Neuromechanical representation of fabric-evoked prickliness: a fiber-skin-neuron model

Hu Jiyong · Li Yi · Ding Xin · Hu Junyan

Received: 13 August 2010 / Revised: 17 November 2010 / Accepted: 20 November 2010 / Published online: 1 December 2010
© Springer Science+Business Media B.V. 2010

Abstract Cutaneous A δ nociceptors encode the material and geometrical features of fiber ends evoking prickliness sensation by generating neural spikes in response to indentation of human skin, however, understanding of the underlying neuromechanism of fabric-evoked prickliness is still far from clear. This work develops and validates a fiber-skin-neuron (mechanosensitive A δ -nociceptors) model that combines an analytical model of fiber-skin indentation, a sigmoidal function of neuronal transduction, and a leaky integrate-and-fire model of neuronal dynamics. Firstly, the model is validated to be capable of capturing the typical neurophysiological features of cutaneous A δ nociceptors and the psychophysical phenomenon. And then, several case studies with respect to statistical features of fiber ends are carried out, and the resulting neural responses are calculated to explore the relationship between statistical features in study and evoked responses. The analysis of predicted action potentials over one second indicates that they systematically change with statistical features of fiber ends protruding above fabric surfaces, and the fitted stimulus–response relationship of A δ nociceptors is highly similar to the stimulus-sensation relationship of prickliness rating magnitude. It follows that there might exist a linear relationship between fabric-evoked neurophysiological responses and psychophysical responses. These results

provide significant new insight into the fabric-evoked prickliness sensation and raise interesting questions for further investigation, and the model described here bridges the gap between those models that transform fiber ends properties to firing rates.

Keywords Prickliness · Fiber ends · Nociceptor · Neurodynamics · Skin

Introduction

Fabric-evoked itch and prickliness sensation, one of main factors for clothing comfort, has been psychophysically widely studied (Hu et al. 2010a, b; Li 2001; Naylor 2010). Itch is defined as a sensation that evokes a desire to scratch, and prickling or stinging is described as sharp sensations that evoke a reflex desire to withdraw rapidly. Very recently, it has been shown that two independent neural coding mechanisms are involved in so-called itch and prickle sensation in clothing comfort, which might be principally associated with separate coding channels: polymodal C-fiber nociceptors for itch sensation, whereas A δ mechano-sensitive nociceptors (A δ nociceptors in following text, if not pointed, are mechano-sensitive) for prickling sensation as the first pain (Garell et al. 1996; Hansen et al. 2007). However, understanding of the underlying mechanisms of fabric-evoked itch and prickliness is still far from clear, the main reason being that itch and prickliness is influenced by many factors besides physical features of fiber ends, including both physiological and psychological factors. Quantitative modeling and simulation of fabric-evoked itch and prickliness sensation are urgently needed before the tactile study of clothing as a science could be established. Here, this study places an

H. Jiyong (✉) · D. Xin
Key Lab of Textile Science and Technology,
Ministry of Education, Donghua University,
201620 Shanghai, People's Republic of China
e-mail: hjydh@126.com

H. Jiyong · L. Yi · H. Junyan
Institute of Textiles and Clothing, Hong Kong Polytechnic
University, Hung Hom, Hong Kong
e-mail: tcli@inet.polyu.edu.hk

emphasis on neuromechanical representation of fabric-evoked prickliness sensation.

Cutaneous A δ nociceptors encode the mechanical prickling of fiber ends protruding above fabric surfaces, and enable us to perceive the prickliness in wearing clothing. The function of nociceptors is not to signal existing tissue damage, but to inform the central nervous system (CNS) when prickling stimuli approach tissue-threatening intensities. It is now clear that the local indentation of skin modifies significantly the subcutaneous stress, and then this stress is further converted into neural signals by a population of mechanosensitive nociceptors innervating the epidermis and shallow dermis, giving rise to nociception sensation at the cortex level (Garell et al. 1996; Lumpkin and Caterina 2007; Slugg et al. 2000). When fiber ends prick human skin's surface, the contact forces propagate through underlying tissues and toward the locations of mechano-sensitive A δ nociceptors, the transduction sites of A δ nociceptors. Each A δ nociceptor transforms forces near its transduction site into a series of neural pulses that carry stimulus information along the afferents to the brain. The pulses are stereotyped all or nothing events, referred to as action potentials or spikes.

