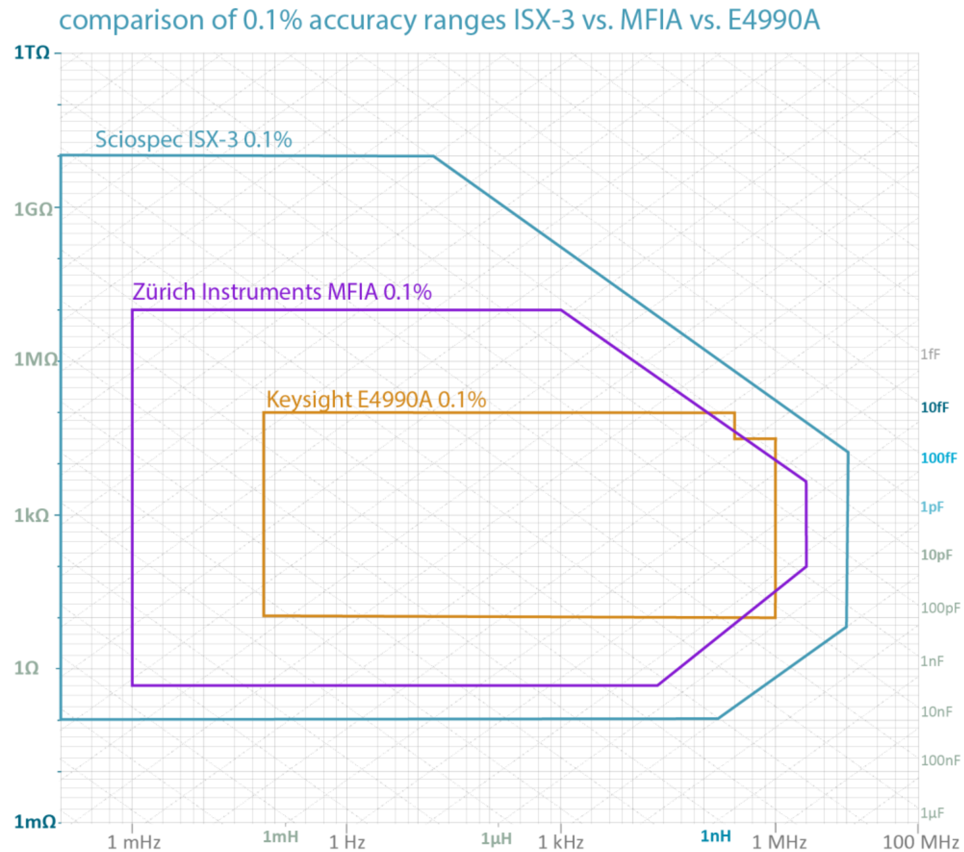
Keysight E4990A	Sciospec ISX-3	Zürich Instruments MFIA
		



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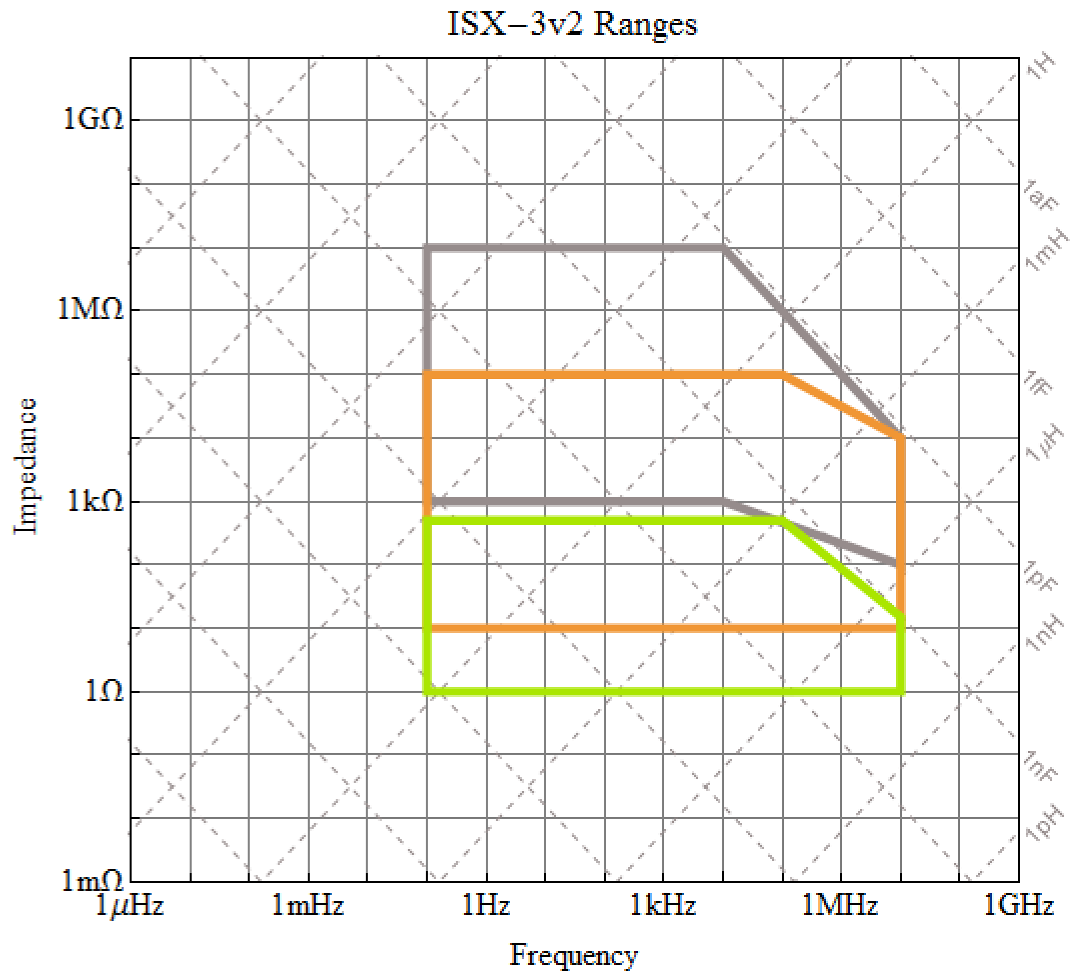
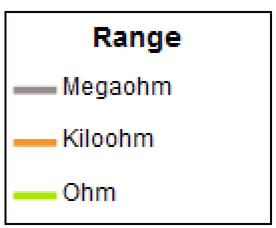
Precision range plots vs. spec summary

- still not unconditionally valid!
- Assumptions include maximum excitation amplitude, optimum settling on a purely resitive DUT and optimum frontend set point (gains, max bandwidth, etc.).
- Some manufacturers will specify these plots separately for different measurement ranges, some will include plots for different precision/ bandwidth settings and some just give you one summary plot.





