

(別記様式-博7)

千葉大学審査学位論文 (要約) (Summary)

基幹工学 専攻 機械工学 コース
Division Department

氏名 キアグス アウファ イブラヒム
Name Kiagus Aufa Ibrahim

論文題名 (外国語の場合は、その和訳を併記)
Thesis Title (foreign language title must be accompanied by Japanese translation)

**Sodium-Ion Concentration Measurement in Skin by Time-constant-domain
Electrical Impedance Spectroscopy (TCD-EIS)**

時定数領域電気インピーダンス・スペクトロスコピー法 (TCD-EIS)による皮
膚内ナトリウム・イオン濃度測定

The aim of this thesis is to develop an accurate measurement technique for sodium-ion concentration in dermis layer using time-constant-domain electrical impedance spectroscopy (TCD-EIS). The aim is achieved by a series of systematic steps of the following objectives: 1) Sodium-ion concentration extraction in the dermis layer by time-constant-domain electrical impedance spectroscopy (TCD-EIS) with dermis separation model (DSM); 2) Skin layer classification in conductivity changes by source indicator trained from feedforward neural network in bioelectrical impedance spectroscopy; 3) Free and bound sodium identification in human skin model by skin dielectric properties separation algorithm of bioelectrical impedance spectroscopy (spa-BIS). The details of present study explained in this thesis can be summarized as follow:

Chapter 1

This chapter has highlighted the significance of sodium-ion concentration in the skin and its association with various skin diseases [1] and systemic disorders [2]. The measurement of each skin layer and identifying free and bound sodium in the skin offer valuable insights into sodium storage, regulation, and potential treatment targets. Sodium-magnetic resonance imaging (^{23}Na -MRI) is commonly used in-situ to measure sodium-ion concentration in the dermis layer of the skin [3]. However, its limitations have led researchers to explore other methods, including bioelectrical impedance spectroscopy (BIS), which is non-invasive, fast, inexpensive, and portable [4]. BIS can overcome the limitation of considering skin as a bulk instead of layer composition, but careful consideration and standardization of testing settings are crucial for accurate and reliable results. Furthermore, accurately determining the electrical properties of each skin layer using BIS can be challenging.

Chapter 2

The chapter discusses the drawbacks of using Electrical Impedance Spectroscopy (EIS) in the measurement of sodium-ion concentrations. One solution to this is using time-constant-domain electrical impedance spectroscopy (TCD-EIS) based on the distribution of relaxation times (DRT) [5], which is a method that can be used to obtain more accurate results in the measurement of sodium-ion concentrations. DRT allows for the characterization of complex systems with multiple relaxation processes [6], which is particularly useful for electrolyte systems [7]. Thus, TCD-EIS can be a viable solution for the measurement of sodium-ion concentrations.

Chapter 3

This chapter focuses on identifying free and bound sodium characteristics based on phantom skin fabrication and the skin dielectric properties separation algorithm of electrical impedance spectroscopy (spa-BIS). The spa-BIS is developed through three stages: 1) conductivity-permittivity

conversion [8], 2) contact impedance compensation [9], and 3) a correlation score algorithm based on a bipolar circle electrode, as shown in Figure 1. Figure 2 shows that the algorithm successfully identifies sodium type: free sodium has a positive, and bound sodium has a negative correlation score trend. The study demonstrates that spa-BIS has a prominent performance to replace ^{23}Na -MRI in terms of free and bound sodium identification.

