Body impedance spectroscopy based on processing of step response

Uwe Pliquett[1], Nguyen Ngoc Duc[2], Trinh Dinh Yen[2], Nguyen Thi Thuong[2], Le Manh Hai[2]

[1]Institut für Bioprozess- und Analysenmesstechnik, Heilbad Heiligenstadt, Germany
[2]Institute of Biomedical Physics, Ho Chi Minh City, Viet Nam
Contact: Uwe.Pliquett@iba-heiligenstadt.de

Introduction

Body composition is an important measure, not only for body building or cosmetics, but mostly for medical reason [*1*]. The body composition, overwhelmingly the fat content and hydration status, can guide rehabilitation therapy but is also used for estimation of risks for patients undergoing surgery or any kind of analgesia.

The use of electrical impedance measurement relays on the fact that different tissues can be discriminated by their electrical impedance [*2*]. Blood has a higher conductivity than muscle and tissues like fat or bone show low conductivity. Even less conductive would be air intaken into the lungs.

At a first glance, modeling of the body seems fairly simple since the geometry of an average body and the electrical behavior of tissues are known. However, with the low number of variables measured, it is not possible to justify a complicate model. If, for instance, only the magnitude of the frequency at one single frequency is measured, modeling cannot access any detail.

Using the phase angle as well, additional information about compartments surrounded by intact cell membranes is possible. This can be used for distinction between water in- and outside of cells. Unfortunately, this is not sufficient for assessment of the fraction of free body water (i.e. inside intestine) and water bound in tissues. Having information of electrical properties over a greater frequency range can considerably increase the significance of the measured properties [*3*].

If impedance spectroscopy at whole body is performed using frequency domain approach, the measurement takes up to more than a minute depending on selected frequencies and integration time. A great uncertainty arises from moving artifacts and body functions like respiration or heartbeat. This can be overcome by fast measurements, at least twice as fast as then the period of such oscillating events or long integration times.

Fast measurements in time domain are common in several fields of bioimpedance measurement but most commercial BIA-devices (body impedance analysis) do not use this approach. Several studies using broad bandwidth excitation with monitoring the response in time domain are reported, mostly by employing multisine signals [*4*]. In general, these signals are Fourier-transformed and further processing is done in frequency domain. Although step voltage or current was employed as well [*5*], it was rejected by most researchers due to the following reasons:

1. If equidistant sampling and Fourier transformation is used, huge noise appears at higher frequency due to the decline of energy with increasing frequency.
2. The use of broad bandwidth amplifiers does not allow for efficient noise reduction as is possible with lock-in amplifiers.
3. The reproducibility, especially in the high frequency range is often poor due to the jitter of low cost acquisition systems (simple digital oscilloscope or data acquisition boards) where the channels are not synchronously triggered.
4. Uncertainties at low frequency arise due to the use of low resolution ADC (i.e. 8-bit).
5. Signals are often not consequently preprocessed, which results in higher quantization noise (e.g. only 6 or 7 bit used because the signal is too small) or aliasing effects occur (insufficient filtering).

All these limitations base on the practical approach but they are theoretically irrelevant, if the signals are processed in a proper way.

When seeking fast methods with minimal energy consumption, employing step response is an excellent choice. This, however, needs a more sophisticated approach than equidistant sampling with 8-bit resolution. A good approach may include:

1. If equidistant sampling is preferred due to the availability of the instrumentation (IO-cards, digital oscilloscope, data acquisition system) at least 12 bit resolution should be used. Moreover, the jitter between signal generation and sampling is critical and should be as small as possible. This should be taken into account for frontends and cabling as well.
2. A transformation into frequency domain is not necessary. Since the response of biological tissue to step functions (current or voltage) is the sum of exponentials, a direct calculation in time domain is much faster and yields adequate information. If needed, a simple calculation yields the impedance spectrum. Critical in this approach is the quality of the excitation signal. The step should be clear without overshoot and the rest of the signal has to be as flat as possible, otherwise more complicate calculations are unavoidable.
3. The highest frequency components appear immediately after the step while later only low frequency compounds are found. Therefore, a high sampling rate is necessary at the beginning of the signal and can slow down by orders of magnitude while the excitation signal lasts. It should be noted, that an anti-aliasing filter should be

adapted to the sampling rate in order to avoid unrecognized errors in the sampled signal.

Although some effort seems unavoidable, step excitation shows important features for upcoming applications. If a broad bandwidth signal like for instance multi sine but also step responses is sampled in order to achieve a frequency range of, for instance, four orders of magnitude (e.g. 100 Hz – 1 MHz), at least 20,000 Samples are necessary. With adaptive sampling, it can be reduced to 4 – 10 samples per decade, where 6 samples per decade yields sufficiently good results. This means, all together for 4 orders of magnitude, only 24 samples are needed. This has two important advantages: Because of the low number of samples, the ADC can be slow with low power consumption. Therefore high resolution ADC (e.g. 16 bit) can be used and the data stream in application with continuous sampling is still acceptable. This, however, requires special hardware where the sampling times are generated and adaptive filtering is accomplished by partial signal integration.

