

## Modeling Gout or Gouty (Acute) Arthritis in Biomedical and Biochemical Infophysics

**Peer review status:**

No

**Corresponding Author:**

Dr. Kang Cheng,  
Scientist, Biomedical and Biochemical InfoPhysics, Science Research Institute - United States of America

**Submitting Author:**

Dr. Kang Cheng,  
Scientist, Biomedical and Biochemical InfoPhysics, Science Research Institute - United States of America

**Article ID:** WMC004893

**Article Type:** Research articles

**Submitted on:** 18-May-2015, 03:35:02 AM GMT **Published on:** 18-May-2015, 10:08:14 AM GMT

**Article URL:** [http://www.webmedcentral.com/article\\_view/4893](http://www.webmedcentral.com/article_view/4893)

**Subject Categories:** RHEUMATOLOGY

**Keywords:** joint, massage, water, warm, meridian channel, entropy, conservation, matter, energy.

**How to cite the article:** Cheng K. Modeling Gout or Gouty (Acute) Arthritis in Biomedical and Biochemical Infophysics. WebmedCentral RHEUMATOLOGY 2015;6(5):WMC004893

**Copyright:** This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC-BY\)](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Source(s) of Funding:**

self

# Modeling Gout or Gouty (Acute) Arthritis in Biomedical and Biochemical Infophysics

**Author(s):** Cheng K

## Abstract

Gout or gouty (or acute) arthritis is one of the most painful diseases experienced by humans. The gouty patients are estimated more than 10 millions in the world. Recent clinic trials have demonstrated the manual therapy or massage (joint mobilization) is significantly more effective than the control treatments for patients with osteoarthritis.

To our knowledge, there is not any model to systematically describe this disease, in a perspective of biomedical and biochemical infophysics, information (entropy expression), laws of conservation of matter and energy; there is not either any more effective clinic treatment than massage or manual therapy (joint mobilization) with the same safety and economy to immediately cure this disease without any side effect.

In this investigation, we systematically model gout or gouty (acute) arthritis, using our previous meridian channel models and traditional theory of Yin and Yang, in a perspective of biomedical and biochemical infophysics. A clinic case report using treatments combined with massage and (warm running tap) water support our gouty models.

## 1. Introduction

Gout is a type of inflammatory arthritis that is triggered by the crystallization of uric acid within the joints and is often associated with hyperuricemia. Acute gout is typically intermittent, constituting one of the most painful conditions experienced by humans [1]. The prevalence of gout among US adults in 2007-2008 was 3.9% (8.3 million individuals) [2].

An overall prevalence of 1.4% in the UK and Germany rises to 3% in women and over 7% in men over the age of 75 years [3, 4].

The dieting and sweating controls are some keys, such as purine amount, water intake and loss, to avoid the gout disease. A lot of studies have performed and showed efficient results about the prevention [1]. Therefore, the prevention of the disease is not the point in this paper.

Recent clinic trials have demonstrated the manual

therapy or massage (joint mobilization) is significantly more effective than the control treatments for patients with osteoarthritis [5, 6].

In traditional Chinese medicine, patients with gout or gouty arthritis are treated with acupuncture and moxibustion (firing Chinese mugwort) at the acupoints of the pain joints, and let the patients drink some warm soup, to get the best results [7]. But, patients suffer from the burning or (and) acupuncture allodynia and many patients can not tolerate the allodynia. Additionally, the treatments have some side effects, such as making skin wounds.

In our previous study [8], we in anatomy and histology modeled meridian channels as a physiological system. We think, the meridian system is mostly constructed with interstices in or between systems of the integumentary, nervous, muscular, cardiovascular, skeletal, lymphatic, endocrine, respiratory, digestive, urinary and reproductive; major components in the meridians are loosen connective tissues that consist of electrolytes, cells and proteins; the electrolytes provide rich fluids and ions for processing, propagation or transportation of information, matter and energy in the meridians. Similar to systems of the nervous, cardiovascular, lymphatic, endocrine, respiratory, digestive and urinary, the meridian system should be unblocked or impeded according to the theory of Chinese medicine. If the systems are blocked, some diseases could occur. We also modeled how massage and acupuncture control or manage pains [8].

In another one of our previous study [9] of meridian channel system, we modeled how information, matter and energy are processed, propagandized or transported in the meridian system in a view of biomedical infophysics.

Although the pathogeny of gout or gouty (acute) arthritis is basically clear in medicine or biochemistry [1], to our knowledge, (1) there is not any model to systematically describe this disease, in a perspective of biomedical and biochemical infophysics, information (entropy expression [9]), laws of conservation of matter and energy; (2) there is not either any more effective clinic treatment than massage or manual therapy (joint mobilization) [5, 6] with the same safety and economy to immediately cure this disease without any side effect. In this investigation, we try to accomplish the above two tasks and discuss a clinic

case report to support our models, using our previous meridian channel models and traditional theory of Yin and Yang, in a perspective of biomedical and biochemical infophysics.

## Methods

Our models in this paper are based on published biomedical gouty data [1- 4] and infophysics [10] as well as biomechanics [11], biodynamics [12], thermodynamics and electrodynamics [13-15], chemistry [16 - 18], neuroscience [19], anatomy and physiology [20 - 22] and histology [23].

## 3 Models

### 3.1 Systematic Sketch

The pathogeny of gout or gouty (acute) arthritis is a complicated topic. It at least involves physiological systems of the nervous, exocrine, endocrine, meridian, cardiovascular, skeletal, integumentary, urinary and muscular. Fig. 1 shows our model of the interactions, or exchanges of information, matters and energies between the systems. Where, anatomical and physiological data are from the published data [20 - 23].

### 3.2 Symptom and Signs of Gout Joints

An obvious symptom of the disease is the concentration of uric acid is higher within the gout joints than other locations of the body and the crystal solids (monosodium urate) precipitate (deposit) on the bones, cartilages and ligaments within the joints and elicit an inflammatory response [1, 16, 20, 21]. Fig. 2 shows our model of the disease within an angle joint. We believe the uric acid or urate within the joints mostly comes from the fluid across the blood vessel walls.

### 3.3 Secondary Flows of Blood Fluid at Curved Vessels

Blood flows in the cardiovascular system are mostly powered by ATP biological energy with a heart pump. We modeled the working mechanism of cardiac muscles of the pump in our previous study [24]. In this paper, we focus on blood flows around curved blood vessels within the joints.

When blood flows enter curved larger arteries, such as aorta, there will be significant secondary flows that migrate across the vessels based on biodynamics [12, 25, 26].

In this study, we extend the secondary flow theory to

the medium arteries and veins such as the vessels within the joints. We have at least 3 reasons to perform this extension.