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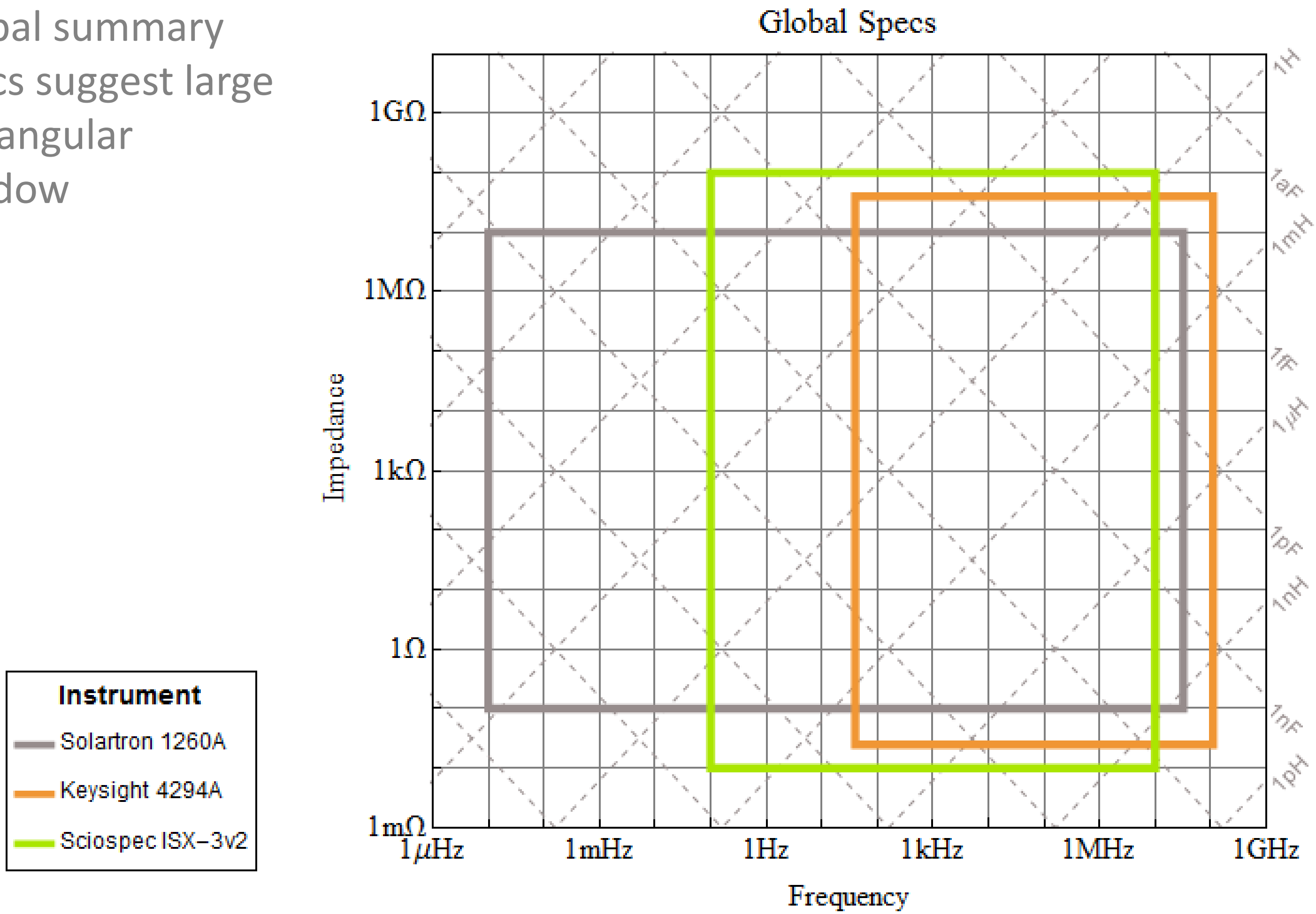
Precision range plots vs. spec summary

- Global summary specs suggest large rectangular window



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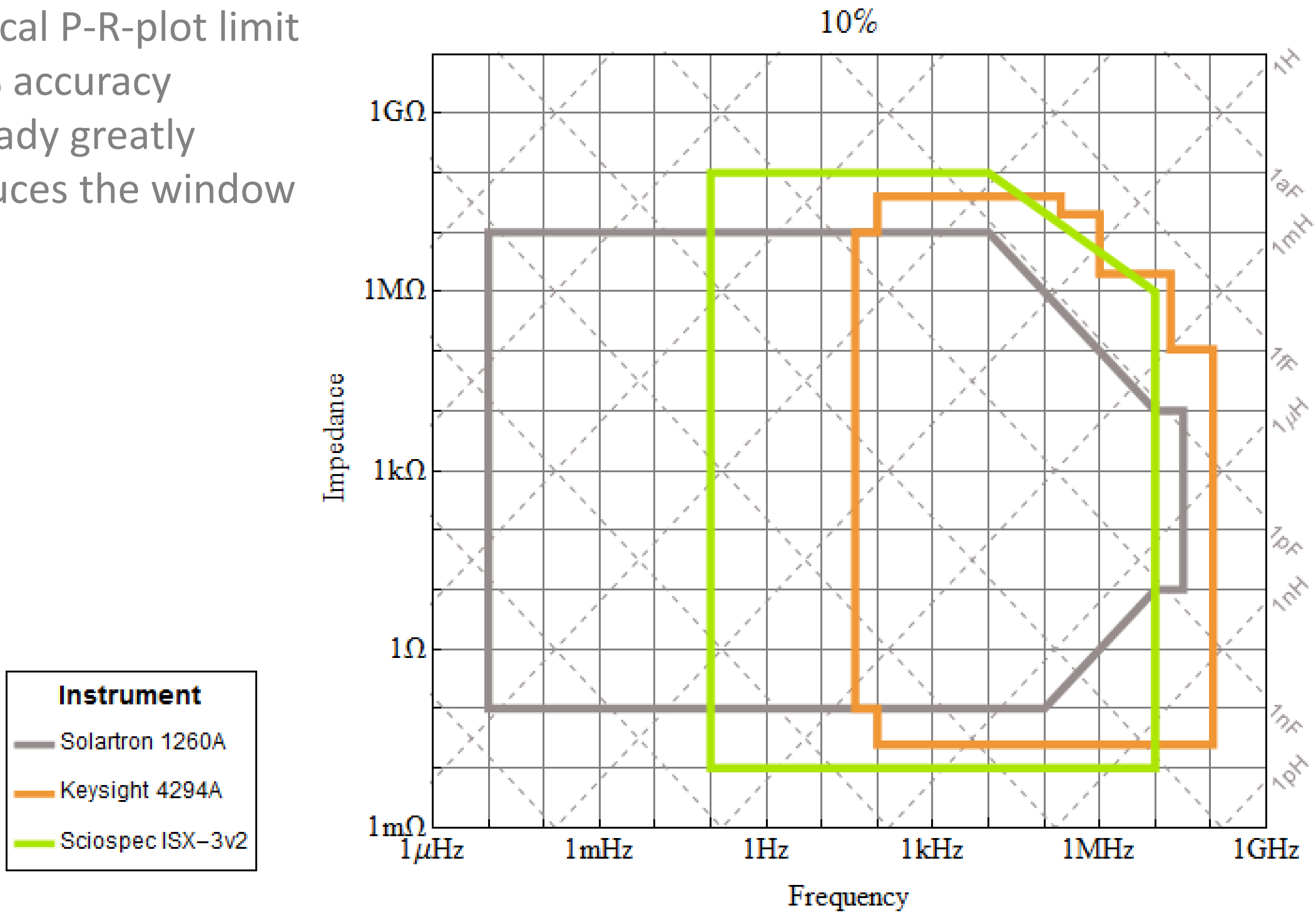