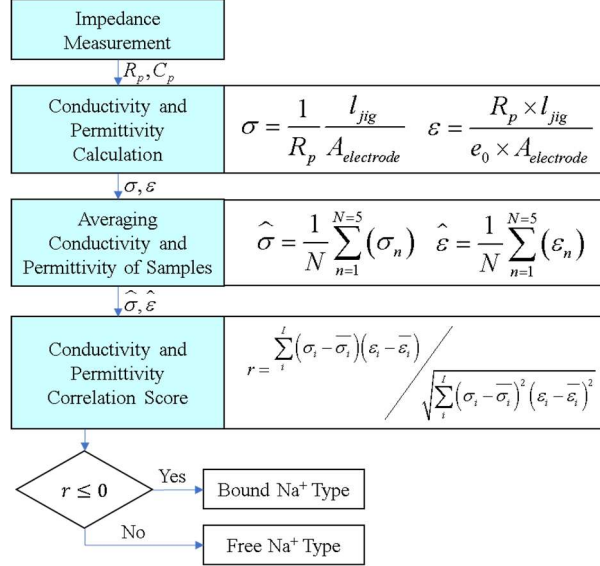


Figure 1. Correlation scoring algorithm based on spa-BIS

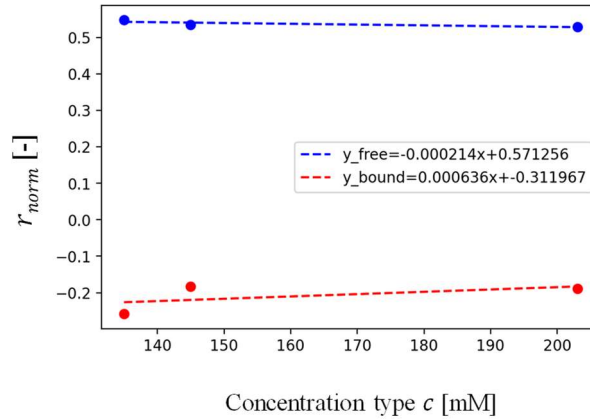


Figure 2. Correlation score between free and bound sodium

Chapter 4

This chapter focuses on developing a technique to measure sodium-ion concentration in the dermis layer of porcine skin using TCD-EIS with DSM. This technique involves three stages: dermis separation formulation, numerical optimizations, and dermis relaxation times with radial base function [10], as shown by Figure 3. The optimized TCD-EIS with DSM is then applied to porcine skin under various conditions, and both simulation and experimental results show that the normalized distribution

function of the dermis decreases with the increase of sodium-ion concentration, revealing the sodium-ion concentration in the dermis layer.