(1) Experimental results demonstrated that uric acids or urate come out of the vessels and the urate crystals precipitate (deposit) on the cartilages, bones, tendons and ligaments within the joints [1, 20].

(2) The flows of the arteries and veins are similar to each other [12].

(3) Human joints, especially, joints of knees, ankles, elbows, wrist, fingers, toes and hips, are often naturally or must be flexed (or curved) sharply. Therefore, there are many bended blood vessels within the joints [20, 21]. The radius of the vessel within the joints is often very small. Therefore, the pressure is stronger and the migration is more efficient at the joints than at other locations when the velocities are comparable.

Therefore, we believe some components of the secondary flows enhance the fluid (including uric acid or urate) migration out of the vessels, (i.e., into the meridian channel system).

Bottom of Fig. 3 and Equ. 1 show our model of the secondary flows at the joints. We can see the pressure against the vessel walls is inversely proportional to the radius of curvature of the streamline according to Equ. 1. This means, the smaller the radius, the more the migration across the vessel walls. When the secondary flows are faster than sweating excretion, for the gouty or acute arthritic patients, uric acid or urate precipitation or deposition may occur.

### 3.4 Uric Acid or Urate Precipitation or Deposition

For the patients with gout or gouty arthritis, the migration fluids across the blood vessel walls have high concentration of uric acid (Fig. 3). We use an extended equation of continuity [24, 27] to model the flow density, concentration and regeneration (+) or recombination (-) of ions at a local area (or meridian channel) of the joint. See Equ. 2.

We model the molecules or ions movements in the interstitial fluids with Fick's first law of diffusion [13 -15] in the meridian channels [8 - 10]. See Equ. 3 - 6 [16 - 18]. Usually, the higher the temperature, the higher the diffusion; the heavier the molecule (ion) weight, the lower the diffusion. The diffusion is caused by thermal movements of the ions in nature [13 - 15] and is an irreversible procedure. Published data demonstrate mobility (equivalent to diffusion here) of water related ions (Fig. 4) is approximately more than 4 times greater than that of sodium ions and uric acid.

Within the joints, there are usually not many fats,

muscles or tissue fluids; bones joints and skins are the major tissues. The sweating is generally easier at the joints than at other body parts. Therefore, after the water and the related ions swiftly flows or evaporates out of the body by sweating through meridian channel and the sweat glands duct, most of the uric acid and  $\text{Na}^+$  are behind the water flow, they are still in the sweat gland duct or meridian channels because of their much slower mobility.

Especially when the sweat gland ducts (0.3 – 0.4 mm in diameter [23]) are (partially) blocked by the uric acid (crystals) or other something, the water fluids can flow through the ducts, but the uric acid can't because of their sizes are much larger than that of water and other small ions; the acid can be repulsed back by a stuck acid too. Therefore, after the concentration of the detained acid is beyond the saturation point, the crystal solids (monosodium urate) form and precipitate (deposit) on the cartilages, bones, tendons, ligaments within the joints, even in the ducts [22] (Fig. 2). The depositions block the channels and the ducts. Therefore, we model the blockers as semipermeable membrane in the channels and ducts to stop excretion of uric acid or urate but to slowly discharge water and other small particles (Fig. 3).

In this investigation, we model the sweat gland ducts as transportation ports of meridian channels for outputs or inputs, to exchange the information, energy and matter with the environments. When the meridian channels or ports are impeded or blocked, gouty or acute arthritis disease occurs for the gouty patients. The precipitation or deposition of urate crystals on the bones, cartilages, tendons, ligaments or synovial membrane, even in the sweat gland duct is equivalent to clog of the meridian channel in Chinese medicine. To remove the clog means to cure the disease [7 – 10].

The clog and its caused inflammation and swelling trigger pain sensors of the nervous system by deforming the receptors and block the blood transportation of the cardiovascular system by externally press the vessels. Therefore, the western and oriental medicines are consistent each other in some ways.

We model the precipitation and dissolution as a reversible procedure regulated by temperature or concentration [16 - 18, 20]. See Fig. 4.

We think the high concentration of the uric acid and the crystal solids chemically, mechanically or thermodynamically trigger the sensors and make the patients to suffer from the allodynia. The stimulations attack nerves, cartilages, bones, tendons and ligaments

### 3.5 Stimulations

Cartilage is a semi-rigid form of connective tissue, provides flexibility and smooth surfaces for movement. The skeletal system is the body system composed of bones and cartilage and performs the critical functions for the human body [20]. Bovine articular cartilage has Viscoelastic shear properties [11]. The normal cartilage filled bovine fluids decrease much of the friction of the joints See Fig. 2.

However, when uric acid concentration is higher than the normal, pH is measured at lower than 7.0 [20], it is possible at a 5 level for a gout or acute arthritis case [28, 29]; the pH value is far below than a normal value of 7.4 in blood vessels [20]. Then, the coefficient of the friction is higher [11]. When the urate crystal solids precipitate in the joints, the friction is higher too. The stronger the friction (shear strain), the more deformation of ion channel of pain sensor and the more signals of ion channel currents; usually, the more (frequent) information of allodynia the brain receive, the more medical care the pain joints receive. Therefore, the pain signals the brain positive curing needs (good thing) as well as negative sufferings (bad things).

Fig. 4 describes possible chemical reactions in the biological fluids within the joints [16-18]. The higher the uric acid, the lower the pH value is; the lower the fluid temperature, the lower the saturation point is and the more crystal solids precipitate (deposit). The both results raise the friction at the joints.

We think the uric acid and urate crystals can respectively stimulate the patients' sensors and tissues chemically, mechanically and thermodynamically.

#### 3.5.1 Chemistry

$\text{H}^+$  or uric acid chemically (electrically) stimulates sensors and tissues. The stimulation is performed by the interaction between the electric charges of  $\text{H}^+$ , uric acid and receptors of the sensors, such as receptor potential cation channel subfamily V member 1, TRPV1 [30]. Experimental results of the sensitivities of the channel in low pH environments supported our model [31, 32]

Drinking alcohol is one of major causes to have gout. Alcohol makes human bodies losing water by inhibiting secretion of antidiuretic hormone (ADH) that is secreted by neurons in posterior pituitary (endocrine system). The secretion results in increased urine production that can eventually lead to dehydration and a hangover [20]. Therefore, the uric acid concentration is higher and pH is lower.

On the other hand, alcohol can decrease the body temperature [33]. The lower temperature decreases the saturation point of uric acid.

Some alcoholic beverages themselves may produce an effect on blood uric acid levels [1] that can lead to gout or gouty arthritis.