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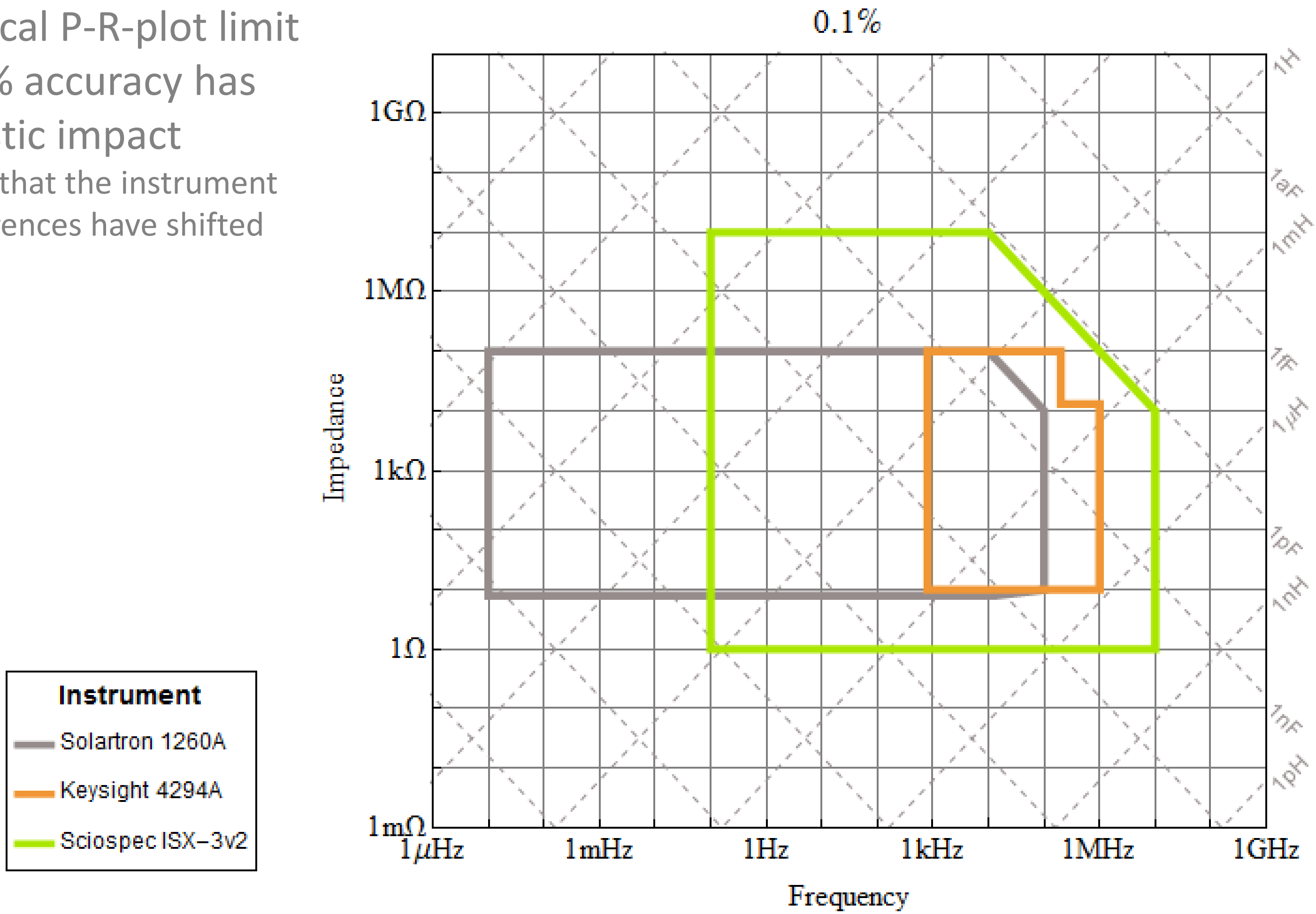
Precision range plots vs. spec summary

- Typical P-R-plot limit 0.1% accuracy has drastic impact
  note that the instrument differences have shifted



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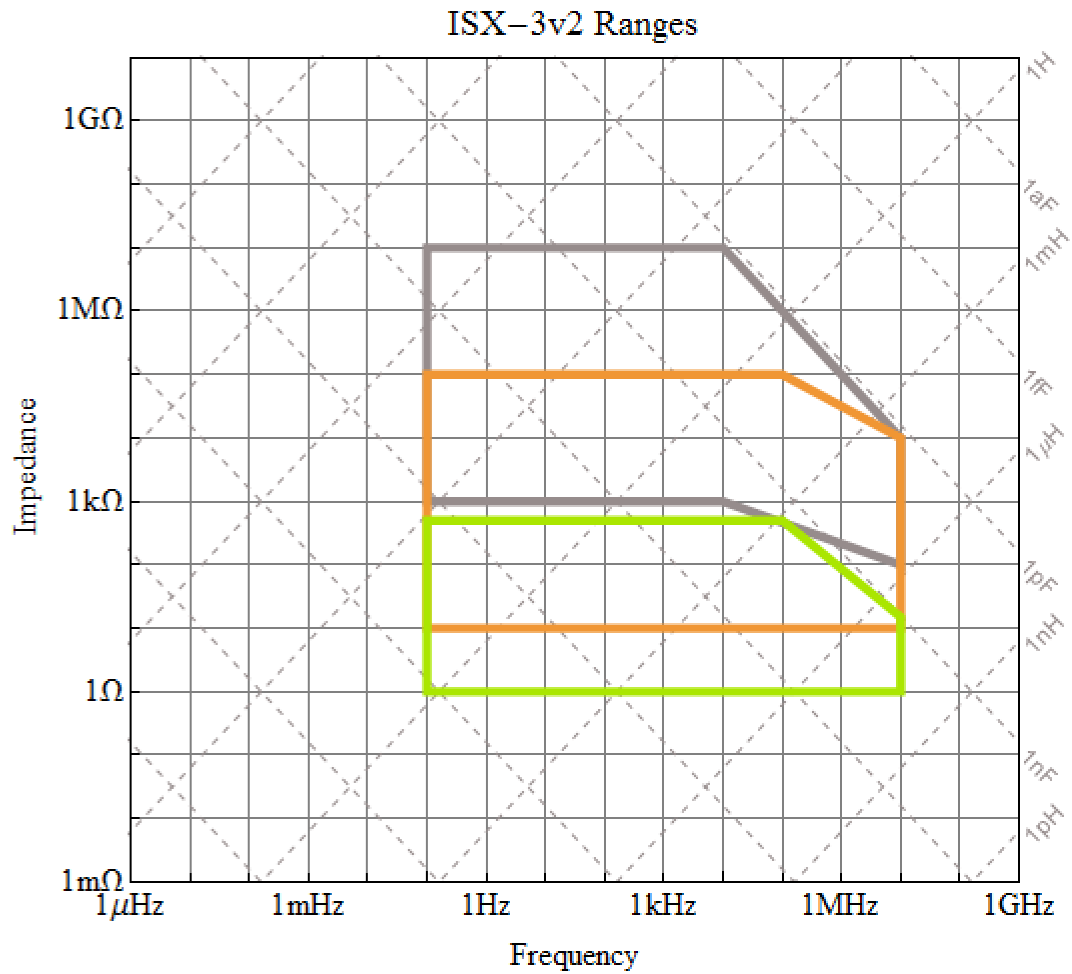