In order to understand the neural coding strategy associated with fabric-evoked prickliness sensation, the best way is to record the signal in each process by which the short coarse fibers protruding above fabric surfaces induce the deformation of soft tissues within skin and elicit the neural signals of nociceptors, whereas the present electrophysiological technologies can not do. The alternative is to simulate the process from the generation of mechanical signal to the evoked action potential of nociceptors, so that it will make clear which physical features of the coarse fiber ends are reflected in the generated bioelectrical signal by the electromechanic transduction process. The simulation method will also allow us to implement a reverse correlation analysis to the pre-neural stage of tactile transduction. Veitch et al. has proposed that the buckling model of a simple Euler slender rod with fixed-hinged constraint can express the critical mechanical behavior of fiber ends prickling human skin (Veitch and Naylor 1992), and our previous study (Hu et al. 2010a, b) has modified the Euler buckling model of a fixed-hinged rod under axial compression by considering the large deformation phenomenon of fiber ends and the boundary constraint conditions of both ends. Therefore, it needs a further step to couple the mechanical behavior of fiber ends with the neural dynamics of cutaneous nociceptor neurons.

From above-mentioned survey, this study places an emphasis on the transduction function of cutaneous A δ nociceptors and the development of nociceptor transduction model, which is composed of three submodels: fibers-skin indentation model, model of biological current

generation, and neural dynamical model of transmission and modulation. And then, the case studies on neural responses of mechanosensitive nociceptors, embedded in soft tissues within human forearm, to typical physical properties of fiber ends protruding above fabric surfaces are carried out, and the predicted responses are compared to existing experimental observations.

Modeling and methods

To simulate the neuromechanical process from the mechanical behavior of fiber ends prickling human skin to the generation of membrane potential of cutaneous nociceptors, the proposed model needs to couple the fiber-skin indentation mechanics, the anatomical mapping and the mechanoelectric transduction of cutaneous A δ nociceptors, and the neural dynamics.

Fiber-skin indentation sub-model

According to our previous study (Hu et al. 2010a, b), the buckling behavior of single fiber end protruding above fabric surfaces and prickling human skin is schematized in Fig. 1, and the boundary constraints at both ends of single fiber ends prickling human skin are equivalent to be either elastic-inclined or elastic-hinged. In this context, the fiber end held in a fabric is elastic-restraint with the elastic rotation stiffness and the other end (against human skin) slipping-sliding (elastic-inclined) or hinged (elastic-hinged). Under each type of boundary constraints at both ends, the buckling behaviors of axial compression of fiber ends between human skin and fabric surfaces have been expressed.

Fig. 1 Schematic of buckling behavior of single fiber end under the compression between the fabric surface and human skin

For elastic-inclined

The force moment balance of a buckling fiber end at the cross-section of x distance away from the origin

$$M(x) = F(\Delta y - y) - Q_s(L_f \cos \gamma_0 - \delta_f - x). \quad (1)$$

The boundary restraints

$$\begin{aligned} Q(0) &= Q_s = \mu F \\ M(0) &= k_e \theta(0) = F \Delta y - Q_s(L_f \cos \gamma_0 - \delta_f) \\ M(L_f) &= 0 \\ \theta(0) &= \gamma - \gamma_0. \end{aligned} \quad (2)$$

$$M(x) = \begin{cases} -Fy - Q(0)x + M(0) & 0 < x < L_\alpha \\ Fy - Q_s g(L_f - \delta_f - x) & L_\alpha < x < L_f \end{cases}. \quad (4)$$

The boundary conditions are:

$$\begin{aligned} Q(0) &= Q_s \\ M(0) &= k_e \theta(0) = Q_s \cdot (L_f - \delta_f) \\ \theta(0) &= \gamma \\ M(L_f - \delta_f) &= 0. \end{aligned} \quad (5)$$