To show the features of impedance measurement with step excitation, we used a continuously sampling system (oscilloscope) but process the data in a way as it would have been with adaptive sampling. This allows us to test critical parameters for future developments of sophisticated hardware. Moreover, it is a good teaching example for those who are not familiar with processing step responses direct in time domain. The results of measurement with step stimulus were validated by comparison with multi sine excitation and Fourier transformation for obtaining the results in frequency domain.

It is the intention of the study described in this paper to show the practical approach of non-equidistant sampling of step functions for impedance calculation. The previous equidistant sampling allowed to process data in different ways for developing optimized algorithms and to learn how to improve the robustness of the method. Measurements at probands were here only used for developing the method. Therefore, results in terms of body composition are behind the scope of the paper.

Materials and Methods

Electrodes Commercial EKG-electrodes (Nikotabs®, Nikomed, USA) were used throughout the experiments. The electrodes have been contacted using miniature crocodile clamps and unshielded wires with the length of 1m.

Electrode placement Five healthy volunteers took place in the study and their body impedance was repeatedly measured using different stimulation signals and measurement procedures. They were connected to the electrodes in one-side arrangement with two electrodes (stimulus and monitor) at the left hand and the complimentary electrodes at the left leg. The whole body was insulated to ground with exception of the unavoidable parasitic capacitances.

The distance between the stimulus and monitor electrodes was 5 cm (Fig.1). The probands were allowed to have about 10 min rest before the measurement started. Always 10 measurements (1 measurement / s) were conducted for each experimental condition.

Using very fast measurement at a frequency of 50 kHz every 1 ms (1,000 measurements/s), we proved a minimum sensitivity to heart activity and respiration during the measurements. However, despite the fact that the measurement is stable against vital body activities, moving artifacts still occur.

In order to cut out these artifacts, we calculated an average spectrum from the 10 single measurements. All spectra which were outside a single standard deviation were removed and the average spectrum was calculated again. In general, not more than one or two spectra per experiment were discarded. If electrode placement was bad or extreme movement artifact occurred, we repeated the entire measurement.



Figure 1 The driving electrodes 1 and 4 inject the stimulus while the voltage dropping across the body was monitored by the electrodes 2 and 3.

Impedance measurement instrumentation

In spite of future developments we took advantage of measurements in time domain. The most critical part for this procedure is the choice of the excitation signal but also the sampling of the response. The suitable frequency range for BIA is between 100 Hz and 1 MHz which is four orders of magnitude. Suitable broad bandwidth excitation signals are for instance step functions, multi sine, maximum length sequence or chirp. All these function are easily implemented in an arbitrary waveform generator. Throughout the experiments reported here, an AWG2021 (Tektronix) was used for generation of the stimulating signal. The response was always sampled by a DPO 2022B – oscilloscope (Tektronix). The two channels of the oscilloscope were used for measuring the voltage across the monitor electrodes and the total current injected. Since both waveforms, voltage and current, may have slow edges (e.g. multi sine) or have a high noise level, we used the trigger output of the generator and the auxiliary input of the oscilloscope for triggering.

The frontend consisted of a differential driver which injected the stimulating waveform (voltage controlled) into the outer electrodes (electrode 1 and electrode 4 in fig.1). The current was monitored as voltage drop across a serial resistor. In order to guarantee symmetric operation, equal resistors were placed at each outputs of the driver. A high impedance, differential amplifier matched the signal to the 50-Ω impedance of the coaxial cable connecting the oscilloscope. An amplifier equal to this for current measurement was used for monitoring the voltage across the monitor electrodes. The input of the oscilloscope was terminated with 50 Ω.

The oscilloscope recorded the waveforms with 125,000 samples in a 8-bit format (without average) or in 16 bit format (32 x Average). It should be noted that the 16 bit format does not necessarily mean that such resolution is indeed reached. This depends on the noise level of the signal and the number of averages.

The stimulus was applied as symmetrical, repeating step functions (square wave) with voltage control at the electrodes 1 and 4 (Fig. 2). Due to the capacitive behavior of the skin and the electrodes, the total current through the body is differentiated. Therefore, the voltage across the inner electrodes is differentiated as well.