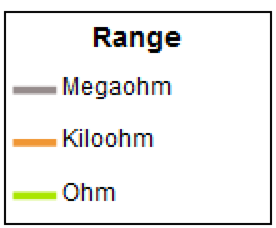

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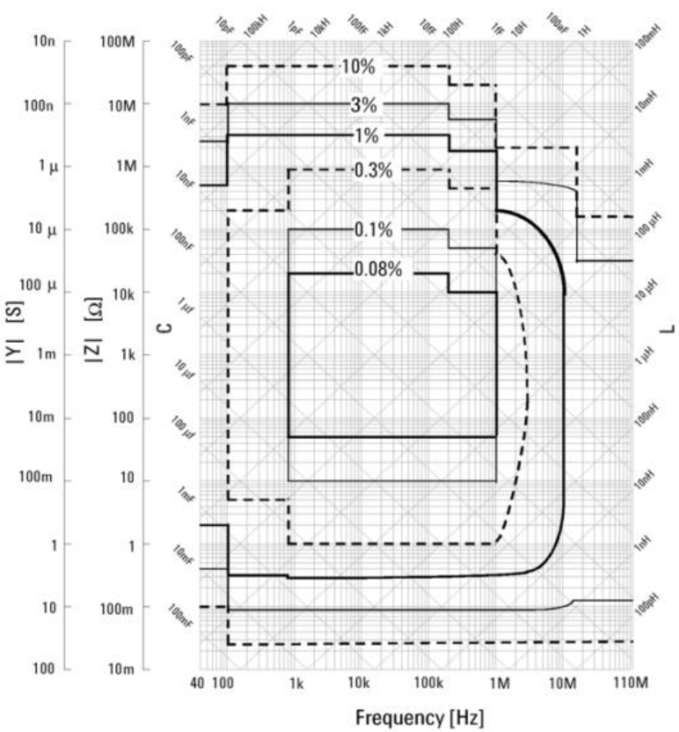
Validity of p-r-plots

- Always check for the conditions!
- Example: note figure desciption - this is only an example and only valid for maximum excitation level and only in voltage mode, also note the difference depending on the connector ports/adapter used (left,right)



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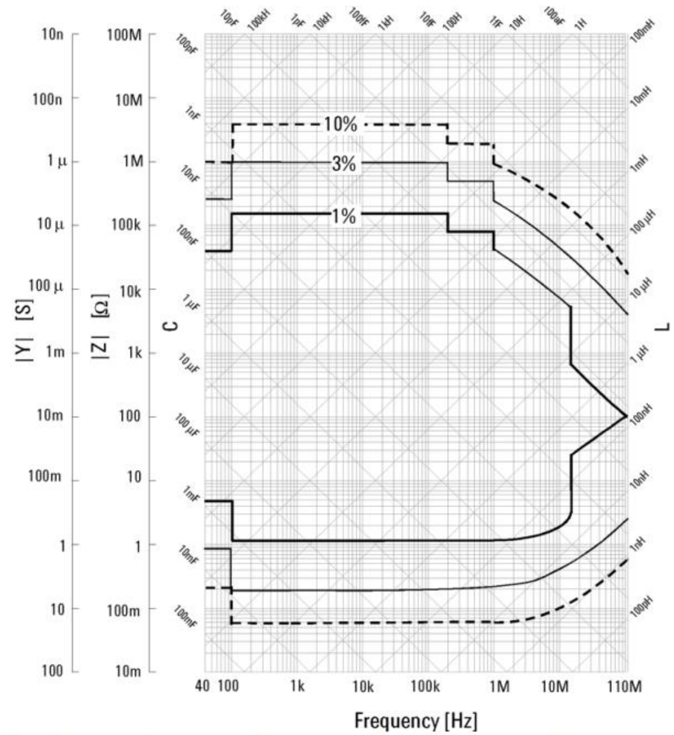

Figure 5. Impedance Measurement Accuracy at 7-mm Port of the Agilent 42942A Terminal Adapter Connected to the Agilent 4294A (Oscillator Level = 0.5 Vrms)

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But wait, there´s more!

- condition for specified measurement accuracy
  - note what happens beyond the temp range

Conditions of Accuracy Specifications

Temperature

Four-terminal pair port of the 4294A's front panel	23 ±5 °C Beyond 23 ±5 °C, the measurement accuracy is twice as bad as described.

