A Novel Mathematical Model to Represent the Hypothalamic Control on Water Balance

Divya Jangid and Saurabh Mukherjee

October 30, 2021

A NOVEL MATHEMATICAL MODEL TO REPRESENT THE HYPOTHALAMIC CONTROL ON WATER BALANCE

Ms. Divya[1], Dr. Saurabh Mukherjee,
Department of Computer Science, Banasthali Vidyapith, Banasthali-304022, Tonk, Rajasthan (India)

ABSTRACT:
For the stability maintenance process of internal environment of Human body various parameters are responsible such as temperature, water, glucose and a number of hormones participated. Homeostasis is an important substantial process which maintains the threshold value for all these basic parameters of human body. Osmoregulation, Energy balance, Respiratory system and appetite control are four major components of Human Homeostasis process. A homeostasis process which balances the water level in Human body is Osmoregulation. The threshold value for the hydration level of each cell is retained by Osmoregulation process. Osmoregulation controls the water level in different internal organs of human body. Some of the internal organs participated in this process such as Hypothalamus, pituitary gland, kidney etc. Osmoregulation starts from the smallest unit like cell till the respiratory system. But the domain for the introduced mathematical model is limited to the organ level only. An Antidiuretic Hormone (ADH) i.e. Vasopressin is the main regulator for the Osmoregulation process at organ level. The Hypothalamic Water control Mathematical Model is being designed and deployed to represent the Water regulation process.
Keywords: Hypothalamus, Hypothalamic hunger Regulation Model, Water Balance, Osmoregulation, Anti Diuretic Hormone (ADH).

1. INTRODUCTION

The stable state of different functions of human body is maintained by the Homeostasis process. The factors which participate in balancing different physiological parameters of Homeostasis are Hunger regulation, Energy Balance, Osmoregulation (Water Balance), Thermoregulation and so on[3][4].Mathematical modeling is an influential and impactful way to define, analyze and postulate the homeostatic and Endocrine functions(Systems)[18] of human body like Hunger Regulation[1][2], Water balance, and HPA(Hypothalamus-Pituitary-Adrenal)System[5].Our major concern is about theWater regulation process (Osmoregulation) with hypothalamic effect. It depends on many parameters like Blood Volume, Blood Pressure, and Osmotic Pressure and so on. Osmotic pressure is the main simulator for Osmoregulation and it quantifies the tendency of water during osmosis. The extra water from Human body is drained out during water osmosis. Osmotic pressure is directly proportional to the water requirement by different internal organs. In other words we can say that osmotic pressure prevents the water level from too much diffusion or too much concentration[8].If the water level is too much higher than the average threshold the osmosis process will start whereas Thirst (Dry Mouth Theory,1779) is a significant indicator for the decrease in water level from the specific threshold value. Thirst helps in maintaining hydration level of human body and stops the osmosis process [10][11]. The negative feedback process of osmolality instigate and regulates the feeling of thirst and it increase the release of ADH on the Circumventricular organs (Hormonal neurons) [17].The Circumventricular organs influence the hunger regulation and initiate thirst signals[16].Water Balance (Osmoregulation) and Hunger regulation are strongly connected. Similarly Hunger and thirst are directly connected in the same way. Now a day this connection is effected by today's eating behavior but the basic parameters for this connection cannot be denied [8][9]. Both Hunger and thirst are very strong sensation but thirst is more stable and effective. Thirst instigates the process of water intake which is further integrated by different nerve, Hormonal and osmotic signals [11]. The osmotic signals (Osmoreceptors)and hormonal signals are received and generated by hypothalamic nuclei respectively. Supraoptic (SON) and Para-ventricular (PVN) nuclei located at the anterior region of Hypothalamus majorly participated in Osmoregulation. The eating behavior and the fluid regulation is executed together efficiently and smoothly by the neuro-signal generated at Subfornical Organs [12]. During the recent studies on mice depicts the effect of sleep and active state on homeostasis level of water regulation. The Vasopressin the Anti-diuretic Hormone, polarizing effect increase the electrical activity of neurons at Subfornical organ during active state which result into more water intake whereas during final state of sleep, Vasopressin,secreted by magnocellular neuro-secretory cells at the hypothalamic nuclei (Supraoptic and PVN), increase the water reabsorption by

[1] Corresponding Author:
Email: jangid.divya@gmail.com.

internal organs (Kidney) until recommence of water intake[13][14].The initial detection of thirst starts from the osmotic signals generated gastrointestinal instigate the throat osmolarity level(dryness in throat) which is further balance by the hypothalamic signals by consumption of water[15].