The relative displacement along y axis direction between both ends of single fiber end as well as the compression force

$$\begin{aligned} \delta_f &= L_f - \left[\int_{\gamma}^{\alpha} f(\theta) \cos \theta d\theta - \int_{\alpha}^{\beta} f(\theta) \cos \theta d\theta + \int_{\gamma}^{\alpha} f(\theta) \sin \theta d\theta / \tan(-\beta) \right] / \sqrt{2}k \\ F &= \left[\int_{\gamma}^{\alpha} f(\theta) d\theta - \int_{\alpha}^{\beta} f(\theta) \cos \theta d\theta + \int_{\gamma}^{\alpha} f(\theta) \sin \theta d\theta / \sin(-\beta) \right]^2 \cdot (E_f I_f / 2L_f^2) \end{aligned} \quad (6)$$

The relative displacement along x axis direction between both ends of single fiber end as well as the compression force

$$\begin{aligned} \delta_f &= L_f \cos \gamma_0 - \frac{1}{k\sqrt{2}} \int_{\gamma}^{\beta} \frac{\cos \theta}{\sqrt{(\cos \theta + \mu \sin \theta + C/F)}} d\theta \\ F &= \left[\int_{\gamma}^{\beta} f(\theta) d\theta \right]^2 \cdot E_f I_f / 2L_f^2 \end{aligned} \quad (3)$$

where μ is the fiber end sliding resistance coefficient against human skin, k_e the rotational stiffness of the fiber end held in fabric surfaces, γ_0 the initial inclined angle, γ the real-time inclined angle, β is the acute angle of fiber end against human skin to y axis, θ the tangential angle at any point along the buckling fiber, E_f tensile Young modulus of fiber, I_f axial moment of inertia of fiber, and

$$\begin{aligned} f(\theta) &= \frac{1}{\sqrt{\cos \theta + \mu \sin \theta - \cos \beta - \mu \sin \beta}} \\ C/F &= -\cos \beta - \mu \sin \beta \\ k^2 &= F/E_f I_f. \end{aligned}$$

For elastic-hinged

The force moment at the cross-section of x distance away from the origin

where α is the tangential angle at the contra-flexure point of buckling fiber.

The buckling deformation energy of fiber ends can only reach the cutaneous nerve endings through the intervening non-nervous tissues, and the triggering responses of nociceptors depend on the mechanical state of tissues in which they reside (Khalsa et al. 2000; Lumpkin and Caterina 2007; Zheng et al. 2002). From the point of view of single nociceptors, the skin is infinite in extent. Considering the small deformation less than 1.0 mm indentation, meanwhile, the mechanical stresses can be derived by the classic linear elastic deformation principles. According to classical elastic mechanics, the stimulus probe with little flat radius tip will nearly produce a constant displacement underlying contact area (Johnson 1985). Therefore, individual coarse fiber ends (less than 50 μm diameter) in the fiber array, which elements are consisted of fiber ends in contact with human skin, are assumed uniform indentations acting on the surface of the skin, and the relationship between the contact force F_s by single coarse fibers and the resulting skin indentation d_s is

$$d_s(r) = \begin{cases} \frac{F_s 1 - \nu_s^2}{2r_f E_s} & r \leq r_f \\ \frac{F_s 1 - \nu_s^2}{\pi r_f E_s} \sin^{-1}(r_f/r) & r > r_f \end{cases} \quad (7)$$

where E_s and ν_s is the Young modulus and Poisson's ratio of forearm skin as an isotropic elastomer, r_f the radius of fabric fiber, and r the distance far away from the fiber end center, respectively. Inversely, the contact force F can be

obtained from Eq. 7. Note, the distribution pattern of the contact pressure over the single contact area is complex and here is not discussed in detail.