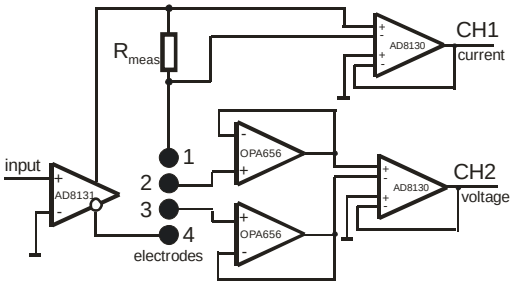


Figure 2 Schematic of the frontend. Although potentiometric stimulus is applied between the electrodes 1 and 4, the exctitation on tissue level depends on the capacitive behavior of the skin. Therefore, measurement of both, voltage and current is required.

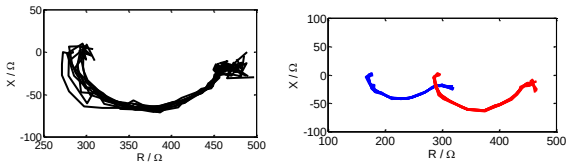
One aim of the measurements was to show that energy minimized solution with low data volume can achieve the same accuracy than reference methods. Therefore, the response to step functions was traced using an oscilloscope and further calculation (sample point, signal integration) was done digitally. Although this does not show any advantage for the particular measurement, it is the basis for future developments, like for instance wearable systems with power harvesting.

Results and discussion

Multisine: The signal with 69 logarithmically spaced frequencies between 100 Hz and 1 MHz was continuously applied. This ensures steady state condition which is required for transformation into frequency domain by fast Fourier transformation. The frequency lines were multiples of 100 Hz with phase optimization in order to minimize the crest factor.

It is important that the time shift between current and voltage is essentially zero which depends on the equipment used and is not always accomplishable. However, the highest jitter between the channels was not more than the time between adjacent sample points, here 80 ns. Further disturbance was prevented by matching the group delay of the voltage and current channel.

Using the recording in sample mode, only 8 bit resolution was available and a higher noise level appeared. Therefore, the reproducibility of the measurements was less (Fig 3 A) than with averaging (Fig 3.B). Having different probands, clear and reproducible differences in impedance were evident (Fig.3.B). Especially big was the difference between male and female test persons.



A B

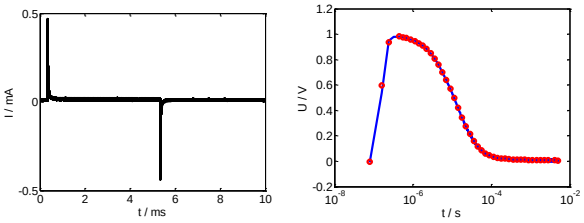
Figure 3 (A) Wessels diagram from 10 single measurements with 1 s spacing and an electrode configuration shown in Fig. 1 without averaging of the current and voltage response (B) Wessels diagram of two persons (measurements with 16 x averaging) (blue male, red female).

Step response: In general, the response of step function can be handled in the same way as the multisine response. In this sense, it does not have any advantage. Quite opposite, the noise level rises dramatically with increasing frequency due to the fast declining energy.

In order to show the way for taking advantage of the step response with respect to energy minimization and minimal data volume, we use a special processing. Currently, we develop hardware solutions for this purpose which is behind the focus of this paper.

Sampling: The idea is to sample fast where fast changes of the signal occur and slow it down with time. Moreover, since we can assume that he signal is symmetrical between the half periods, only one half period needs to be sampled. With the sample vector obtained in this way, FFT is impossible and needs to be replaced by analytic integration of the product between measured signal and test function (sine and cosine function). This implies that, in opposite to FFT, the time point where the step is applied is 100% known and set to t=0s. It would be simple if the hardware does not show any jitter. However, in our experiments a jitter of $\pm\Delta t$ = 80 ns for a sampling rate of 12.5 MS/s was unavoidable.

Using a fit procedure, the exact time point t_0 of the step was calculated. Rounded to the next integer, it was used to extract exactly a half wave from the signal. The time vector was subsequently adjusted with the fractional part of t_0.



A B

Figure 4 (A) current response of the step voltage and (B) processed response with partial averaging in a logarithmic scale

A sole processing of one half period requires complete offset compensation. Since it is our intention to show ways for efficient hardware and data processing in the future (ultra-broad bandwidth, lowest energy consumption),

we resample the equidistantly spaced vector using a logarithmic function. Since simple sampling with increasing sample interval would violate the sampling theorem, adaptive low pass filtering was realized by integration over the entire sampling interval. This is a critical step, which is also required for future hardware solutions.
Both, the current and voltage were traced and processed as shown in Fig.4 for the current. The integration intervals were logarithmically distributed.