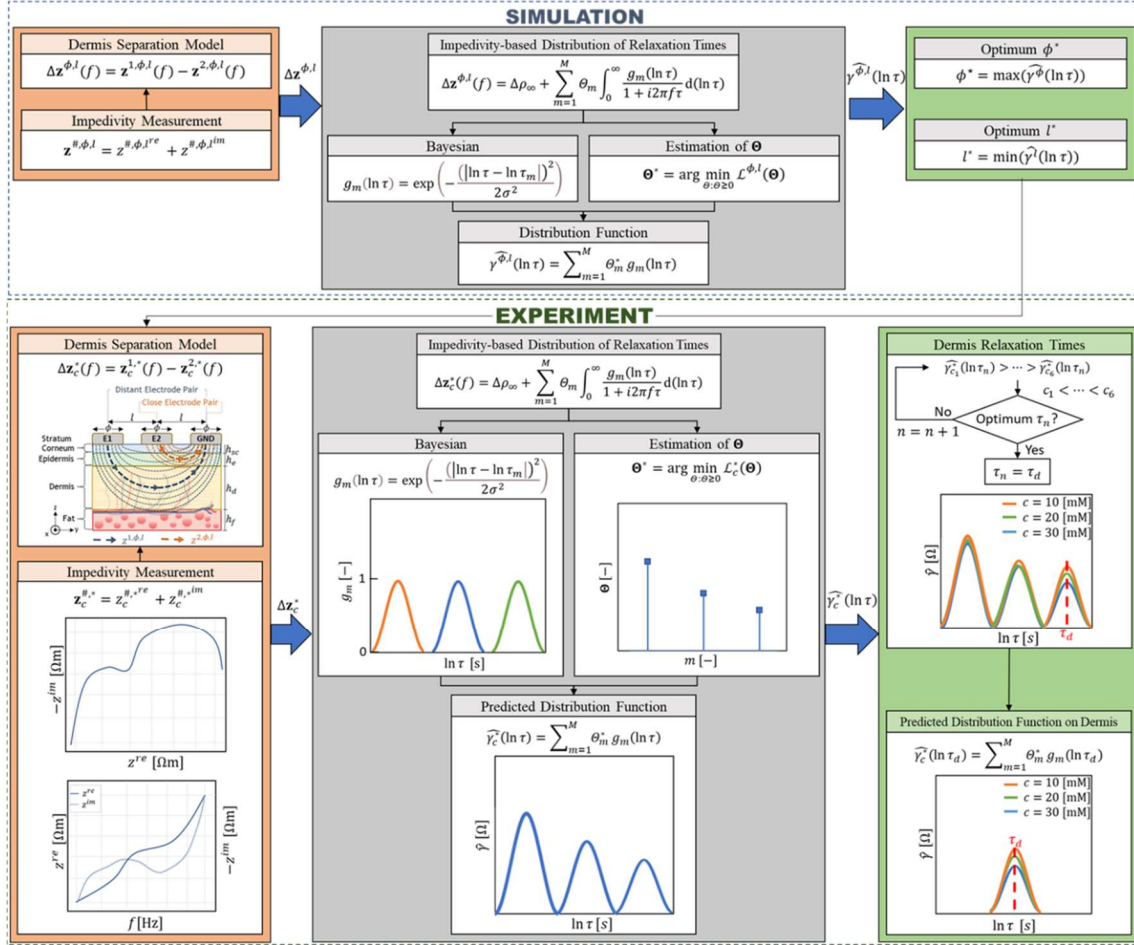


Figure 3. Conceptual figure of TCD-EIS with DSM

Chapter 5

This chapter presents a method to classify skin layers based on conductivity change using bioelectrical impedance spectroscopy (BIS) and a feedforward neural network (FNN). The study involved developing four impedance input profiles [11] and selecting frequency pairs using distribution of relaxation time (DRT), as shown by Figure 4. The FNN was trained using numerical simulations and validated through BIS experiments with porcine skin [12]. The proposed method successfully classified conductivity changes in the dermis layer with high accuracy, and the selected frequency pair based on DRT minimized measurement noise and systematic error.

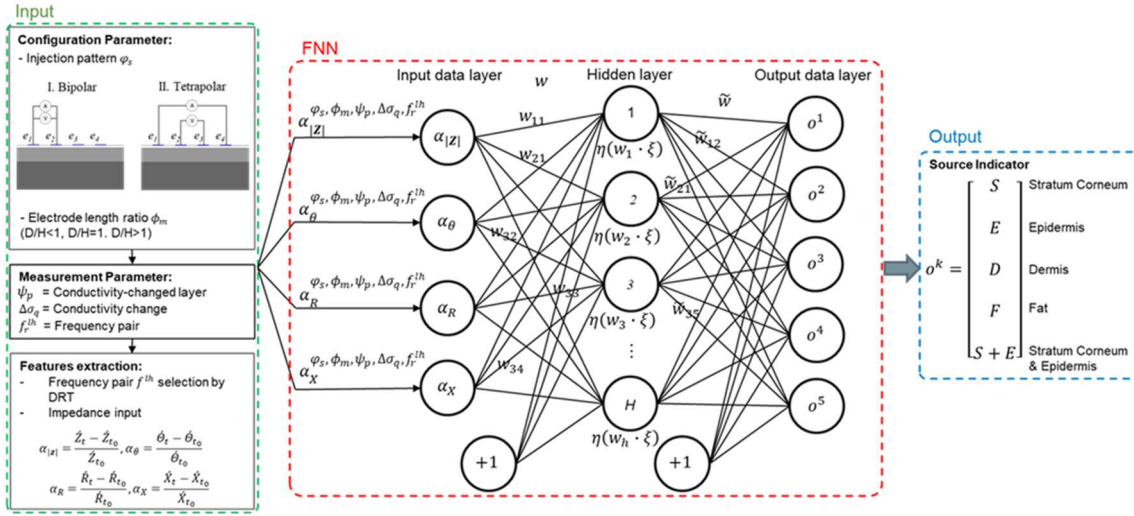


Figure 4. Schematic flow of skin layer classification of conductivity change

Chapter 6

This chapter presents another application of planar sensors in industrial applications. The copper (Cu) particles have been detected among significant aluminum (Al) particles in a wet-type gravity vibration separator utilizing an integration of generative adversarial network and electrical impedance tomography (GAN-EIT) [13]. GAN-EIT generates two kinds of images of different Cu positions among significant Al particles, which are 1) the photo-based GAN-EIT images, and 2) the simulation-based GAN-EIT images. In static conditions, the proposed GAN-EIT is utilized to evaluate the performance of the metal detection method with different positions of Cu particles. In conclusion, the results showed that the GAN model successfully enhanced the EIT images, resulting in more feasible images for distinguishing between the different Cu positions.