- Speed vs. frequency & bandwidth vs. accuracy

Measurement Time

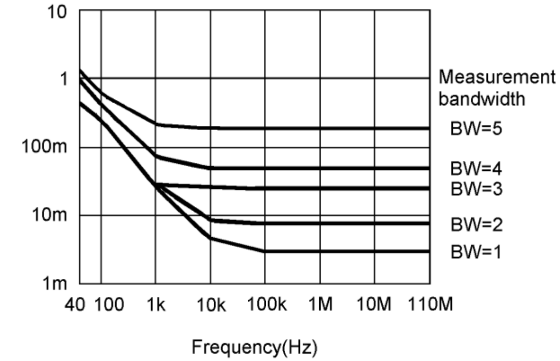
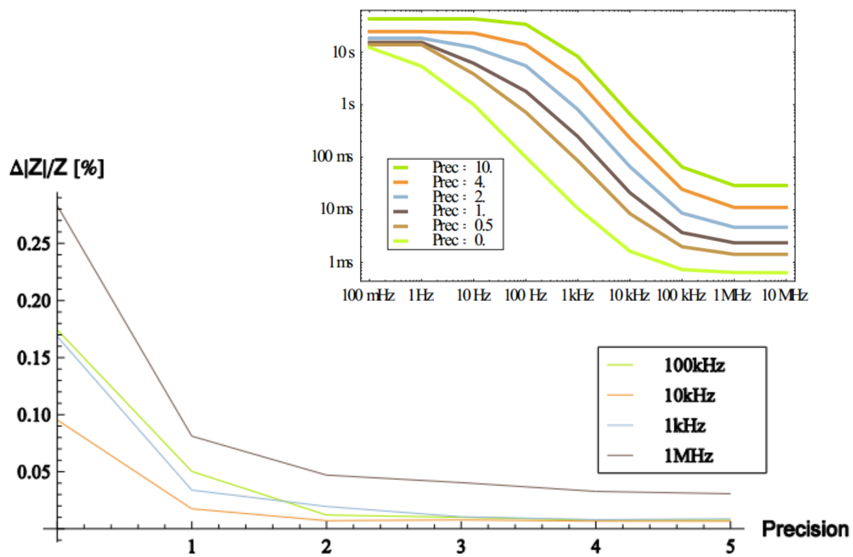


Figure 2. Measurement Time (SPC)

NOTE
When the Agilent 42941A Impedance Probe or 42942A Terminal Adapt
used, measurement time is 1.5 times longer than the value in Figure 2.



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More speed issues

- Lower frequencies take longer to measure (who would have thought)
- single period acquisition time is possible, but yields high influence of harmonics, distortion, coupled noise
- In general single sine remains the most precise
- Settling time and phase synchronisation

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beyond the analyzer - mind the overall setup

- Specs we saw so far are only specified up to connector of the analyzer
- but ENTIRE setup influences your results
- non-ideal setups are the reality!
- bad setup can ruin the best analyzer specs

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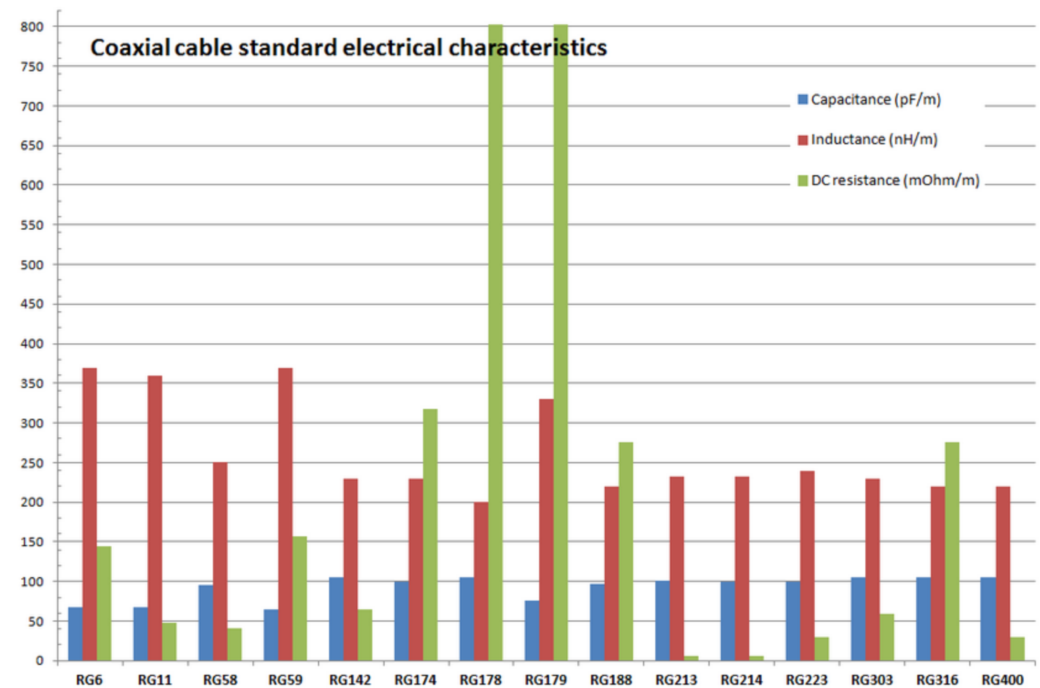
beyond the analyzer - cabling

- Cable parasitics
  - Capacitance to shield, other cables, ground structures, etc.
  - DC resistance
  - Inductive component
  - All are distributed (ladder network) -> concentrated component equivalent model does not perfectly fit
  - The longer, the worse
- Example:

  Typical coax cable types



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beyond the analyzer - multiplexing

- types of switches/multiplexers
  - Mechanical, magnetic relays, semiconductor switches, reed contact switches, semiconductor multiplexers
- parasitics of switches
  - Ron, Cpar, noise coupling, finite off-isolation through capacitive coupling and substrate leakage
- either bulky and cost intensive with high grade relays or small, but higher parasitics with semiconductor switches
- careful: even though relays can have low parasitics themselves, their bulkiness requires larger pcb area and longer wires for their routing which in turn again leads to increased parasitics!
- rule of thumb: the higher the channel count, the higher the parasitic influence

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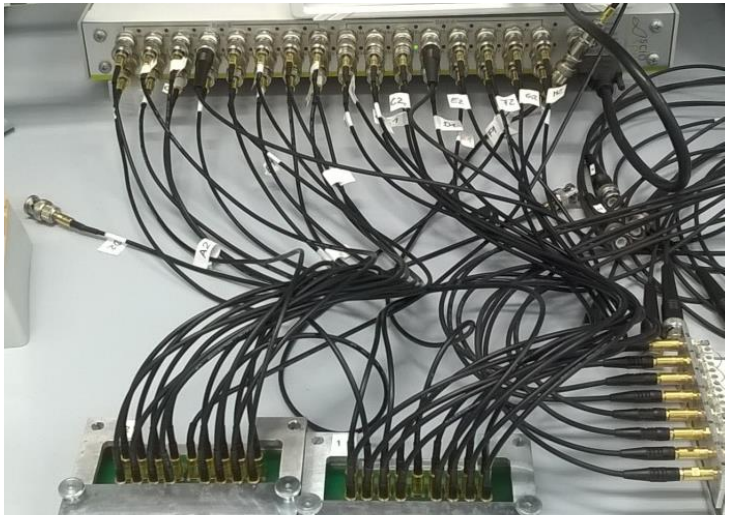
beyond the analyzer - multiplexing

- way out: optimized mux structures with a mixture of relays, semicondutor muxes and buffers
- Example below is old and new for a multiplexed chip based cell culture impedance measurement setup



From this parasitic nightmare

to this clean and simple 50 x multiplexing chip adapter

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beyond the analyzer – 2,3 or 4 pt. electrodes?