2. OBJECTIVE

The objective of Our Model (HWBMM) is to present a base mathematical model which describes the hypothalamic impact in maintaining the water balance at homeostatic level. It also represent the mapping between theosmotic signals and hormonal signals, the spikes generated and regulatedat hypothalamus for the feeling of thirst (Water requirement) and water balancingin human body. We also consider some basic parameters for the analysis report which only gives hypothetical validation.

3. MOTIVATION

For Hunger regulation a general mathematical representation was being introduced, named HhRM (Hypothalamic Hunger Regulation Model) [1]. Our Model (HWBMM) i.e. Hypothalamic Water Balancing Mathematical Model is also dependent on the concept of HhRM and the optimized HhRM [1][2]. Moreover, at physiological level Osmoregulation process for human has been studied regularly with psychological and analysis perspective but this physiological process was never described from the mathematical aspect. However some of the researchers has represented mathematical model on Endocrine system. These models concentrate on the impact and functioning of Hypothalamus and pituitary gland in endocrine functioning in human body. A mathematical model based on the physiology of HPA systems are defined where the positive and negative feedback of homeostasis used as the key regulator [16]. A differential equation based mathematical is used to define the Endocrine system where all the hormone-concentrationand endocrine gland represented via differential equations (linear and nonlinear) [18].

4. HYPOTHALAMIC WATER BALANCE MATHEMATICAL MODEL

The methodology for the development of the Mathematical model can be explained in multistep process. Each step is specific to the activity of thirst and osmosis process. The presence of the Vasopressin Hormone and change (increase/decrease) in its secretion start the process at physiological level. The whole process of HWBMM (Water Balance) is explained with block diagram in *Figure1*.

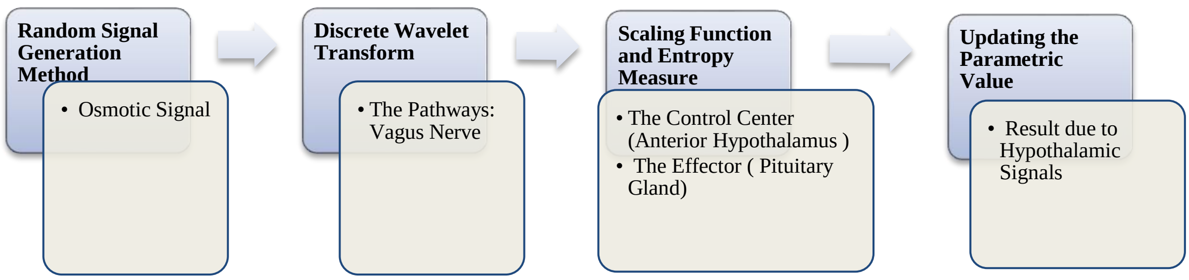

Figure 1: The Steps for HWBMM with the mathematical Terms

Step-1:
Osmotic Signal: Increase and decrease in the Water level from its homeostatic level identify by the negative feedback homeostatic level (Negative feedback process for Water Regulation). The parameters participate in this process, osmotic pressure, updated from it stabilized value.This change perceived by Osmoreceptors i.e. homeostatic neurons. Vasopressin Hormone secretion also update from the homeostatic level.The non-uniformly generated random numbers are used for the parametric value of Osmotic Signals.

Step-2:
Pathway for the Signal: The osmotic signals from the Osmoreceptors further regulated to Hypothalamic Nuclei, Supraopticand Paraventriculer Nuclei via Vagus Nerve. The Osmotic Signal travels the path of Vagus nerve by blood stream which destined the Osmotic signals to Forebrain. The Discrete wavelet transform is being used to represent the Osmotic signal with fractal constant.