And then, the contact force of each fiber end in fiber array will be computed by the discrete numerical method in contact mechanics (Johnson 1985). Briefly, the indentation under each fiber end locus is taken to be the additive effect of component forces exerted by all fibers in contact, and the mechanical influence coefficients between any two fibers are expressed as a matrix C , of which element c_{ij} expresses the indentation at the fiber end i produced by a unit force at the fiber end j . The skin indentations under all of fiber ends are then formulated as

$$D_s = CF \quad (8)$$

where D_s is an array containing skin indentations underlying fiber ends in contact, F is an array of the resulting contact forces and C is an influence coefficient matrix derived from Eq. 7. Thus, the array of contact forces, F is the form of

$$F = C^{-1}D_s. \quad (9)$$

For the mechanical system consisted of fiber ends and skin, on the other hand, the skin indentation under each fiber end can be expressed as the displacement of fiber end held in fabric surfaces (in this context, the external displacement loadings), by

$$D = D_s + \Delta_f \quad (10)$$

$$D = [d_1, d_2, \dots, d_n], D_s = [d_{s1}, d_{s2}, \dots, d_{sn}], \Delta_f = [\delta_{f1}, \delta_{f2}, \dots, \delta_{fn}], F = [F_{s1}, F_{s2}, \dots, F_{sn}]$$

where D and Δ_f is the set of displacement at the end of fiber end held in fabric surface and the approaching distance of one end of fiber end to the other, respectively, and the value of n represents the real-time number of fiber ends prickling human skin. In this context, the size of each element in array D as the loading displacement is calculated from the same reference plane as the fabric surfaces, therefore, their sizes are same. In this way, once the loading displacement D is given, the contact forces can be numerically and iteratively solved by taking Eq. 3 (or Eq. 6) and Eq. 10 into Eq. 9.

After the contact force acted by each fiber end on human skin is obtained, the stress–strain states underlying skin soft tissues will be calculated by the superposition principles in linear elastic mechanics. The stresses at any location of skin in the local coordinate system for each fiber end are given by

$$\sigma = 2FG/\pi \quad (11)$$

where $\sigma = \{\sigma_{ij}\}_{i,j=1,2,3}$, and the matrix $G = \{g_{ij}\}_{i,j=1,2,3}$, and each value of index i, j represents the direction along the x, y and z axis, respectively. Each element in matrix

G is the form of $g_{11} = \frac{3r^2z}{R^5} - \frac{1-2\nu}{R^2+zR}$, $g_{22} = (1-2\nu)(\frac{1}{r^2} - \frac{z}{r^2R} - \frac{z}{R^3})$, $g_{33} = \frac{3z^3}{R^5}$, $g_{13} = g_{31} = \frac{3rz^2}{R^5}$, $g_{12} = g_{21} = g_{23} = g_{32} = 0$. In Cartesian coordinates (x, y, z) , $r = \sqrt{x^2 + y^2}$, $R = \sqrt{r^2 + z^2}$. The z magnitude represents the depth of nociceptors below skin surface. And then, the stresses produced by multiple point loads can be added after each stress tensor is transformed into the global coordinates.

As for the case of multiple fiber ends simultaneously prickling human skin, on the other hand, an array consisted of pairs of coordinates will be used to describe the spatial distribution location of the protruding coarse fiber ends over fabric surfaces. These fiber ends are assumed to be randomly distributed over fabric plane, and the diameter dimension d_f of each fiber end in the array is statistically assumed to be normal Gaussian distribution. Besides, the values of each pairs of elements in this array depend on the spatial density of protruding coarse fiber ends per unit area of fabric surface (simply referred to fiber ends density, hereafter) and the diameter dimensions of adjacent fiber ends. Meanwhile, the assigned diameter dimension of fiber ends is limited by the following conditions: (1) the diameter of any fiber end is ranged from 30 (d_{fmin}) to 50 μm (d_{fmax}); (2) the center-to-center distance between any two fibers is larger than the sum of the radius of these two fibers. Mathematically these conditions can be described by

$$\begin{aligned} \text{(i)} \quad & d_{fmin} < d_{fi,j} < d_{fmax}, \\ \text{(ii)} \quad & d_{ij} > (d_i + d_j)/2, \quad d_{ij} = \sqrt{(x_{fi} - x_{fj})^2 + (y_{fi} - y_{fj})^2} \end{aligned} \quad (12)$$

where (x_{fi}, y_{fi}) and (x_{fj}, y_{fj}) are the location coordinates of the i th and j th coarse fiber end, respectively.