- unlike in classical electrochemistry in EIS we want electrodes to be passive (they´re not!)
- lots of arguments on which is the right method to contact for EIS - almost religious beliefs that one or the other config is the ultimately right choice
- careful: no easy answer to which one is right!
- some arguments from a strongly simplified perspective:
  - 2 pt … series parasitics & double layer capacitance at an electrode to liquid interface
  - 4 pt. … additional capacitance -> limit dynamic at higher frequencies
  - VERY general assumption might be: use 4 point for NF and 2 point for HF
  - BUT: series parasitics might be especially high impact at higher frequencies (inductive component) and thus contra indicate 2 point setup AND especially in BIOimpedance spectroscopy typical DUTs have capicitive character and will have lower impedance at higher freuqencies, which in turn might make the effect of additional parallel capacitance of 4pt setups negligible

- Always consider overall setup including the frequency dependant DUT and the cable parasitics

- Model overall impedance structure with simple equivalent circuit models - can also be simulated (SPICE) and while they will never be an exact match to the real world, they typically give "good enough" approximations to make educated decisions on the structure of the setup, cable types and electrode configuration

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beyond the analyzer – electrode choice

- electrode material, surface structure and geometry will greatly influence your measurements
- beware:
  - only because a certain chip is available in your lab it does not mean it´s the right choice
  - only, because someone has been using a certain chip for years and made lots of publications, this does not mean it´s a good choice - even if you want to do a similar experiment
- if no a priori knowledge for the measurement to be done is obtainable, than trial and error is an option: take several common geometries and test which gives good results - if needed reiterate with variations of the best working structure
- Chip contacting is important: Can you stick to an established format and use existing optimized adapters?

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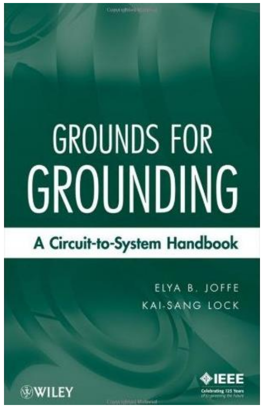
beyond the analyzer – shielding & guarding

- shielding in general is supposed to reduce effects of noise coupling
- mechanisms: capacitive and inductive coupling
- general shielding approach (active or passive): conductive material in between source and receiving end of possible distortion
- optimum shield topology & grounding strongly depends on the situation
- for EIS: shielding will also play a crucial role in terms of parasitic effects
- active guarding will limit stray capacitance effect
- special care when connecting multiple devices – multi point grounding might interfere with shielding topology and in case of multiple power sources several noise coupling mechanisms can be amplified
- in general: in order to get maximum performance, the setup needs an overall grounding and shielding concept incorporating all system and setup components as well as surrounding/supporting structures and machinery

great read: “Grounds for Grounding”
by Elya B. Joffe & Kai-Sang Lock



beyond the analyzer – temperature

- Conductivity may increase or decrease with temperature depending on material
  -> strongly depends on the charge transfer mechanism
- Dominating mechanism/mode of conduction changes over frequency
  -> tempco depends on frequency as well
- same with permittivity (depends on polarization mechanism)
- Example:
  - Conductivity tempco of electrode materials:
    …0.39%/K (copper, platinum), 0.34%/K (gold)
  - electronic PCBs, coax cables, insulation and housings or chip substrates:
    …0.01%...several %/K for both conductivity and permittivity
    …e.g. silicone has a conductivity tempco of 7.5%/K at low frequencies

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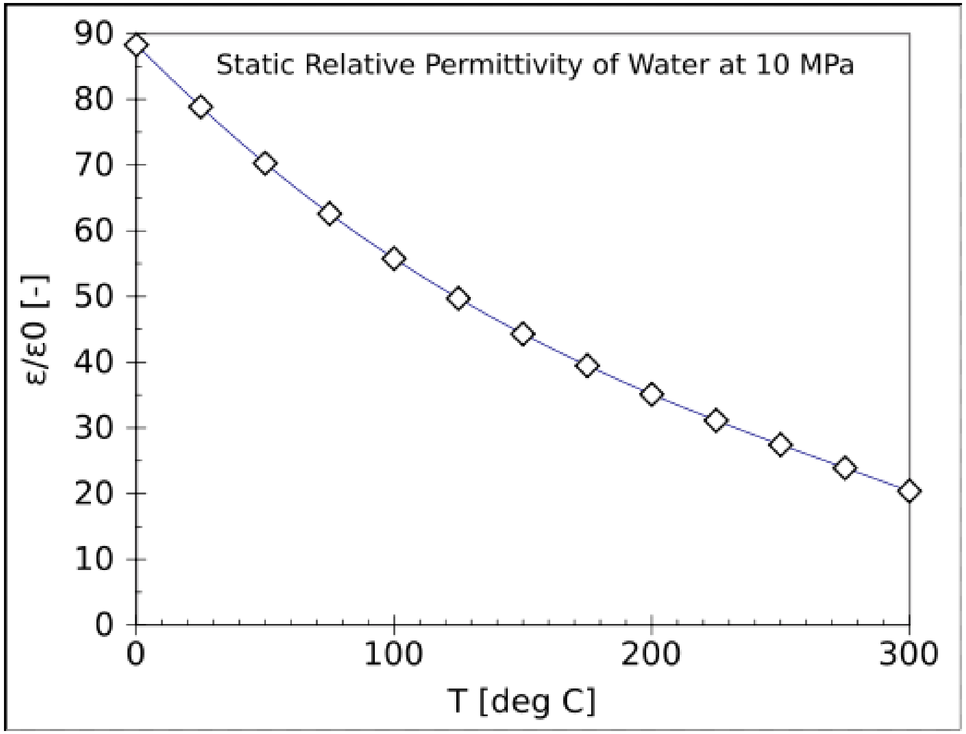
beyond the analyzer – temperature

- Example:
  fluidic media - relative permittivity of water will change at approximately 0.5% per Kelvin around room temperature



