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Review Article

Mathematical methodology in dermatology and electronic skin

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Abstract

Notwithstanding the considerable advances witnessed within the domain of information engineering, the fundamental concept of information itself has become obscured by the extensive utilization of specialized terminology. Mathematical methods in the analysis of skin pathology offer a perspective that goes beyond mere observation. The potential for computer-controlled electronic skin to monitor lesions through the skin and facilitate novel approaches to treatment is significant. The construction of mathematical models and computer simulations based on them may contribute to predicting the effects of transdermal drug administration, and to improving our understanding of inflammation, skin lesions, and the mechanisms of skin homeostasis. This review examines the potential contributions of mathematical science and computer technology to dermatology, drawing upon extant reports.

Key words: Artificial intelligence, internet, mathematical model, simulation, electronic skin, deep learning

Introduction

The number of reports pertaining to the application of artificial intelligence (AI) to medicine has increased rapidly in recent years. Nevertheless, the term “AI” is scientifically ambiguous. A more precise characterization would entail the designation of the subject as numerical analysis, construction of mathematical models, and computer simulation. It is imperative that a comprehensive numerical analysis is conducted in order to ascertain the objective characteristics that are inherent within the data. In recent years, significant advancements have been made in the field of deep learning technology, thereby enabling more sophisticated approaches to image analysis and pattern recognition. Mathematical models have been shown to play a pivotal role in the identification of the salient factors underlying complex biological phenomena. Computer simulations, derived from these models, play a pivotal role in exploring medical approaches to nonlinear phenomena i.e., as is the case with most biological phenomena, processes where input and output are not proportional—such as those involving the nervous or circulatory systems.

In this review, the potential impact of recent advancements in mathematical science methodology on dermatology is examined, drawing upon the insights of in this field.

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1. The morphology of nerve fibers

The application of mathematical methods in pattern recognition offers a valuable avenue for elucidating fundamental principles of skin biology. As has been previously documented, the pruritus experienced by patients with atopic dermatitis was previously attributed to increased peripheral nerve fiber density within the epidermis [1]. Thin tissue sections have traditionally been used to observe nerve fibers in the skin. However, the arrangement of nerve fibers in the skin may be similar to the branching structure of a tree, thereby hindering the acquisition of precise information without the observation of their three-dimensional configuration.

A comparative and numerical three-dimensional structural analysis of peripheral nerve fibers in the epidermis of patients with atopic dermatitis was performed, revealing a lower density in their epidermis [2] (Fig. 1). Initially, three-dimensional images volunteers and in non-lichenified and lichenified lesions of patients. Subsequently, immunostaining of the nerve fibers within each tissue sample was conducted using an anti-PGP9.5 antibody. Three-dimensional images of nerve fibers measuring 320 × 320 μm with a depth of 100 μm were obtained. In order to facilitate the numerical analysis, sequential 10 μm cross-sectional images of the nerve fibers in the epidermis were constructed from 100 μm thick skin specimens. Subsequently, the images were processed using a binary method, and the length and density of the fibers were evaluated using ImageJ, a digital imaging software developed by the National Institutes of Health (NIH).

A subsequent report demonstrated that nerve fiber density was reduced in the skin of patients with atopic dermatitis and psoriasis, as revealed by three-dimensional analysis of cutaneous nerves via optical clearing and imaging [3]. We previously hypothesized that epidermal keratinocytes may contribute to cutaneous sensory functions. In keratinocytes, transient receptor potential (TRP) channel activated by mechanical stimuli, temperature, and chemical stimuli such as low pH and capsaicin are functionally expressed.