Step-3:

Control Center and Effectors: The Hypothalamic signals generated atanterior part i.e.SupraopticandParaventriculerNuclei which further communicate with the Posterior Pituitary Gland to release Vasopressin, theAntidiuretic Hormone into the Blood stream. The Scaling function with Entropy measure is applied for the activation of the Hypothalamic Signal. The variance property of the scaled signals is also used to optimize the parametric value of the signals.

Step-4:

Updating the Parametric Value: The Vasopressin hormonal signals are transferred from the internal organs (Adrenalgland (kidney), Lungs)to Hypothalamic Nuclei (PVN and SON).It decreases the rate of loss of water from the and vice-versa.

The physiological effect of ADH on the internal organs is either water absorption or water secretion. Increase in ADH is responsible for decrease in loss of water and decrease in ADH is responsible for increase in loss of water from different internal organs which participated in Osmoregulation process (Figure 2).

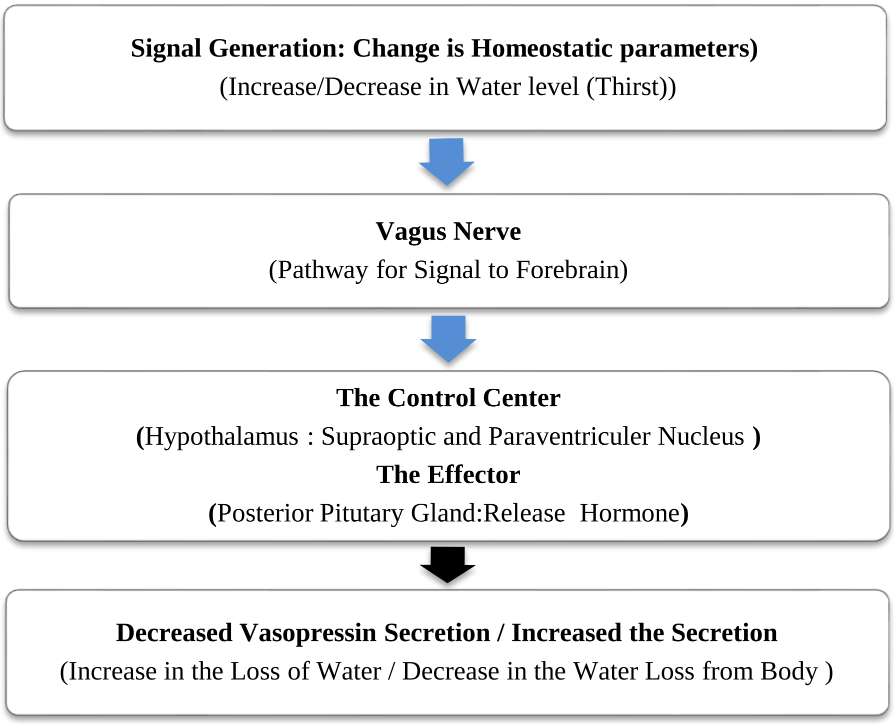

Figure 2: Block Diagram for the Hypothalamic Water Balance process

The HWBMM includes the following Assumptions and functions:

The process starts with the Assumption that Vasopressin hormone release positively. Osmoregulation can be divided into two sub processes HyperOsmolality and HypoOsmolality. A binary function **f(o)** is used to start the process after Vasopressin Release and identification between HyperOsmolality (Increase in secretion of Vasopressin concentration (VC)) and HypoOsmolality (suppress the secretion of Vasopressin concentration):

$$\mathbf{f\,(o)} = \begin{cases} \mathbf{1} & \textbf{for} \quad \textbf{ST} <= \textbf{VC} <= \textbf{HT (HyperOsmolality (Thirst))} \\ \mathbf{0} & \textbf{for} \quad \textbf{LT} <= \textbf{VC} <= \textbf{ST (HypoOsmolality)} \end{cases}$$

Where ST= Stable Threshold Value for VC, LT= Lowest Threshold Value for VC, HT= Highest Threshold value for VC according to Homeostasis process i.e. Osmoregulation.