Additionally, the acidity of the ethanol can directly stimulate the receptors (e.g., TRPV1) of sensors [34]. The receptors signal to brains [19]. We believe the charges of the molecules play a role (Fig. 5)

### 3.5.2 Mechanics

A gouty patient usually feels more allodynia at knee and ankle joints with a standing posture than the sitting and lying, because the more gravitational forces (or stress, static or dynamic frictions) or shear strains applied on the joints [11, 20] (Fig. 2). The patients often feel more allodynia at wrist and elbow joints than at the other joints, because they use their wrists or elbows more often than their other joints. Therefore there are more dynamic frictions and tissue erosions or damages, wounds or inflammations at the joints.

The mechanical stimulated allodynia is probably signaled by TRPV1 in a view point at a molecular level [35, 36].

### 3.5.3 Cold Temperature

Our hands, feet and joints of ankles, knees, elbows and wrists are about 5 to 10 degrees (oC) lower than that of the body core in a cold environment (e.g. 20 oC), [21]. Therefore, in cold days, we feel much colder in or within our joints than others in our bodies because lower temperature is over there. We think The lower temperature are because less warm tissues, such as fats, muscle, tissue fluids and less clothes cover are within or around joints than other locations. Therefore, heat is difficult to keep and easier to lose at joints than at other body parts.

When the body temperature is low, the solvability of the monosodium urate is low too. Therefore, more urate crystal precipitate (deposit) on the bones, tendons, ligaments and other tissues; there are more frictions at the joints; and the patients feel more allodynia. On the other hand, the sensor, such as TRPV1 [37], can directly signal the cold information at 19 oC.

Osmotic pressures across the sensor membrane and structure of the sensor receptor are functions of temperature [13- 15]. When the temperature changes, the structure also changes or the pressure changes the structure, to respond the thermodynamic stimulation.

### 3.5.4 Hot Temperature, Moist (Humid) or Stuffy

## Environment

Sweat glands are important exocrine pathway to excrete heat, wastes (including urate or uric acid) by sweating (evaporating (vaporizing), or flowing). The excretion usually works normally on dry or cool days or under a ventilating condition. However, if the skin environment is hot, moist or stuffy, such as hot weather, humid days, over covered skin, or over flexed (e.g., < 45o) joints (interior surfaces), the sweat ducts may be (at least partially) blocked by the sweated wastes because the evaporation or excretion is (at least partially) stuck with too much sweating or the environmental saturated water [20, 38]. See Fig 3.

Therefore, the urate crystals are more or uric acid concentration is higher on hot or humid days or in a stuffy environment than that in a dried skin condition, at the joints. High concentration of uric acid or urate crystals respectively chemically or mechanically stimulate sensors (e.g., TRPV1) and hurt other tissues. The final result is gout or gouty (acute) arthritis is prevalent under these conditions.

### 3.5.5 Combination

All of the stimulations may actually act together. For instance, mechanical and chemical stimulations involve thermodynamic stimulation. They change the structure or conformation of the sensor channels, such as TRPV1. Our previous theoretical investigation show the effective radius of the channels change only 13 %, the effective channel currents will change 10000 times [39-40]. Sensor channels (e.g., TRPV1) and neurons play roles to signal the stimulation to the brains [19].

## 3.6 Treatment

We think one of efficient treatments to immediately cure the disease is to remove deposits or blockers from the sweat gland (ducts) ports and meridian channels; to decrease the concentration of the uric acid (and the urate) and to excrete the uric acid and urate out of the joints and the body; and to maintain channels and ducts opening and ventilating under a suitable temperature and unstuffy environment.

Fig. 6 illustrates our model of treatment. The skin tissue or anatomic data are from the published data [20 - 23]. The blockers are removed from the duct to excrete uric acid or urate by the massage and running water. The massage (joint mobilization of manual therapy) is performed with a pleasant or mild pain feeling of force and repeated from 6 to 10 moving strokes, rubs, or kneads between fingers and thumb at a pain joint at a rate about one stroke per second. The running tap water is warm (30 – 40 oC), cool (20 – 30 oC) or no water.

We model the momentum transfer equation of ions approximately as Equ. 6. We believe, the massage or fluid force is the dominant force to remove wastes of the stocker, crystal acid or crystal solids from the epithelial exocrine (sweat) glands duct or meridian channels (interstices) and to clear out the deposits on the bones, cartilages and ligaments within the joints (Fig .6).

The warm running water and the friction increase the fluid temperature and the saturation point. The warm running water treatment decreases the concentration of the uric acid and migrate the uric acid or urate out of the body. A total energy equation [41] can be used to model this process, see Equ. 7.

We use Equ. 8 to model the rate of change of entropy in time domain. The change rate is mostly managed by the heat of warm water or friction cost in our model. In information theory [42], the entropy represents a state of the order of matters; the entropy change is equivalent to information change (amount). Based on our previous models [8-10], entropy is one of expressions of information. In this model, warm water and friction heats increase the entropy of the ions, such as uric acid and Na<sup>+</sup>. The results are the ions become more disorder (de-crystallized) [15], so that they are removed from the tissues, move randomly in the meridian channels, by the heats; and finally they are cleared out of the body by the massage force and fluid flow.

After the treatments, dry the joints with towels and keep the joints warm (about body temperature) and ventilating without sweat (a little normal sweat can evaporate easily).

We think, our treatment method is similar to clean our eyes with running tap water, to clear out some sands or dirty things that are accidentally blown into; or is similar to clear out kidney stones by drinking (water) and walking more. But the models in this paper are more efficient than that in our previous study to manage pain with massage without any water [8, 10].

## 4 Discussions

### 4.1 A clinic case report

A patient has major symptoms and signs of the gout or gouty (acute) arthritis, such as having a joint pain feeling after walking or (labor) working long time, sweating, eating purine rich foods or drinking alcohol, especially in a cold environment. The patient is a middle aged man and has the symptoms for about 3 decades and he often cures or suppresses the pain by himself with the methods in this paper.

Table 1 shows the results. The treatments using massage with warm, cold running tap water, or wet towel are more effective than the massage (joint mobilization of manual therapy) alone. No treatment result is the worst among the methods. The reason could be the no treatment takes much longer time to passively obtain enough tissue fluids without or with little uric acid to clear out the fluids with the high concentrated uric acid or urate crystals. But the other methods could be to actively remove and (or) wash out the high concentrated uric acid or urate crystals from the joints.

After curing or suppressing the pain, the patient often feels warm and comfortable at the joints.

If the pain relapses, cure or suppress it again using the active treatments. Our treatment methods are very safe and have not any side effect; and they are very economical if self serves. They can be accomplished in a common family bathroom or with tap (running) water. Our clinic case report is at least significant in a perspective of individual medicine.