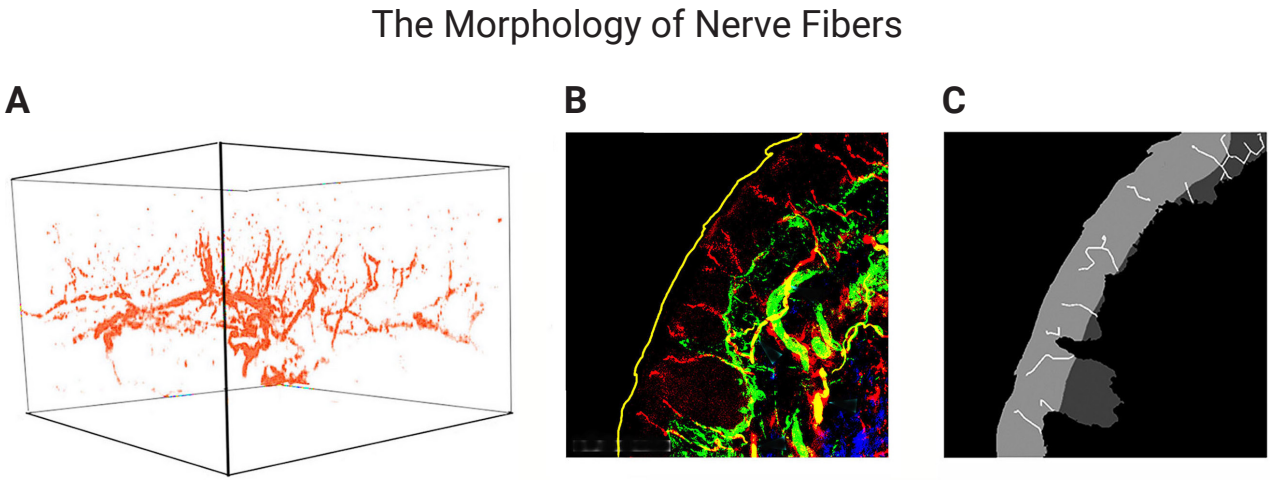

Figure 1. The morphology of nerve fibers. Mathematical analysis is effective in evaluating the three-dimensional structure of nerve fibers in the skin. **A)** Three-dimensional representation of representative nerve fibers obtained by two-photon microscopy. **B)** Cross-sectional images of multi-stained skin. Nerve fibers appear in red. Collagen green. Yellow lines: skin surface. **C)** Processed binary images showing epidermis in gray with fibers in white.

Moreover, toll-like receptors (TLRs) are also expressed in keratinocytes [4]. These results suggest an important role of keratinocytes in pruritus associated with these skin diseases.

In view of these results and our present three-dimensional structural and numerical analyses, which indicate that the density and distribution of nerve fibers in the epidermis are decreased in lesional skin of patients with AD compared with healthy skin, it seems reasonable to speculate that predisposing factors for pruritus in AD are associated with keratinocytes.

The findings of this report indicate that mathematical analysis is useful for quantitative image analysis.

2. The internet and electronic skin

2.1 Internet and dermatology

A substantial body of literature has proposed that the integration of internet systems into clinical dermatology would prove advantageous for the diagnosis and treatment of skin diseases. Data obtained through electronic engineering methods can be readily digitized and processed by computers, and shared extensively over the internet [5, 6].

A recent study demonstrated the efficacy of the "Internet of Medical Things" (IoMT) in skin lesion segmentation and classification, a field in which medical equipment and software share data over the internet [5]. A further report indicated that convolutional neural networks were useful for capturing subtle representations of images when trained end-to-end on this dataset. The authors of the study hypothesized that the integration of the IoMT will facilitate the provision of real-time patient data, thereby enabling healthcare professionals to deliver more efficacious care and permitting patients to consult with dermatologists remotely. The convolutional neural network (CNN) is a deep learning model constructed with three layers: convolution, pooling, and connected layers [7]. As demonstrated in previous reports, CNN has been shown to demonstrate equivalent proficiency in the identification of melanoma to that of dermatologists [8]. The model has been demonstrated to possess the capacity to learn spatial hierarchies of visual features.

VECTRA WB360 (Canfield Scientific, Inc.), a recently developed 3D imaging scanner, also holds the potential to bridge clinical dermatology and mathematical methods. This technology utilizes multiple cameras arranged in a 3D configuration within a stationary unit to instantly capture the subject's entire skin surface in high-resolution 3D; for instance, it is a device capable of detecting melanoma with 95% sensitivity [9].

2.2 Electronic skin

A substantial corpus of literature has recently emerged on the subject of electronic skin (e-skin) [10]. The majority of these reports indicated that thin, light, and flexible wearable devices have the capacity to monitor systemic health conditions from the skin's surface. Conversely, we recently proposed that e-skin could be a new skincare device [11]. As demonstrated in previous studies, the

application of appropriate temperature, electric potential, visible radiation, and sound has been shown to accelerate the recovery of barrier function after damage [12–15]. Recent advancements in materials science have resulted in the development of fibers that are capable of emitting visible radiation or sound [16, 17]. These fibers have the potential to be utilized in the fabrication of wearable skin care devices.