O(s) is Osmotic signals generated from Osmoreceptors and projected to Hypothalamic Nuclei. AD(s) represent the Antidiuretic Hormonal Signals. We also use Daubechies Wavelet function D4 (AD(s)) and Scaling Function Sf (h) for Hormonal Signals. Constant fractals function frac (h) used with Wavelet transformation pattern to generate the hypothalamic signal. An Entropy function **E (h)** is also used to measure uncertainty for the physiological data i.e. hormonal signals. $\boldsymbol{Co(O(s), AD(s))}$ is used to represent the covariance and correlation between the Osmotic Signal and Hormonal Signals.

Since hormonal signal dependent on the osmotic signals, we use coefficient of correlation and determination to verify the utility of our model. The Equation for the Hypothalamic Water Balancing Mathematical model is as follows:

$$\boldsymbol{HT = D4(O(s)) * frac(O(s)) + Sf(AD(s)) * E(h)} \quad \textbf{........ (1)}$$

$$\frac{\boldsymbol{dHT}}{\boldsymbol{dt}} = \boldsymbol{frac(h)D4'(O(s) + \mathrm{E(h)}Sf'(AD(s))}$$

5. RESULT AND DISCUSSION

For the development phase and analysis phase of our model we use MATLAB 2018a.For analysis we consider Coefficient of Correlation, Entropy, Variance and Skewness. These parameters depict different features of Osmotic Signals (O(s)) and Hypothalamic Signals (H(s))which are as follows:

- Coefficient of Correlation between the Osmotic Signal, O(s) and Vasopressin Hormonal Signal at Hypothalamus, ADH(s)),is the correlation numerical measure to define the dependence and independence between both of the signals. For HWBMM if the value of N (Total number of signals) is increased then there is also an increase in Coefficient of Correlation. HWBMM the correlation calculated within the range of 60-80 percent.
- Variance of Hormonal signal increases the impact of the scaling function as it shows the variation between different Hormonal signal values. Skewness gives us the asymmetricnature of the data (Signals) towards the mean.
- The four different Entropy measure are used for the hypothalamic Hormonal signals, Scalar Entropy: EM = -3.4900e+03, Threshold Entropy at 0.06: EMt = 2677, Log entropy: EMl = -3.4900e+03, Shannon Entropy: EMs = -2.2536e+03.Threshold entropy gives positive correlation whereas Scalar, Shannon and Log Entropy give negative correlation. So for the result it is being analytically decided to apply Threshold Entropy. For our randomly generated dataset, the Threshold entropy is calculated at threshold value 0.06. Entropy measure provides more uncertainty and variation to our data set (Figure 3,Figure 4 and Figure 5).