### 4.2 General

Sporty [43] and labor men [1] often have high concentration of uric acid or urate in their sweats. We believe they often unconsciously do massage with a towel or (and) wash out or dilute the uric acid with warm running water when they a shower after hard work to prevent the gout or gouty (acute) arthritis.

We think the gouty allodynia can be alleviated by extending long time flexed joints, because the extension reduces the secondary flow and sweating blockers, and increases sweat evaporation, so that the uric acid concentration or urate crystals at the joints could be decreased.

Although our models of massage with warm running tap water in this article target joint gout or gouty (acute) arthritis, we believe the models are also helpful to relieve the pain from the muscle gout or arthritis and some other urgent or chronic pains such as the headache, neuritis, arthritis, back, waist, limbs and frozen shoulders as well as to clean or open the meridian channels. Therefore, we recommend the patients to perform some massages or manual therapy at any pain sites when having a shower.

According to traditional Chinese theory of Yin and Yang, Yin and Yang represent two complimentary concepts [7, 10]. For instance, respectively, Yin represents humidity, stuffy, cool or cold; Yang represents dry, ventilation and warm or hot. Therefore, in Chinese medicine, to cure a disease is to find a balance between Yin and Yang, i.e., to treat a disease with a Yin characteristic using a complimentary

method with a Yang characteristic; vice versa. We applied the theoretical principles in our models and treatments in this study.

The principles of our models and treatments in this investigation could be also used to transport some medicine into subcutaneous tissues or meridian channels to target some diseases without any invasion.

Future studies could be focused on higher phases of clinical trials.

## 5 Conclusion

In this paper, we systematically model gout or gouty (acute) arthritis in a perspective of biomedical and biochemical infophysics. Comparing the treatments with medicine, our models are very safe and easy to accomplish, to immediately cure the without any side effect; and the models are also very economical when perform self treatments. A clinic case report using treatments combined with massage and (warm running tap) water support our gouty models.

## References

1. Choi HK, Mount DB and Reginato AM, 2005. Pathogenesis of gout. *Ann Intern Med.*, 143:499-516.
2. Zhu Y, Pandya BJ and Choi HK, 2011. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007-2008. *Arthritis Rheum*, 63(10):3136-41. doi: 10.1002/art.30520.
3. Annemans L, Spaepen E, Gaskin M, et al, 2008. Gout in the UK and Germany: prevalence, comorbidities and management in general practice 2000-2005. *Ann Rheum Dis*, 67:960-6
4. Mikuls TR, Farrar JT, Bilker WB, et al. 2005. Gout epidemiology: results from the UK General Practice Research Database, 1990-1999. *Ann Rheum Dis*, 64: 267-72
5. Poulsen E, Hartvigsen J, Christensen HW, Roos EM, Vach W and Overgaard S, 2013. Patient education with or without manual therapy compared to a control group in patients with osteoarthritis of the hip. A proof-of principle three-arm parallel group randomized clinical trial. *Osteoarthritis and Cartilage*, 21: 1494 - 1503. <http://dx.doi.org/10.1016/j.joca.2013.06.009>.
6. Rhon D, Deyle G, Gill N and Rendeiro D, 2013. Manual physical therapy and perturbation exercises in knee osteoarthritis. *Journal of Manual and Manipulative Therapy*, 21(4):220-228. DOI 10.1179/2042618613Y.0000000039.
7. Cheng Z. Chinese Medicine of Acupuncture and Moxibustion. People's Health Publishing, Beijing, China, 1958, (Chinese).
8. Cheng K and Zou C, 2010. Information models of acupuncture analgesia and meridian channels. *Information*, 1(2):153-168. doi:10.3390/info1020153.
9. Cheng K and Zou C, 2011. Biomedical infophysics models of meridian channel system. *WebmedCentral BIOPHYSICS*, 2(12):WMC002555.
10. Cheng K. Biomedical InfoPhysics. CreateSpace, Charleston, NC, USA, 2012.
11. Fung YC, Biomechanics, Mechanics Properties of Living Tissues. Springer, New York, NY, USA, 1996.
12. Fung YC, Biodynamics Circulation. Springer, New York, NY, USA, 1984.
13. Barrow G. Physical Chemistry. McGraw-Hill College, New York, NY, USA, 1996.
14. Moore WJ. Physical Chemistry. Longman Publishing Group, New York, NY, USA, 1998.
15. Van Holde KE. Principles of Physical Biochemistry. 2nd Ed. Prentice Hall, Upper Saddle River, NJ, USA, 2006.
16. Nelson DL and Cox MM. Lehninger Principles of Biochemistry, W.H. Freeman & Company, New York, NY, USA, 2008.
17. Sorrell TN. Organic Chemistry, University Science Books, Sausalito, CA, USA, 2006.
18. Holtzclaw H, Robinson R and Odom J. General Chemistry with Qualitative Analysis, 9th ed., D.C. Heath and Company, Lexington, MA, USA, 1991.
19. Purves D. Neuroscience. 4th Ed. Oxford University Press. New York, NY, USA, 2007.
20. OpenStax College, Anatomy & Physiology. OpenStax College. 25 April 2013. <<http://cnx.org/content/col11496/latest/>>.
21. Kapit W, Macey RI and Meisami E. The Physiology Coloring Book, Murray, New York, NY, USA, 1987.
22. Goyal MR. Biofluid Dynamics of Human Body Systems. Apple Academic Press, Boca Raton, FL, USA, 2013.
23. Ross MH and Pawlina W. Histology: A Text and Atlas: With Correlated Cell and Molecular Biology, 5th Ed., Lippincott Williams & Wilkins: Philadelphia, PA, USA, 2006.
24. Cheng K and Zou C, 2009. Four dimensional (4-D)