- In ionic solutions this gets a lot more complicated

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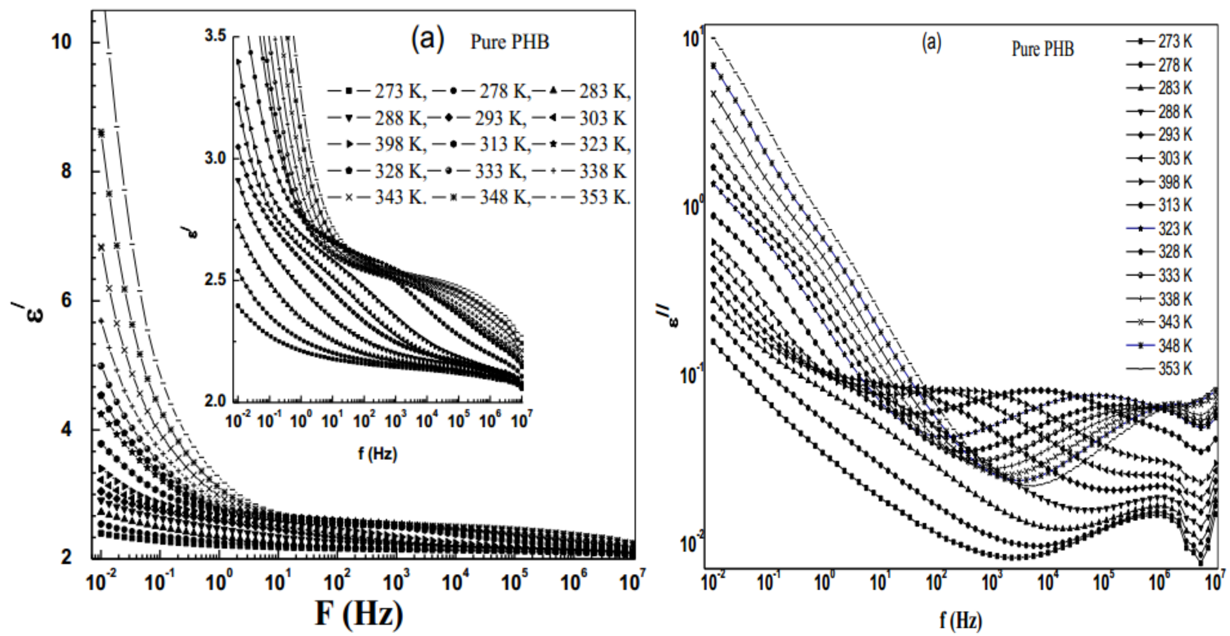
beyond the analyzer – temperature

- Example: biochip/fluidic channel
  Poly (hydroxyl butyrate) – aka "PHB" is widely used for disposable items and biomedical applications
- Shows highly complex frequency-dependant temperature behavior



published by Fahmy, Ahmed and colleagues (International Journal of Physics and Applications. ISSN 0974-3103 Volume 8, Number 1 (2016), pp. 1-14)

beyond the analyzer – temperature

In conclusion

- temperature dependence of conductivity and dielectric constant have largely complex behavior and will be in ranges that might well affect your results
- Material mix makes it all the more complicated
- Might be a good idea to closely control temperature

- Side Note: Similarly severe influences can be expected from humidity changes around the electrodes, contact boards or any other non-sealed portion of the measurement setup.

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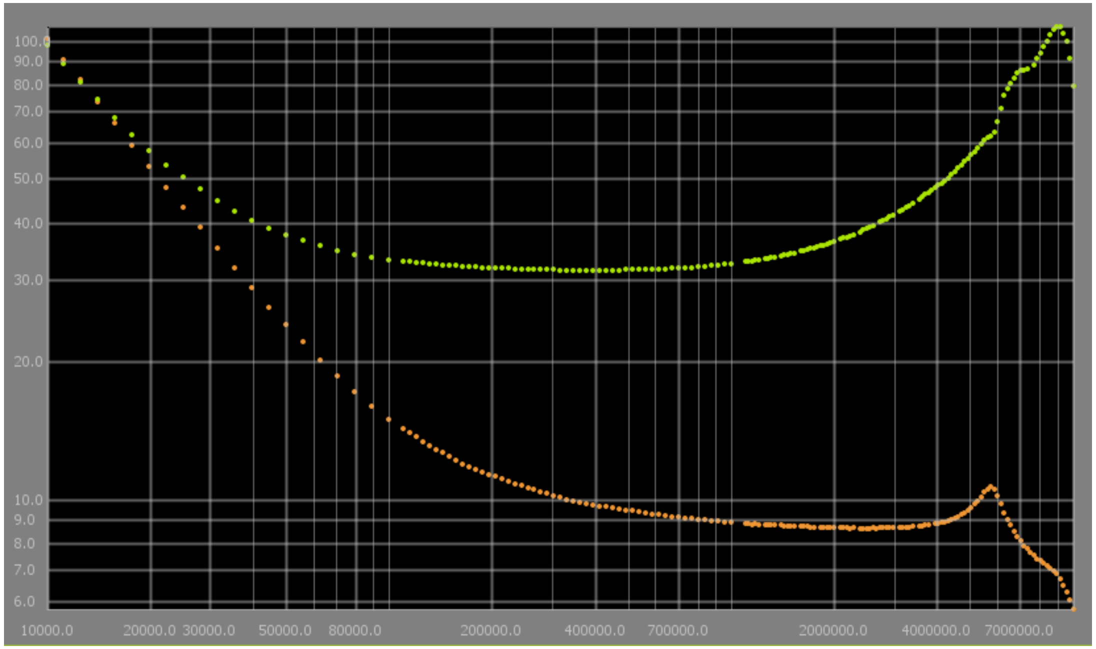
Why calibration does not magically fix it all…

- Calibration measurements are susceptible to same noise and distortion effects
- temperature dependency
- Is the calibration object and its contacting ideal? Almost never! – example shows result after calibration with badly contacted cal piece on chip electrodes (green) and specifically adapted cal chip (orange)



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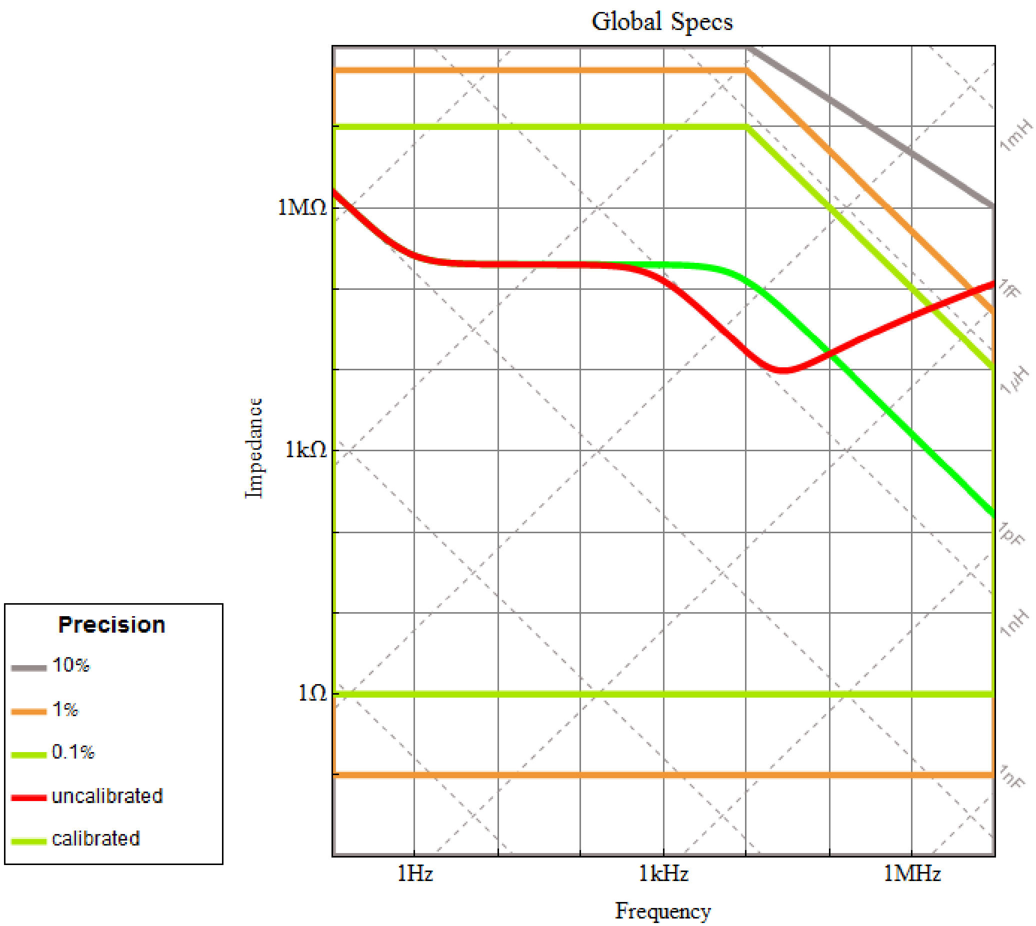
Why calibration does not magically fix it all…