Anatomical mapping of nociceptors

In literatures there is not a clear description of spatial distribution pattern of cutaneous A δ nociceptors, and the Gaussian distribution pattern has been proposed to describe the change in spatial innervation density of low-threshold mechanoreceptors and free nerve endings in the extremities (Burgess and Perl 1973; Güçlü and Bolanowski 2002; Goransson et al. 2004; Lauria et al. 1999). In this context, all of A δ mechanosensitive nociceptors can be assumed to distribute in a plane parallel with forearm skin surface, and the y -coordinates are assumed to be uniformly distributed along the medio-lateral line across human forearm, and the density of x -coordinates decreases proximally from the maximum at distal ventral forearm (near to wrist) to the minimum at the proximal forearm by obeying a half-Gaussian peak function. In terms of an independent x - and y -coordinate anatomical distribution, moreover, the joint

probability density of A δ nociceptors mapping into anatomical organization is

$$g_S\{x_i = x, y_i = y\} = \frac{1}{w} \cdot \left(\frac{\alpha_s}{\sigma_s \sqrt{2\pi}} e^{-x^2/2\sigma_s^2} + \beta_s \right) \quad \text{for } 0 \leq x \leq L \cap 0 \leq y \leq w \quad (13)$$

and

$$\begin{aligned} \beta_s &= d_{\max} - \alpha_s / \sigma_s \sqrt{2\pi} \\ \lim_{x \rightarrow \infty} g_S(x, y) &= d_{\min} \\ \frac{1}{L \cdot w} \int_0^L g_S(x, y) dx &= d_{\text{mean}} \end{aligned}$$

where L , w the length and width of human forearm skin domain in study; α_s , β_s , σ_s constants dependent on density $d_{\max}$, $d_{\min}$ and d_{mean} .

In Eq. 13, the A δ -fiber RFC density $d_{\max}$ and $d_{\min}$ are respectively the upper and low quartile and estimated from the average innervation density (d_{mean}) as a parameter variable, here an estimation $d_{\text{mean}} \approx 0.05$ A δ -fibers/mm² on human forearm skin. Parameters α_s and β_s are determined by the integral of the density function being unity ($\alpha_s = 6.7416$, $\beta_s = 34.8368$) (Hu et al. 2010a, b).

Transduction sub-model

The transduction sub-model transforms stresses in the vicinity of the nociceptors to biological current entering the nociceptive fibers through its membrane, a quantity known as the receptor current. In the model, inputs are filtered separately, then summed and converted into current to form the input into neural dynamical sub-model with IF mechanism in next section.

While all types of in vivo observations match mechanical stimuli in the skin with the generated spikes at A δ fibers—the gross input–output relationship (Khalsa et al. 2000; Zheng et al. 2002), other intermediate transformations are not currently observable. For example, we can neither measure the specific forces local to the A δ nor observe the transformation of those local forces to the timing of elicited spikes. It is reported that the compressive or tensile component of stresses dominates the responses of cutaneous A δ -fiber nociceptor (Khalsa et al. 2000; Zheng et al. 2002). While the relationship between stresses and receptor current is unknown—because the nociceptors is not accessible to whole-cell recording, sensory cells such as hair cells and pain receptors exhibit sigmoidal stimulus–current curves (Holt and Corey 2000; Roberts and Rutherford 2008; Siemens et al. 2006), and the same trend of tension–Voltage for muscles exists (Karagueuzian and Katzung 1982). For this reason, this work employs a sigmoidal function

$$I_c(\sigma_I) = \alpha_I \frac{1}{1 + e^{\gamma_I(\sigma_{I0} - \sigma_I)}} \quad (14)$$

where α_I , β_I , and γ_I specify the shape of the transduction function, and σ_I is the stresses that give rises to the receptor current I_c . Before case studies, firstly the model parameters α_I , β_I , and σ_{I0} are modified, so that it is capable of capturing the typical physiological properties of nociceptors.