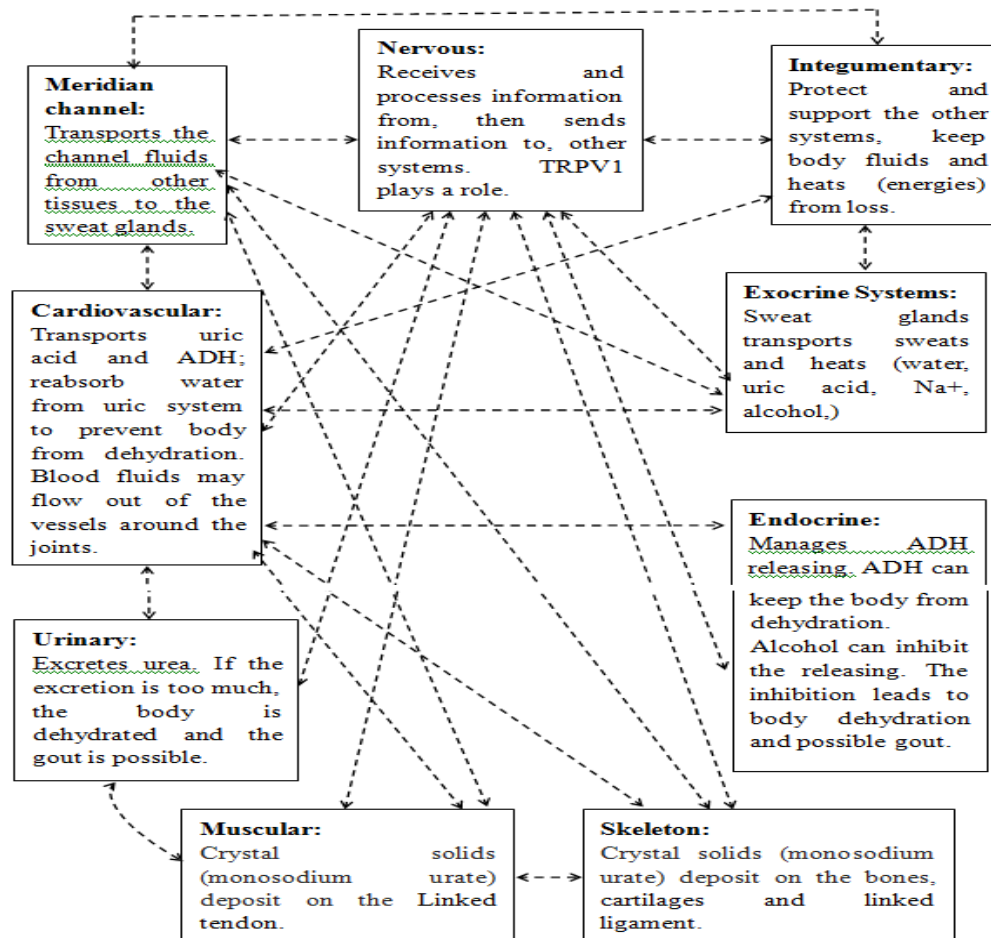
- BioChemInfoPhysics models of cardiac cellular and sub-cellular vibrations (oscillations). *OnLine Journal of Biological Sciences*, 9(2):52-61.
25. Pedley TJ, *The Fluid Mechanics of Large Blood Vessels*. Cambridge University Press, New York, NY, USA. 1980.
26. Wood NB, 1999. Aspects of fluid dynamics applied to the larger arteries. *J Theor Biol*, 199:137-161. Article No. jtbi.1999.0953.
27. Sokolnikoff IS and Redheffer RM, *Mathematics of Physics and Modern Engineering*, McGraw Hill, New York, NY, USA, 1966.
28. Kanbara A, Miura Y, Hyogo H, Chayama K and Seyama I, 2012. Effect of urine pH changed by dietary intervention on uric acid clearance mechanism of pH-dependent excretion of urinary uric acid. *Nutrition Journal*, 11:39. <http://www.nutritionj.com/content/11/1/39>
29. Clark J. My Gout Kill Formula - Changing Your Body pH, Home / Body Health. <http://www.healthalkaline.com/my-gout-kill-formula-changing-your-body-ph/>
30. Sardar P, Kumar A, Bhandari A and Goswami C. 2012. Conservation of tubulin-binding sequences in TRPV1 throughout evolution. *PLoS ONE*, 7(4):e31448. doi:10.1371/journal.pone.0031448.
31. Caterina MJ, Schumacher MA, Tominaga M, Rosen TA, Levine JD and Julius D, 1997. The capsaicin receptor: a heat-activated ion channel in the pain pathway. *Nature*, 389:816-824.
32. Tominaga M, Caterina MJ, Malmberg AB, Rosen TA, Gilbert H, Skinner K, Raumann BE, Basbaum AI and Julius D, 1998. The cloned capsaicin receptor integrates multiple pain-producing stimuli. *Neuron*, 21:531-543.
33. MD Health.com, Sweating after drinking alcohol, Mar 21, 2015, <http://www.md-health.com/Alcohol-Sweating.html>
34. Trevisani M, et al, 2002. Ethanol elicits and potentiates nociceptor responses via the vanilloid receptor-1. *Nat Neurosci*, 5(6):546-51.
35. Wu SY, Chen WH, Hsieh CL and Lin YW, 2014. Abundant expression and functional participation of TRPV1 at Zusanli acupoint (ST36) in mice: mechanosensitive TRPV1 as an "acupuncture-responding channel". *BMC Complementary and Alternative Medicine*, 14:96. <http://www.biomedcentral.com/1472-6882/14/96>.
36. Jiang YL, Yin XH, Shen YF, He XF, and Fang JQ, 2013. Low frequency electroacupuncture alleviated spinal nerve ligation induced mechanical allodynia by inhibiting TRPV1 upregulation in ipsilateral undamaged dorsal root ganglia in rats. *Evidence-Based Complementary and Alternative Medicine*. <http://dx.doi.org/10.1155/2013/170910>.
37. Oseguera AJ, Islas LD, Garcia-Villegas R and Rosenbaum T, 2007. On the mechanism of TBA block of the TRPV1 channel. *Biophys J*, 92:3901-3914.
38. Zhang YQ, Chaisson CE, Chen CA, McAlindon TE and Hunter DJ. High humidity and high temperature increase the risk of recurrent gout attacks: The Online Case-crossover Gout Study. Presentation Number 707. American College of Rheumatology Annual Scientific Meeting, Washington, DC, November 2006.
39. Cheng K, Tarjan PP and Zou C, 1993. Schrodinger equation, Maxwell-Boltzmann distribution and single channel current. *Biomed Sci Instrum*, 29:361-367.
40. Cheng K, 1997. Improved 3-D quantum mechanical models of ion movements in a cylindrical ion-channel. *Proceedings of 16th Southern Biomedical Engineering Conference*. pp. 220-223.
41. Whitaker S. *Introduction to fluid mechanics*, Prentice-Hall, Englewood, NJ, USA. 1968.
42. Shannon CE, 1948. A mathematical theory of communication, *Bell System Technical Journal*, 27: 379-423, 623-656.
43. Huang LL, Huang CT, Chen ML, and Mao IF, 2010. Effects of profuse sweating induced by exercise on urinary uric acid excretion in a hot environment. *Chinese Journal of Physiology*, 53(4): 254-261, 2010. DOI: 10.4077/CJP.2010.AMK060.
44. Sigma Aldrich, Uric acid sodium salt. <http://www.sigmaaldrich.com/catalog/product/sigma/u2875?lang=en&ion=US; Santa>.
45. Cruz Biotechnology, Uric acid sodium salt (crystals), <http://www.scbt.com/datasheet-202711-monosodium-urate-crystals.html>.