- might bring result into a region, where accuracy upon uncalibrated result is much lower
- Careful: lowers your dynamic headroom and hides the impact on accuracy



- @ 1 MHz uncalibrated curve is at 100 kOhm and thus outside 1% accuracy range
- Calibration now "calculates" the parasitics out and gives green curve, but in reality the actual measurement still yields the red curve!
- calibrated curve gives 100 Ohm @ 1 MHz corresponding to 0.1 % of measured value and thus factor 10 below the accuracy rating for this measurement

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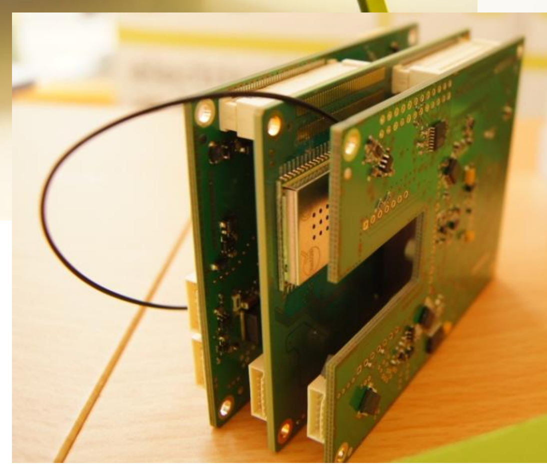
what else you should consider aka "the last 10% are the hardest"

- multichannel measurements, portability, atypical measurement modes
- Scalability: how to go on after proof of principle (field work, upscaling, specializing)
- Typical lab impedance analyzers are not scalable without extreme cost/effort
- Sciospec approach: built in modularity and flexibility.



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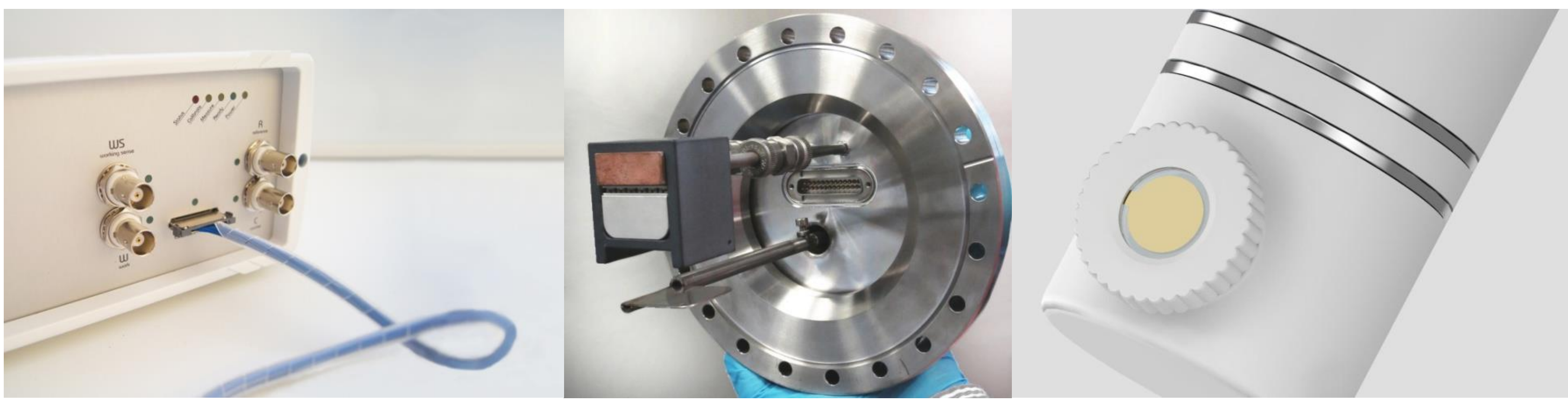
Making it fit: application specific frontends in combination with standard instruments

- some instruments offer specific support for extensions through external add-ons like adapters, temperature controllers etc.
- even better could be a solution that involves specifically designed frontend electronics, which is not impossible with standard instruments, but a little more challenging
- Sciospec approach:
  - example: extension port for application specific
  - specifications for all ports and interfaces are open access enabling users to build their own application specific modules like adapters, multiplexers, fluidic chambers, amplifiers etc.



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OMG – how can I handle all this?!

- complex measurements have complex have implications, dependencies that will greatly impact your results. Ignoring them leads to misinterpretations and wrong conclusions! Be aware of them and don´t ignore it just because it is not your primary research goal
- "Do I really need to know all this in depth?" Not necessarily. You must be aware of the influencing factors and be able to identify possible problems when interpreting your data.
- consult with an impedance expert on the **overall measurement setup** -> your chances will increase significantly
- How to deal with your dealer:
  - The sales personal problem
  - After sales support
  - beware of simplifications: When the instrument sales guy tells you only a price a that it will all pan out - be suspicious

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OMG – how can I handle all this?!

- The further down the chain of components the solution reaches the higher the chances for good results: Best fit will most likely be application specific solution.
- Example 1: Chip adapters with optimized multiplexer structures
- Example 2: Mimetas OrganoTEER® Lab on a chip solution measuring TEER
- Example 3: Nanion CardioExcyte 96 Lab on a chip solution Cardiomyocyte analysis


- **You don´t have to handle all this complexity by yourself: Ask an expert - this way you can focus on your core expertise.**
- **Don´t just buy an instrument, talk to the manufacturer about your application**

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Thank you for your attention.