Neural dynamics sub-model

The modified integrate-and-firing equations are particularly useful in clarifying the time-dependent behavior of nerve excitation (Izhikevich 2004). Here, the Izhikevich's equation is employed to transform receptor current to spikes, and achieves to transduce a diverse range of physical energy into action potentials in somatosensory nociceptors. In essence, whenever the membrane potential, $V(t)$, is driven to the spike initiation threshold (V_0) by the current (I), a neural spike is recorded. The modified integrate-and-firing model by Izhikevich [Izhikevich, 2004] is

$$\begin{aligned} \frac{dV}{dt} &= 0.04V^2 + 5V + 140 - U + I_{ex} \\ \frac{dU}{dt} &= a(bV - U) \end{aligned} \quad (15)$$

$$\text{if } V \geq V_0 = 30 \text{ mV, then } \begin{cases} V \leftarrow c \\ U \leftarrow U + d \end{cases}$$

where a the rate of recovery, 1.0e-3; b the sensitivity of the recovery variable U to the subthreshold fluctuations of the membrane potential V , 0.1; c the after-spike reset value of the membrane potential V caused by the fast high-threshold K⁺ conductances, -70 mV; d after-spike reset of the recovery variable U caused by slow high-threshold Na⁺ and K⁺ conductances, 2.0; V membrane potential (depolarization positive) (mV); t time (ms); I_{ex} the external stimulus induced current density, positive outward ($\mu\text{A}/\text{cm}^2$), namely I_c in this contest. An action potential (spike) is produced when the membrane voltage reaches the voltage threshold and corresponds to the first-passage time for the associated stochastic process describing the voltage. In the moment of spike generation, the voltage is instantaneously reset to the resting membrane potential c .

Firing activity analysis

Some measures such as mean firing rates and entropy have been proposed to quantify the neural activities, and the correlation intensity between the external stimulus and neural activities.

From the output membrane potential of transduction sub-model, the peak firing rates of each nociceptor are

firstly calculated by spiking times averaging over one stimulus period. When the voltage reaches a threshold V_0 , the neuron emits a spike and the voltage is reset to a reset potential c after an absolute refractory period. The action potentials of each nociceptor are summated over the stimulus time and averaged over all activated nociceptors. And then, the stimulus–response data are fitted by the equation

$$ips = ax^b \quad (16)$$

where x the fiber feature values for one stimulus case, ips the averaging action potentials under each stimulus case.

Case study

Problem description

As the intrinsic reaction of human, once one or more of fiber ends prickling skin reach the force threshold of one of nociceptors responsible for fabric-evoked prickliness, we will perceive the prickliness and try to withdraw from the fiber end. Meanwhile, the maximum deflection angle of fiber end against skin is no more than $\pi/2$, otherwise it will slip along skin surface or the contact domain will abruptly increase by the point-face to line-face contact mode. Additionally, considering the little contribution of content of thin or long fibers to contact forces, it will only be simulated for the buckling behavior of short fiber end in the coarse edge of fiber diameter distribution, which prickles human forearm skin domain with a length of 100 mm and a width of 50 mm.

Observations are made at a series of sets of statistical features of coarse and short fiber ends as effect factors: the fiber end density, the mean lengths and the standard deviation, the mean diameters and the standard deviation. The forearm-skin Young modulus of 0.05 MPa (Jachowicz et al. 2007) and fiber-end Young modulus of 3.54 GPa (Veitch and Naylor 1992) keep invariant. With reference to previous studies (Garnsworthy et al. 1988; Naylor 1992a, b; Naylor et al. 1995), the typical statistical features of fiber ends generating prickliness are: mean length 2.0 mm and standard deviation 0.7, mean diameter 36 μm and standard deviation 6 μm , the fiber ends density 10 ends/10 cm^2 . In one set of study cases, one of the typical statistical features of fiber ends protruding above fabric surfaces changes systematically, and the others keep a constant level. Besides, both fiber ends length and fiber end diameter change consequentially in a normal Gaussian distribution and a limited range: the diameter of fiber ends ranges from 30 to 50 μm , and the length from 0.2 to 3 mm. These values represent not only the typical statistical features of fiber ends which contribute to fabric-evoked prickliness,

and also allow to obtain a more complete visualization of how the changes in each type of fiber end feature affect the neural responses of cutaneous A δ nociceptors.