# Illustrations

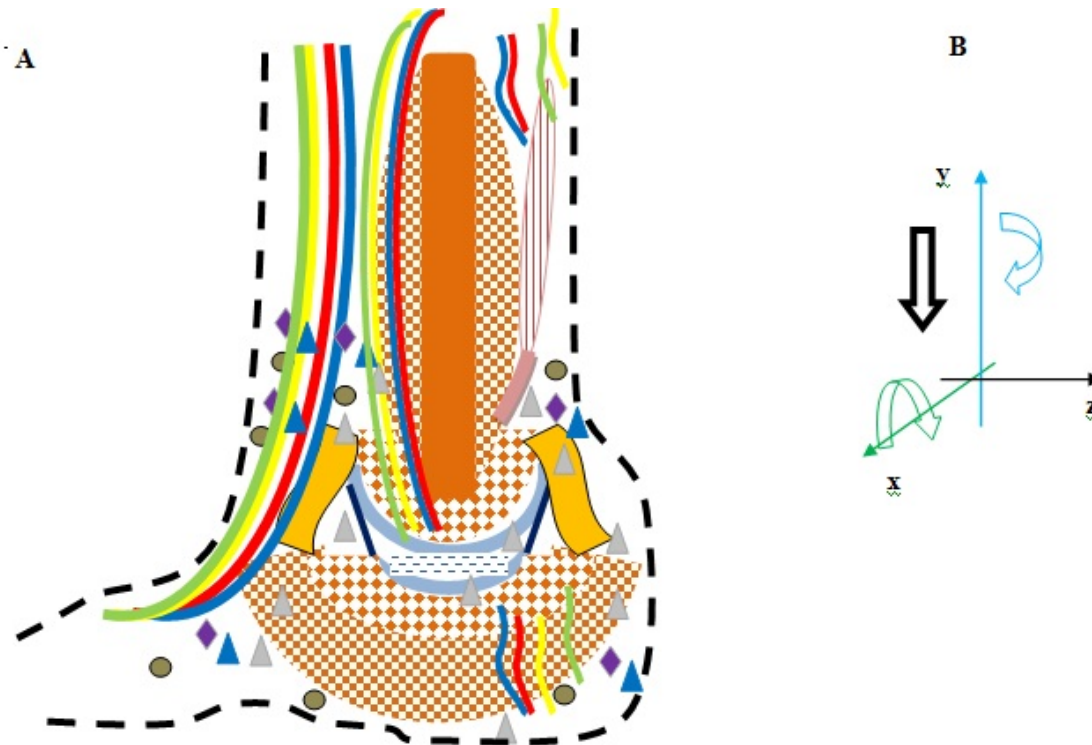
## Illustration 1

Fig. 1. Our main framework of human systems that are mostly involved in gout or gouty (acute) arthritis. The dashed arrow lines denote possible exchanges of information, matters or energies. See texts.



## Illustration 2

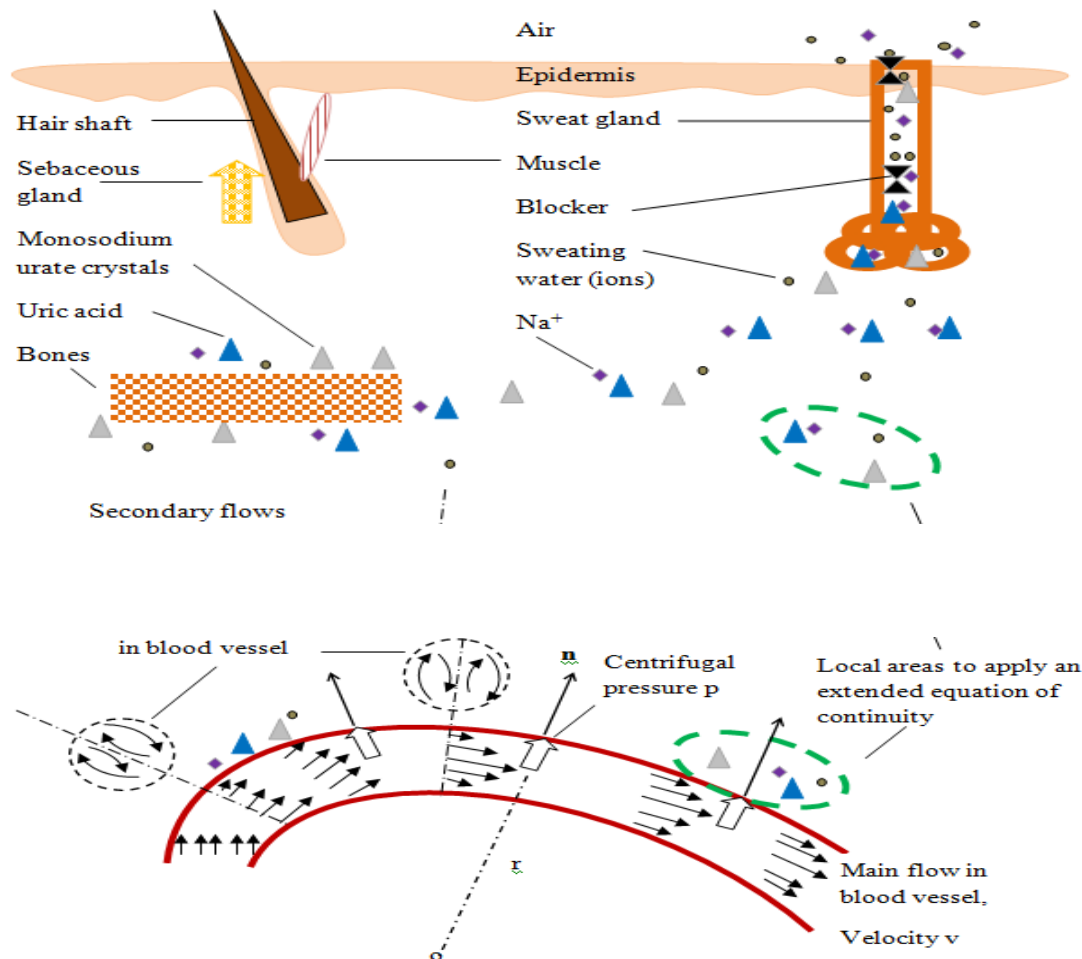
Fig. 2. A. Ankle joint (between tibia and talus) is a synovial joint [11, 20]. B. Rotation about y axis (vertical direction, blue), wastes of uric acid and (or) urate crystals are within the joint; rotation about x axis (comes out of the paper, green); and stress in y- direction. See the text. The draw is not to the scale.