In summary, three different studies aimed to extract and identify sodium-ion concentration in the dermis layer of the skin. The first study employed a skin dielectric properties separation algorithm called spa-BIS. The second study used TCD-EIS with DSM, while the third study utilized skin layer classification in conductivity changes through feedforward neural network in bioelectrical impedance spectroscopy. All three studies showed promising results in accurately identifying and classifying sodium-ion concentration in the dermis layer of the skin. These findings could be useful for improving the diagnosis and treatment of skin diseases and for gaining a better understanding of skin pathophysiology. Another study conducted to apply planar sensor in industrial applications.

References

- [1] Maifeld A, Wild J, Karlsen T V., Rakova N, Wistorf E, Linz P, et al. Skin Sodium Accumulates in Psoriasis and Reflects Disease Severity. *J Invest Dermatol* 2022;142:166-178.e8. <https://doi.org/10.1016/j.jid.2021.06.013>.
- [2] Hanson P, Philp CJ, Randeve HS, James S, O'Hare JP, Meersmann T, et al. Sodium in the dermis

- colocates to glycosaminoglycan scaffold, with diminishment in type 2 diabetes mellitus. *JCI Insight* 2021;6. <https://doi.org/10.1172/jci.insight.145470>.
- [3] Qirjazi E, Salerno FR, Akbari A, Hur L, Penny J, Scholl T, et al. Tissue sodium concentrations in chronic kidney disease and dialysis patients by lower leg sodium-23 magnetic resonance imaging. *Nephrol Dial Transplant* 2021;36:1234–43. <https://doi.org/10.1093/ndt/gfaa036>.
- [4] Tsai B, Xue H, Birgersson E, Ollmar S, Birgersson U. Dielectrical properties of living epidermis and dermis in the frequency range from 1 kHz to 1 MHz. *J Electr Bioimpedance* 2019;10:14–23. <https://doi.org/10.2478/joeb-2019-0003>.
- [5] Boukamp BA. Fourier transform distribution function of relaxation times; application and limitations. *Electrochim Acta* 2015;154:35–46.
- [6] Ciucci F, Chen C. Analysis of electrochemical impedance spectroscopy data using the distribution of relaxation times: A Bayesian and hierarchical Bayesian approach. *Electrochim Acta* 2015;167:439–54.
- [7] Ramirez-Chavarria RG, Sanchez-Perez C, Romero-Ornelas L, Ramon-Gallegos E. Time-Constant-Domain Spectroscopy: An Impedance-Based Method for Sensing Biological Cells in Suspension. *IEEE Sens J* 2021;21:185–92. <https://doi.org/10.1109/JSEN.2020.3014569>.
- [8] Neuman MR, others. Biopotential electrodes. *Med Instrum Appl Des* 1998;4:189–240.
- [9] Bennett D. NaCl doping and the conductivity of agar phantoms. *Mater Sci Eng C* 2011;31:494–8. <https://doi.org/10.1016/j.msec.2010.08.018>.
- [10] Wan TH, Saccoccio M, Chen C, Ciucci F. Influence of the Discretization Methods on the Distribution of Relaxation Times Deconvolution: Implementing Radial Basis Functions with DRTtools. *Electrochim Acta* 2015;184:483–99. <https://doi.org/10.1016/j.electacta.2015.09.097>.
- [11] Ollmar S. Methods of information extraction from impedance spectra of biological tissue, in particular skin and oral mucosa - A critical review and suggestions for the future. *Bioelectrochemistry Bioenerg* 1998;45:157–60. [https://doi.org/10.1016/S0302-4598\(98\)00082-8](https://doi.org/10.1016/S0302-4598(98)00082-8).
- [12] Wake K, Sasaki K, Watanabe S. Conductivities of epidermis, dermis, and subcutaneous tissue at intermediate frequencies. *Phys Med Biol* 2016;61:4376–89. <https://doi.org/10.1088/0031-9155/61/12/4376>.
- [13] Sejati PA, Baidillah MR, Prayitno YAK, Ibrahim KA, Kawashima D, Takei M. Copper particle detection method by in-situ resistance background implemented in conductance-path recognition algorithm (iRB-CPR) among dominant aluminum particles. *Measurement* 2022;193:110983. <https://doi.org/10.1016/j.measurement.2022.110983>.