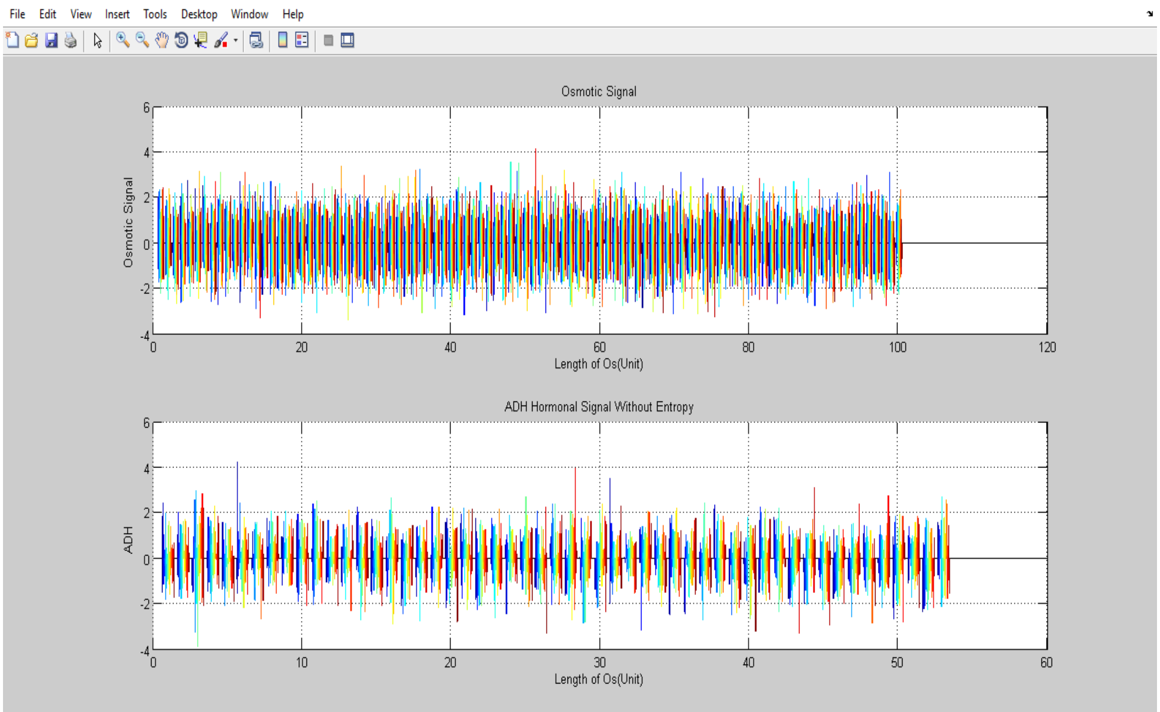

Figure 3 : (a) and (b) shows the Osmotic Signal and ADH Hormonal Signals respectively (2-D Discrete Wavelet Transforms).

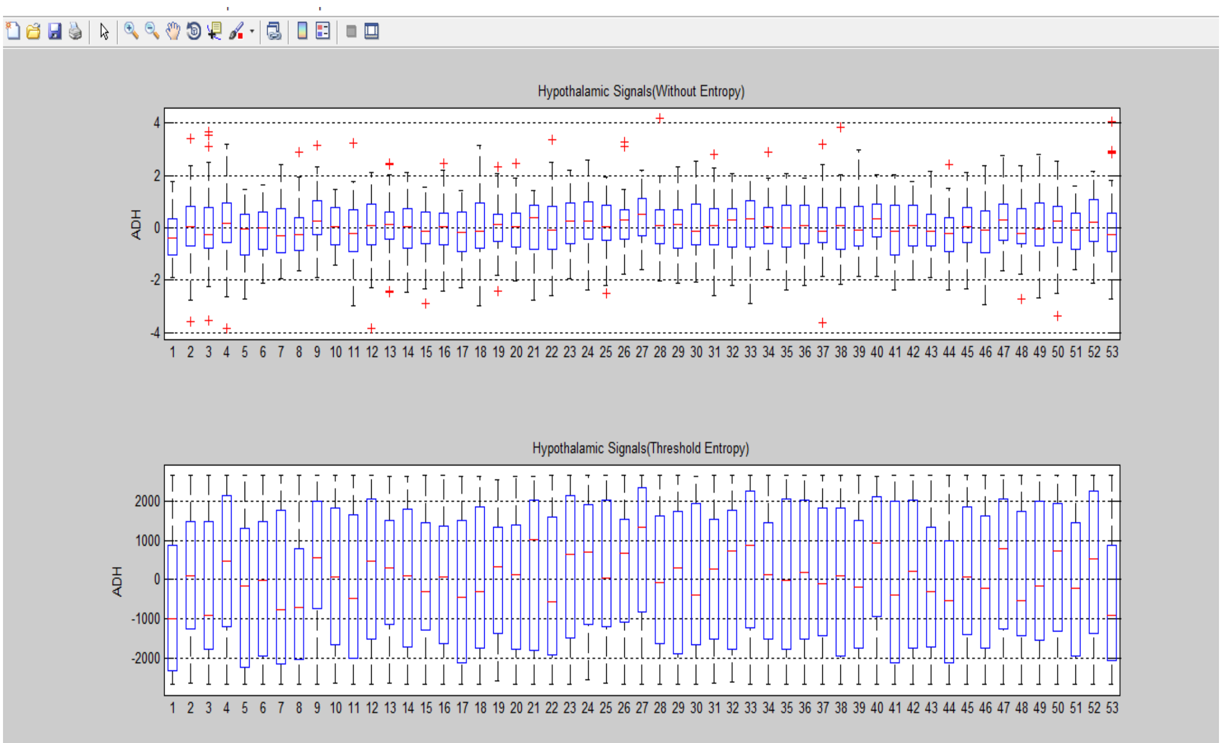

Figure 4 : Hypothalamic Hormonal Signal (a) Without Threshold Entropy (b) With Threshold Entropy at 0.06(minimum)