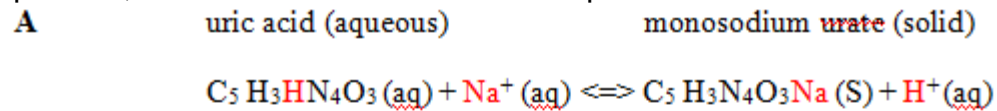
### Illustration 3

Fig. 3. An entry flow into a bended blood vessel within a joint, the velocities of the main flow are proportional to the arrows [12, 20, 25, 26]; and diffusions of water, uric acid, Na or urate in or under skin and transportations or evaporations through the sweat gland ducts. Blockers are modeled as semipermeable membrane in the ducts or ports. The draw is not to the scale.

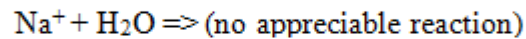
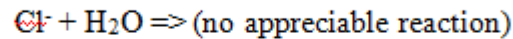
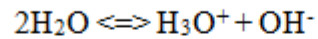


## Illustration 4

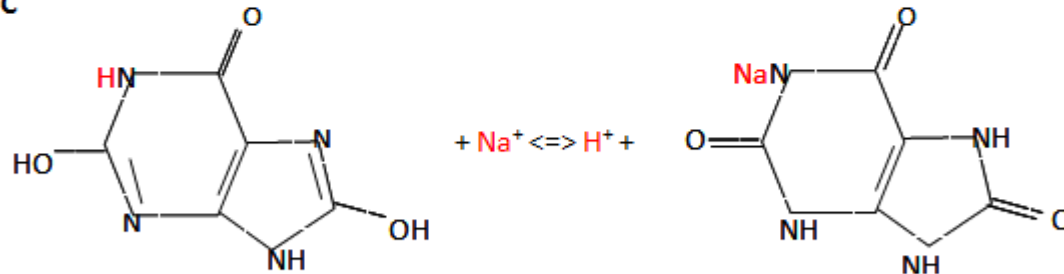
Fig. 4. Chemical reactions of mixture of uric acid and monosodium urate in biological fluid (H<sub>2</sub>O, ions of sodium Na, hydrogen H, hydroxide OH<sup>-</sup> and hydronium H<sub>3</sub>O<sup>+</sup>). The reactions are reversible and regulated by the temperature or concentration [16- 18, 44-45]. When the temperature is low, more crystal urate solids precipitate (or deposit) because of the saturation. A and B: Chemical equations; C and D: Chemical Structure equations



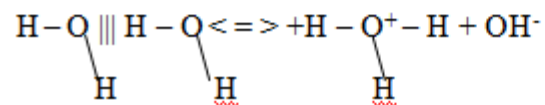
**B**



**C**



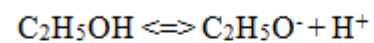
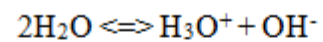
**D**



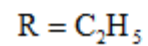
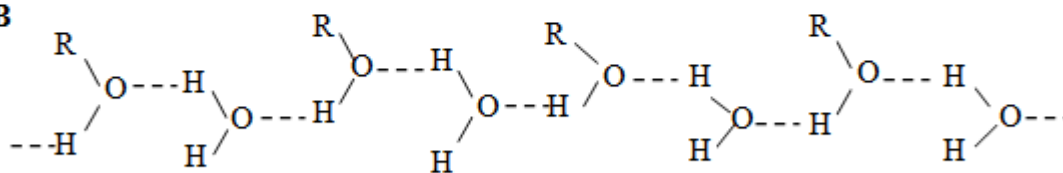
## Illustration 5

Fig. 5. Mixture of ethanol and Water [16]. A. Chemical formula or equation of ionic water and acidity of ethanol; B. Chemical Structure of ethanol in water. The dash lines denote the hydrogen bond. The draw is not to the scale.

**A**

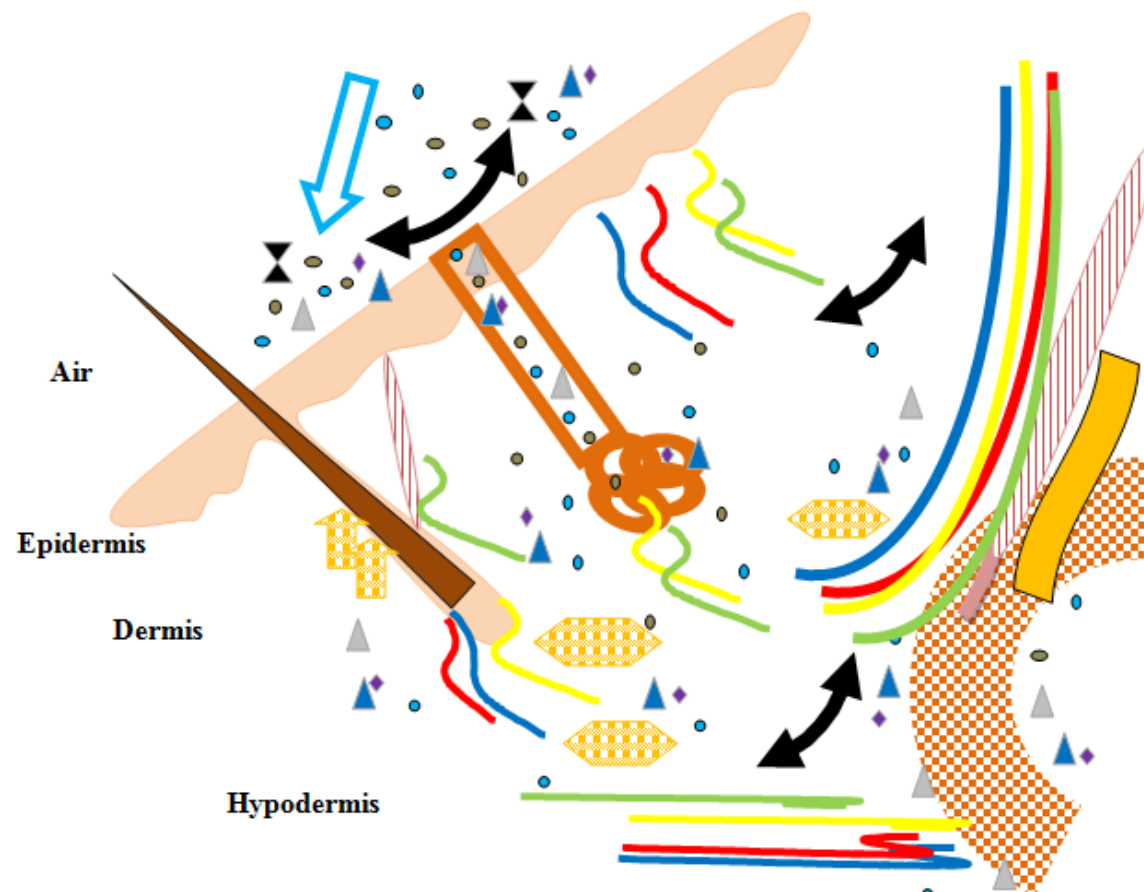


**B**



## Illustration 6

Fig. 6. Our model to treat gout or gouty (acute) arthritis. The draw is not to the scale.