Furthermore, a recent review suggested that a new type of e-skin with dynamic, versatile, multimodal haptic displays (e.g., texture, temperature, vibration) and a tactile sensing system (e.g., active electronic skin, ae-skin) would serve as a new interface between human physiology, psychology, and the digital environment. This interface would facilitate more natural and intuitive interaction with the surrounding environment, thereby enhancing the user experience through increased authenticity and immersion [18]. As a preceding review indicated, haptic stimuli, that is to say massage, have been demonstrated to be an efficacious therapy for general health [19]. E-skin using a series of physical displays, has the potential to benefit not only the skin itself but also overall health, including emotional well-being (Fig. 2**).**

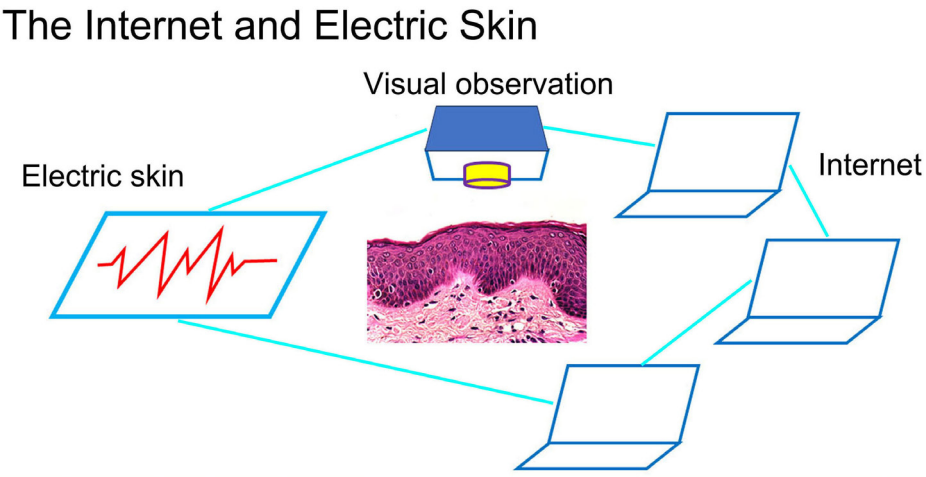

Figure 2. Internet and electric skin. Connecting electric skin with diverse functions to the Internet will bring about major advances in clinical dermatology.

3. Simulation

3.1 Drug delivery

In the early 1990s, researchers utilized a mathematical model to evaluate a transdermal drug delivery system to predict the efficacy of a chemical permeation enhancer (CPE) [20]. The intercellular lipid lamellar structure in the stratum corneum (SC) plays a crucial role in the skin's barrier function. Recently, a more sophisticated methodology has been established through the use of computer simulation. The interactions between CPEs and SC lipids were investigated using MD simulations [21]. The partitioning and diffusion coefficients of CPEs in SC lipids were found to be highly dependent on size and structure. The aforementioned dependencies are elucidated in terms of structural properties, including the radial distribution function, the area per lipid, and the order parameter (Fig. 3).

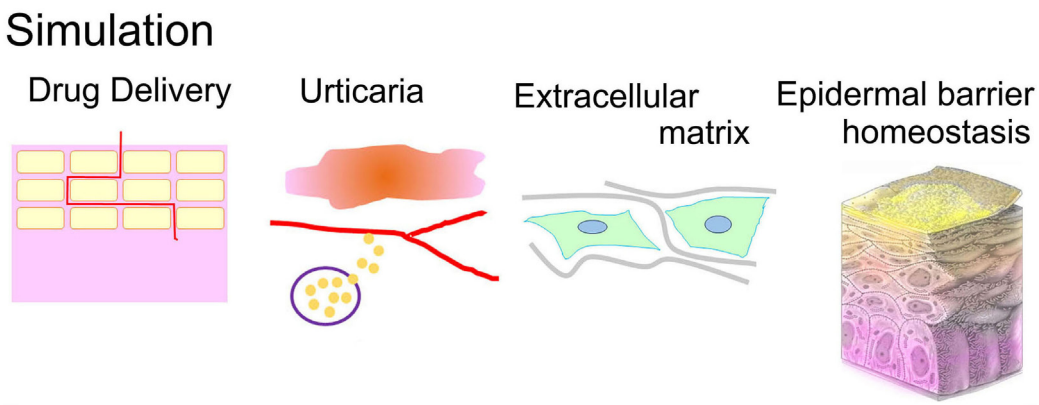

Figure 3. Simulation. Constructing mathematical models and computer simulations based on these models will be useful in elucidating the mechanisms of drug penetration, urticaria, analysis of the intercellular matrix, and epidermal barrier homeostasis.

3.2 Urticaria

Even common dermatological conditions can exhibit complex and variable patterns of clinical manifestation. A multitude of factors must be taken into consideration, as the situation varies depending on each individual patient's medical history and environmental context. In such cases, the identification of key factors can be facilitated through the utilization of mathematical models and simulations. Urticaria, a prevalent dermatological condition, manifests in diverse macroscopic eruptions that vary in their presentation among patients. A preceding study utilized a reaction-diffusion model to elucidate the multifarious eruptions of urticaria, proposing a self-activation and self-inhibition mechanism for the regulation of histamine release from mast cells [22]. The authors of the study indicated that the model parameters could explain the various shapes of the eruptions (Fig. 3).