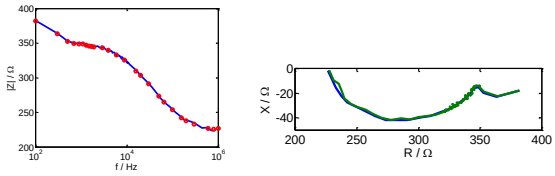
The re-sampled vector with logarithmic spacing (Fig.4) cannot be transformed with methods like Fast Fourier Transformation. Here, we solved the Fourier-integral partially between adjacent time points. The processing of the data included:
- determine the exact time of stimulating step
- resample with logarithmic spacing in time
- calculate the Fourier-coefficients

$$A(\omega_k) = \sum_{i=2}^{N-1} \int_{t_{i-1}}^{t_{i+1}} (a_i t^2 + b_i t + c_i) e^{-j\omega_k t} dt \qquad i = 2,4,\dots,N-1$$

where A is the real Fourier-coefficient for the k[th] harmonic frequency. In this approach, a square approximation of f(t) using three samples was used. Other functions like linear or exponentially can be used as well. Besides, the A-coefficients, also the B-coefficients (imaginary part) had to be calculates for current and voltage as well.
- calculate the impedance (or transfer function) by

$$Z(j\omega) = \frac{U(j\omega)}{I(j\omega)} = \frac{(A_U + jB_U)}{(A_I + jB_I)}$$

Although, it seems complicate, it is a pure analytical solution and needs minimal resources of an FPGA or microcontroller. The ratio of the Fourier transformed voltage and current (F(U) / F(I)) yields a transfer function having the unit of impedance but is physically not really an impedance due to the electrode placement.
A typical result is presented in Fig. 5.



A B

Figure 5 (A) Magnitude of the transfer function using the electrode configuration in Fig.1 for a healthy volunteer. The blue line is calculated a reference using ordinary FFT with logarithmic averaging of the unprocessed signal while the red circles show the result of data processing introduced above. (B) Wessel diagram for the same data in comparison between the both ways of processing.

The reproducibility of the results is critical but also the robustness against uncertainties in the measurement chain. Here, mostly timing errors and noise have been prominent sources of uncertainties. We repeated all measurements 10 times with 1 s spacing (Fig.6). A high impact on the high frequency part of the spectrum was found when the exact timing of the signals, especially the time when the step occurs (t_0), was not exactly calculated.

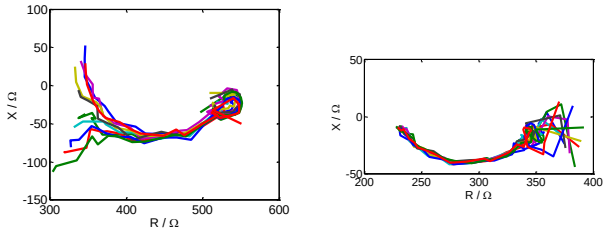


Figure 6 (A) Wessel diagram with 10 subsequent measurements with 1 s spacing without processing of time vector and trigger condition t_0, (B) corrected jitter.

The uncertainty of the results depends on both, the measurement method and the way of data processing. Moreover, at high and low frequency, uncertainties are more prominent. In the low frequency region, mostly the high resistance of the electrodes overwhelms any influence from inside the body and at high frequency, cable effects and the influence of parasitic capacitances, for instance between the body and ground become important.

Conclusions

Despite impedance measurements are long under investigation and are used for many applications, equipment for fast, broad band measurements with high repetition rate but ultralow power consumption is still missing. A candidate concept is the use of step functions for excitation together with adaptive sampling, aiming in nearly equally distributed energy throughout the spectrum for the sampled response. With timing as hardware solution, this concept is feasible for ultralow power applications, such as distributed system with energy harvesting.

Having only minimal data volume, the bottleneck of data transmission and processing becomes irrelevant.

References

1 Jacobs, D. O. (1993) Bioelectrical impedance analysis: a way to assess changes in body cell mass in patients with acquired immunodeficiency syndrome?, *JPEN. J. Parenter. Enteral. Nutr. 17*, 401-402

2 Gabriel, S., Lau, R. W., and Gabriel, C. (1996) The dielectric properties of biological tissues: II. Measurements in the frequency range 10 Hz to 20 GHz, *Phys. Med. Biol. 41*, 2251-2269

3 Cornish, B. H., Ward, L. C., Thomas, B. J., Jebb, S. A., and Elia, M. (1996) Evaluation of multiple frequency bioelectrical impedance and Cole-Cole analysis for the assessment of body water volumes in healthy humans, *Eur. J. Clin. Nutr. 50*, 159-164

4 Bragos, R., Blanco-Enrich R., Casas, O., and Rosell, J. (2001) Characterisation of dynamic biologic systems using multisine based impedance spectroscopy Instrumentation and Measurement Technology, 1 ed., pp 44-47,

5 Pliquett, U., Gersing, E., and Pliquett, F. (2000) Evaluation of fast timedomain based impedance measurements on biological tissue., *Biomed. Techn. 45*, 6-13