To compute the evoked action potentials and the information content of cutaneous A δ nociceptors, in each study case, a set of assigned properties of fiber ends is firstly input into the developed sub-model of fiber-skin indentation, and then its outputs into the transduction and modulation model. The simulation flow for each case is schematized in Fig. 2.

Validation

Since A δ nociceptors have often been associated with the first “quick” pain, it is interested in their dynamic responses to the rising phase of mechanical stimulus. That is to say, the activated nociceptors should show the highest firing (discharging) rates at the first seconds of stimulus. When fiber ends prick skin surface, the deformation of skin tissues and the resulting biological current are illustrated in Fig. 3a. It can be seen that the induced biological current into nociceptors changes with different fiber ends in contact, and also gradually with the contacting time. It can be inferred, if the fiber end is easily buckled, a weak current is generated, and the vice versa. Once the induced biological current is above the threshold of current, where the cell membrane of nociceptors will open, the action potential with a burst will generate, as shown in Fig. 3b. Apparently, the triggered neural responses are intense when the induced biological current change rapidly over the prickling time, and will greatly decrease once the induced current enters a stable level. The dynamic component of neural responses has been observed in some published electrophysiological recordings of A δ nociceptors in skin (Adriaensen et al. 1983; Garell et al. 1996;

Fig. 2 Simulation flowchart

Fig. 3 illustration of physiological responses of A δ nociceptor under population of fiber ends prickling skin.

a Induced biological current;
b triggered firing response of two typical nociceptors

Gentle et al. 2001), muscle (Khalsa and Ge 2004). On the other hand, the order of magnitude of firing rates in Fig. 3b is compared to those of A δ nociceptor in the experimental recording results of human forearm skin (Adriaensen et al. 1983) and the others (Garell et al. 1996; Khalsa et al. 2000). Therefore, the developed fiber-skin-receptor model is simple and capable of producing rich spiking dynamics exhibited by A δ nociceptors, and then can be used to predict the neural responses of A δ nociceptor when fiber ends prick human skin.

Fiber ends density

The spatial distribution density of fiber ends with diameter larger than a certain value (e.g. 30 μ m) is identified as an index judging fabric-evoked prickliness (Garnsworthy et al. 1988; Naylor 1992a, b; Naylor and Phillips 1997; Naylor et al. 1997). Figure 4 shows a significant power

Fig. 4 Relationship between fiber end density and number of triggered action potentials over 1.0 s. Each data point represents the triggered neural responses from one simulation of a set of fiber ends features as an input, hereafter

dependence of the triggered responses of nociceptors on the fiber ends density, and the fitted power index is 0.67. This stimulus–response relationship of nociceptors is highly similar to that between perceived prickliness magnitude and fiber end density, where the power index as seen in Garnsworthy’s Fig. 9 is 0.66 (Garnsworthy et al. 1988). Unfortunately, it is unknown of what is the relationship between firing rates of nociceptors and the resulting subjective sensation of prickliness. Although the experimental results observed by Garnsworthy et al. (1988) shows an accelerating increase of the action potentials with three different fiber ends density, it is not enough for the numbered three data to represent the general stimulus–response relationship, so that the relationship between fiber ends density, action potentials and subjective sensation of prickliness can not be deduced from their neurophysiological and psychophysical experiment results.

On the other hand, many authors observed a quasi-linear relationship between neural responses (commonly firing rates) of populations of low-threshold mechanoreceptors and perceived sensation magnitude in psycho-physiological studies with respect to the modalities of tactile sensation such as pressure and roughness (Johnson et al. 2002), itch (LaMotte et al. 2009). In this sense, there probably exists a linearity between perceived prickliness and the neural activity of A δ nociceptors, therefore, it can be inferred from the psychophysical power law proposed by Garnsworthy that the action potentials of A δ nociceptors depend on the fiber end density in a power law. In this sense, these phenomena further validates that the developed fiber-skin-receptor model is capable of simulating the stimulus–response phenomenon of A δ nociceptors triggered by the protruding coarse fiber ends above fabric surfaces.