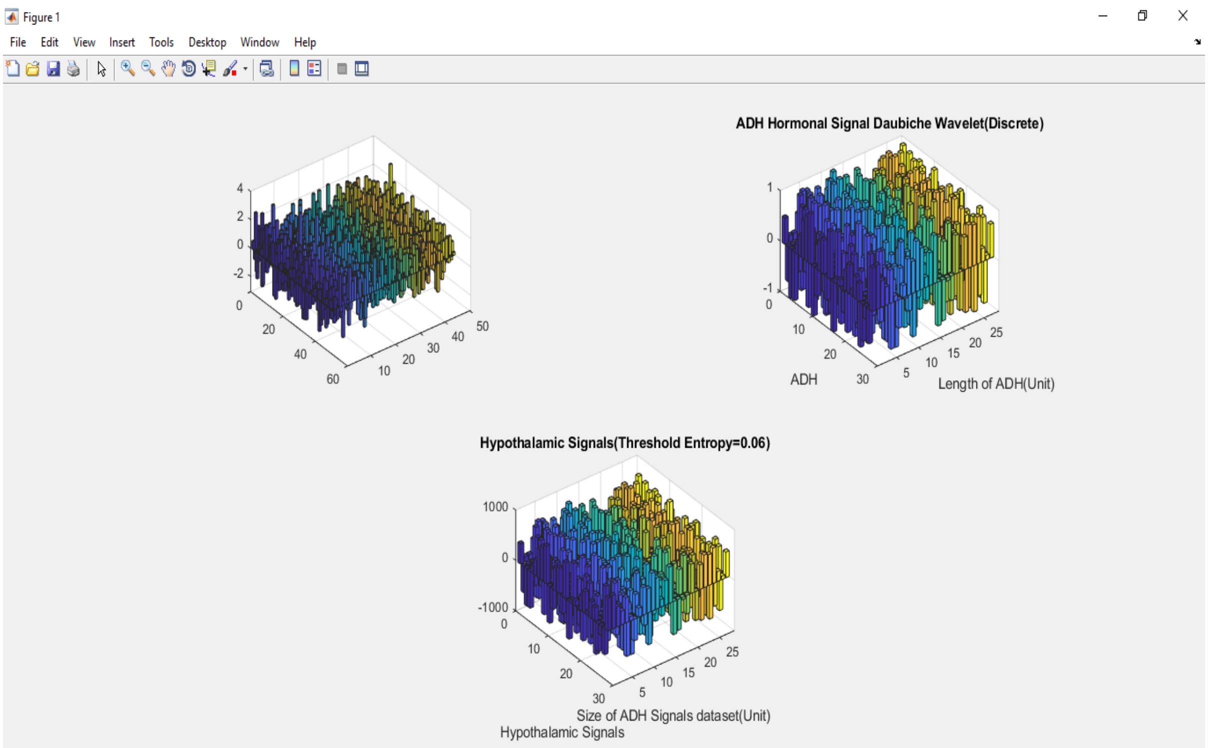

Figure 5 : The Signals in 3-D representation
(a) Osmotic Signal which start the process of Osmolality
(b) The ADH signal generated with the help of scaling function and Wavelet Transform (Without Entropy)
(c) Hypothalamic Signal with Threshold Entropy

6. CONCLUSION

HWBMM describes the physiological process, Osmoregulation (Water Balance), in basic scenario only. For an optimized and high utility model we need to add more complex parameters which give more accuracy and efficient result. This version of HWBMM can be used as the basic study and implementation only as it gives the correlation between the Osmotic Signal and Hypothalamic Signals with in an average range i.e. 60-80 percent. Entropy is an important parameter which shows the repeated values and pattern. A simple scaling function can represent data but for better result we need to introduce a scaling function with spatial parametric values. Also Entropy an impactful parameter for Hormonal signals.