Blocker:



Massage force:



Warm tap water:



Monosodium Urate crystals:



Uric acid:



Na<sup>+</sup>:



Compact bone:



Sweat glands:



Sweat water:



Hair shaft:



tendon:



muscle:



ligament:



Ascending nerves:



Descending nerves:



artery:



vein:



Hair follicle:



Subcutaneous Fat<sup>37</sup>



Sebaceous gland:





## Illustration 7

Table 1. A clinical case report of a patient with symptoms of gouty (acute) arthritis or gout.

<b>Rank (10 = Best)</b>	<b>Treatment Methods</b>	<b>Averaged Results (in 10 seconds after treatment).</b>
10	Massage with warm running tap water (30 – 40 °C).	Feel more than 90% relief of the pain soon.
8	Massage with cool running tap water (20 – 30 °C).	Feel more than 80% relief of the pain soon.
7	Massage with a wet towel (30 – 37 °C).	Feel more than 70% relief of the pain soon.
5	Massage without any water.	Feel more than 60% relief of the pain soon.
3	Warm running tap water without any massage.	Feel about 30% relief of the pain soon.
0	No any treatment.	Feel the pain for hours or longer without any relief.

## Illustration 8

### Equations

## Equations

The migration equation is approximately modeled as,

$$\frac{\partial p}{\partial n} = \rho \left( \frac{v^2}{r} \right) \quad (1)$$

where  $p$  is the centrifugal pressure,  $n$  is a normal direction to the streamline, i.e. in the radial direction;  $r$  is the radius of curvature of the streamline,  $v$  is the velocity along the streamline at a point;  $\rho$  is the fluid density [26]. See Fig. 3.

The extended equation of continuity [24, 27] represents the law of conservation of matters in a point form, and it is,

$$Div J_i = \left( \frac{\partial C_i}{\partial t} \right) + g_i C_i \quad (2)$$

Where,  $Div$  means a divergence operator;  $J_i$  and  $C_i$  respectively denote the flow density and concentration of a kind of ions or molecules,  $g_i$  denotes a hydrodynamic growth factor of the ions. The term at the left side of Equ. 2 represents the ion flows through the areas; at the right side of Equ. 2, the first term represents the ions cross (out of) the vessels, and the second term represents the regeneration (+) or recombination (-). See Fig. 3 and Fig. 4.

The diffusion equations of a kind of ions in the biological fluid in one dimension are approximately modeled as [13 – 15],

$$J_i = -D_i \left( \frac{\partial C_i}{\partial x} \right) \quad (3)$$

$$D_i = \left( \frac{kT}{Q_i} \right) u_i \quad (4)$$

$$u_i = \frac{1}{6\pi\eta r_i} \quad (5)$$

where,  $k$  is Boltzmann constant and  $T$  is an absolute temperature;  $D_i$ ,  $Q_i$ ,  $u_i$ ,  $v_i$  and  $r_i$  respectively denote the diffusion coefficient (it plays an important role for the diffusion), charge, mobility, viscosity and radius of the ions. The 3 dimensional modes are similar to the above. The temperature gradient induced diffusion (Onsager method) in Equ. 3 is ignored to simplify our model.

We model the momentum transfer equation of ions approximately as [24],

$$\frac{d(m_i v_i)}{dt} = F_i + P_i - f_i \quad (6)$$

Where  $F_i$ ,  $P_i$ ,  $f_i$ ,  $m_i$  and  $v_i$  respectively denote the mass force, pressure, friction, mass and velocity of the ions (Fig. 6).

A total energy equation [41] obeys to the law of conservation of energy in a point form. It is,

$$\rho_i \frac{d}{dt} \left( e_i + \frac{v_i^2}{2} + \phi_i \right) = -\text{Div}(q_i) + \text{Div}(Tv_i) \quad (7)$$

Where,  $\rho_i$ ,  $e_i$ ,  $v_i$ ,  $\phi_i$ ,  $q_i$ ,  $T$  and  $v_i$  respectively denote mass density, internal energy, velocity, potential energy, transferred heat, stress and velocity of the ions per unit volume. The terms at the left side denote time rate of change of internal, kinetic and potential energy; the first term at the right side denotes the rate of heat transferred to the ions and the second term denotes the rate of surface work. The heat is mostly transferred by warm water or friction and the work is mostly performed with the massage force in our model.

A rate of change of entropy [41] in a point form is approximately as,

$$\rho_i \frac{ds_i}{dt} = \frac{1}{T} [-\text{Div}(q_i) + \Phi_i] \quad (8)$$

Where,  $\rho_i$ ,  $s_i$ ,  $q_i$ ,  $\Phi_i$  and  $T$  respectively denote mass density, entropy, transferred heat, friction cost energy and temperature of the ions per unit volume. The heat conduction (Onsager method) in Equ. 8 is ignored to simplify our model.

NHANES 2007–2008, all participants were asked about a history of health professional or physician-diagnosed gout. Our primary definition of hyperuricemia was a serum urate level of  $>7.0$  mg/dl for men and  $>5.7$  mg/dl for women. We explored potential secular trends in these estimates and their possible explanations by comparing them with estimates based on 18,825 participants in NHANES-III (1988–1994). Results. The prevalence of gout among US adults in 2007–2008 was 3.9% (8.3 million individuals). The prevalence among men was 5.9% (6.1 million), and the prevalence among women was 2.0% (2.2 million). The mean serum urate levels were 6.14 mg/dl among men and 4.87 mg/dl among women, corresponding to hyperuricemia prevalences of 21.2% and 21.6%, respectively. These estimates were higher than those in NHANES-III, with differences of 1.2% in the prevalence of gout (95% confidence interval [95% CI] 0.6, 1.9), 0.15 mg/dl in the serum urate level (95% CI 0.07, 0.24), and 3.2% in the prevalence of hyperuricemia (95% CI 1.2, 5.2). These differences were substantially attenuated after adjusting for body mass index and/or hypertension. Conclusion. These findings from nationally representative samples of US adults suggest that the prevalence of both gout and hyperuricemia remains substantial and may have increased over the past 2 decades, which is likely related to increasing frequencies of adiposity and hypertension.