3.3 Extracellular matrix

The anatomical configuration of the skin is closely associated with various dermatological conditions. However, in certain instances, the etiology of the lesions may not be directly associated with the biochemical factors that typically underlie such conditions. For example, thymic stromal lymphopoietin (TSLP) released from epidermal keratinocytes can trigger a range of allergic reactions and inflammation [4]. In such cases, the analysis of factors contributing to skin structure formation using a mathematical model has proven to be an effective method.

The extracellular matrix (ECM) is a complex structure through which biochemical and mechanical signals are transmitted. A recent study proposed several models – continuum, discrete agent-based, mechanical, and hybrid – to explain biological dynamics such as cell migration, developmental processes, cancer formation and migration, and wound healing [23]. The aforementioned models are predicated on observations of the ECM state. In order to ascertain the veracity of the content presented in this paper, experimental verification of each individual phenomenon is required. However, it should be noted that this process would serve to demonstrate the manner in which the combination of mathematical models and simulations can provide diverse perspectives (Fig. 3).

3.4 Epidermal barrier homeostasis

Prior experiments and observations have indicated a close relationship between the function of the epidermal barrier and the dynamics of the epidermal calcium gradient [24]. For instance, in a healthy epidermis, calcium ion concentration is high in the uppermost layer; however, the gradient disappears immediately after disruption to the barrier. It is acknowledged that the calcium gradient resumes its normal state once the barrier has been restored. For a considerable duration, the mechanism underlying this phenomenon remained unelucidated.

In order to comprehend the mechanism of barrier homeostasis, an *ex vivo* study was conducted using hairless mouse skin cultures. The present study revealed that calcium pumps and channels play crucial roles in maintaining the calcium gradient in the epidermis [25].

Subsequently, an *in vitro* study was conducted using a human keratinocyte monolayer culture system, which revealed the pivotal role of adenosine triphosphate (ATP), inositol 1,4,5-trisphosphate (IP3), calcium ions, and their receptors in calcium dynamics between keratinocytes [26, 27].

In light of the findings, a mathematical model of the calcium dynamics of the epidermal water-impermeable barrier homeostasis was formulated [28, 29], and computer simulations were conducted [30, 31]. The simulation results predicted that the undulatory pattern of the papillary layer beneath the epidermis is a key determinant of epidermal thickness. In order to test this prediction, human keratinocytes were seeded on polyester textiles with various fiber-structural patterns in culture dishes. The findings were consistent with the predictions of computer simulations, indicating that a textile substrate with fiber thickness and inter-fiber distance matching the simulations resulted in a three-dimensional epidermal-equivalent model characterized by a thick stratum corneum and an intercellular lamellar lipid structure [31].

Furthermore, a three-dimensional, agent-based computational model of the epidermis was presented, with consideration given to dermal deformability. The model simulates the formation of a corn (clavus) by assuming hyperproliferation and rapid differentiation. In addition, experimental data on human corns are provided, which support the model assumptions and simulation results [32].

These findings suggest that mathematical models and computer simulations are effective tools for applied medical science (Fig. 3).

4. Risks of computer technology in dermatology

The advent of sophisticated computing technology has rendered feasible the remote, large-scale manipulation of the physical and mental health of a population by means of computer systems. Recently, research findings have been reported indicating that the misuse of social media can be a risk factor for eating disorders [33]. The scope of contemporary information engineering is constrained to the domain of audiovisual information. This phenomenon has the potential to result in deviations from the fundamental interests of human beings. Nevertheless, the incorporation of skin information into information engineering in a more expansive sense has the potential to engender a more human-centric information society.

5. Conclusion

In comparison to the rapid advancements being made in the field of information science and technology, the application of these technologies in dermatology remains at an early stage. Nevertheless, the mechanisms underlying many skin diseases remain to be elucidated, and treatment frequently relies on symptoms. Furthermore, the foundational approach of Western medicine is reductionist; however, the intricate interplay of numerous factors is imperative for comprehending human health. A subset of dermatology researchers has focused extensively on identifying genetic factors associated with disease. Understanding genetic factors is important for advancing research into disease mechanisms. Nevertheless, the etiology of diseases is determined by the interaction between genetic predisposition, environmental and biological factors.

The application of information science has the potential to contribute substantially for the diagnosis of skin diseases and the development of novel treatments. Further research is needed to validate these computational approaches and establish their clinical utility in dermatology.

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Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Artificial Intelligence (AI) use

The authors accept full responsibility for the content of the manuscript, including the disclosure of any use of AI.
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Author contributions

M.D.: writing – original draft and writing – review and editing.

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Data availability

All of the data that support the findings of this study are available in the main text.
Data base: I used PubMed and Google Scholar. Data range is until July 10th 2026.