7. FUTURE WORK

Since it's a base model, there is a lot more scope for optimization in our model. We can analyze it with a different and multi parameter Scaling function, Multi-scale entropy measure and fractal geometry. For more compatible model to real life application, our model also needs to validate clinically with the help of an actual medical data i.e. fMRI images.

REFERENCES:

[1]. Divya, Saurabh Mukherjee, "Mathematical Model to represent the role of Hypothalamus in Hunger Regulation", National Seminar Proceeding "Information Technology Applications: Strategies, Issues and Challenges", Published in Conference Preceeding, ISBN: 978-93-85000-08-9, (2015).

[2]. Divya, Saurabh Mukherjee, "Optimizing and Validating the Hypothalamic Hunger Regulation Mathematical Model", Journal of Network Communications and Emerging Technologies (JNCET) , Volume 5, Special Issue 2, ISSN: 2395-5317,203-207 ,EverScience Publication(2015).

[3]. W.S. Michael, S.C. Stephen, D Porte Jr, Randy, Denis, "Central nervous system control of food intake", Nature, Volume 404,661-671(2000).

[4]. Joseph J Feher, "Quantitative Human Physiology: An Introduction", Edition 2, Chapter 9.2, "Hypothalamus and Pituitary Gland", 777-786 (2012), ISBN-10:0128008830, ISBN-13:9780128008836, Publisher: Elsevier Science (2016).

[5]. M. Conrad, C. Hubold, B. Fischer, A.Peters,"Modelling the hypothalamus–pituitary–adrenal system: homeostasis by interacting positive and negative feedback". Journal of Biological Physics, 35(2), 149–162, (2009).

[6]. R.A. Thuraisingham, G.A. Gottwald,"On multi-scale entropy analysis for physiological data. Physica A: Statistical Mechanics and Its Applications", 366, 323–332,(2006).

[7]. W. Jänig,"The integrative action of the autonomic nervous system: neurobiology of homeostasis", Cambridge University Press, Cambridge, UK (2006).

[8]. M.J. McKinley, A.K. Johnson,"The Physiological Regulation of Thirst and Fluid Intake", Physiology, 1–6,(2004).

[9]. F. McKiernan, J.A. Houchins, R.D. Mattes, "Relationships between human thirsts, hunger, drinking, and feeding", Physiology & Behavior, 700–708,(2008).

[10]. D.G. Bichet, "Vasopressin and the Regulation of Thirst", Annals of Nutrition and Metabolism, 72(2), 3–7(2018).

[11]. D.E. Leib, C.A. Zimmerman, Z.A. Knight," Thirst", Current Biology, 26(24), R1260–R1265 (2016).

[12]. C.A. Zimmerman, Y.C. Lin, D.E. Leib, L. Guo, E.L. Huey, G.E. Daly,Z.A. Knight," Thirst neurons anticipate the homeostatic consequences of eating and drinking", Nature, 537(7622), 680–684(2016).

[13]. C.A. Zimmerman,D.E.Leib,Z.A. Knight, "Neural circuits underlying thirst and fluid homeostasis", Nature Reviews Neuroscience, 18(8), 459–469 (2017).

[14]. C. Gizowski, C.W. Bourque, "Hypothalamic neurons controlling water homeostasis: it's about time", Current Opinion in Physiology,5, 45–50,ScienceDirect(2018).

[15]. C.A. Zimmerman, E.L. Huey, J.S. Ahn,L.R. Beutler,C.L. Tan, S. Kosar, L. Bai, Y.Chen, T.V. Corpuz,L. Madisen, H.Zeng, Z.A.Knight," A gut-to-brain signal of fluid osmolarity controls thirst satiation", Nature, 568(7750), 98–102(2019).

[16]. M.J. McKinley, D.A. Denton, P.J. Ryan, S.T. Yao, A. Stefanidis, B.J. Oldfield, "From sensory circumventricular organs to cerebral cortex: Neural pathways controlling thirst and hunger", Journal of Neuroendocrinology, e12689(2019).

[17]. D.G. Bichet, "Regulation of Thirst and Vasopressin Release", Annual Review of Physiology, 81(1), 359–373(2019).

[18]. I. Koós,"Mathematical Models of Endocrine Systems", Journal of Universal Computer Science, vol. 12, no. 9, 1267-1277(2006).