Fiber end diameter

The effect of diameter of fiber ends on the activation of A δ nociceptors beneath them includes two folds: one is to increase the bending rigidity, so strengthen the stimulus

intensity to skin surface; the other is to distribute stimulus intensity impinging on nociceptor sheets by changing contact area. Figure 5 shows the change of neural responses of triggered nociceptors with the mean diameter of fiber ends. Each point in Fig. 5 represents the mean action potentials over all of triggered nociceptors when populations of fiber ends protruding above fabric surfaces prickle human skin. Apparently, although the differences of the diameter of fiber ends in effect leads to a large variation of action potentials of triggered nociceptors, totally the neural responses sigmoidally increase with the mean diameter of fiber ends protruding fabric surfaces (goodness of fit test: $F(4, 1) = 1.8e+4$, $P \approx 0.005$, Adj. R -square ≈ 0.84). When the mean diameter of fiber ends increase by 67%, the mean action potentials over triggered nociceptors. Of course, an increase of mean diameter by 67% greatly increase the number of coarse fiber ends (Naylor 1996), and an increasing number of coarse fiber ends will change the stimulus sites, the resulting deformation degree of skin and the stimulus intensity to nociceptors. As a result, an increase of mean diameter can not always increase the neural responses. Considering the linear neural-response relationship, anyway, the high dependence of neural responses on the mean fiber diameter (Pearson $r = 0.92$, $P < 0.03$) is consistent with the good correlation between perceived prickliness magnitude and the mean fiber diameter observed by De Boos et al. (2002) and Naylor (2010).

The magnitude of the standard deviation of fiber ends diameter changes the content of coarse edge of fiber ends, and an increasing standard deviation will increase the absolute number of coarse fiber ends when the total number of fiber ends is constant. Figure 6 shows a sigmoid increase of neural responses of triggered nociceptors with the standard deviation of the diameter of fiber ends (goodness

Fig. 5 Effect of mean diameter of fiber ends on neural responses of triggered nociceptors

Fig. 6 Effect of standard deviation of the diameter of fiber ends on neural responses of triggered nociceptors

of fit test: $F(4, 2) = 5.5e+4$, $P \approx 0$, Adj. R -square ≈ 0.98). Experimentally, Naylor et al. observed that the variations in the content of coarse edge of fiber ends at a given mean fiber diameter can lead to a significant difference in fabric-evoked prickle (Naylor et al. 1992, 1997), however, it is needed to identify the psychophysical sensitivity of human perceived prickliness to the variation of content of coarse edge of fiber ends. In fact, the effect of mean fiber diameter on neural responses of nociceptors is interchangeable with that of its variation, as Naylor et al. have suggested that the percentage point shift in the standard deviation of diameter is equivalent to a micrometer order of magnitude change in mean diameter (Naylor et al. 1995).

Fiber end length

The lengths of fiber ends protruding above fabric surface determine to some degree their capability against buckling deformation. Relatively, a short fiber end can resist against a high compression force, and this will lead to intense neural responses of nociceptors. Figure 7 shows that the mean length of fiber ends has a significant effect on the neural responses of triggered nociceptors (one-sample Chi-Square test for variance, $P < 0.05$). It can be seen that there are two extreme values along the mean length of fiber ends where the neural responses increase with the mean length of fiber ends, as seems to contract with the mechanical model explaining fabric-evoked prickliness on the basis of the classical buckling stability theory of a slender rod (Veitch and Naylor 1992). Note, two end-constraint parameters, i.e. the intensity of fiber ends held in fabric surfaces and the slipping or sliding resistance of fiber ends against human skin surface, are involved in our

Fig. 7 Effect of the mean length of fiber ends on neural responses of triggered nociceptors

developed fiber-skin model, and the added constraint conditions lead to a complex buckling deformation of fiber ends in control. Although it is unknown of the determinant effect of mean length of fiber ends on neural responses, it is sure that the buckling mechanics of a simple fixed-hinged or fixed-free slender rod is not appropriate to simulate the mechanical behavior of fiber ends prickling human skin, as has been validated in our previous work (Hu et al. 2010 a, b).

When the standard deviation of fiber end length is considered, it has a significant and consistent effect on the neural responses of nociceptors, as shown in Fig. 8. It can be seen from Fig. 8 that the neural responses decrease with an increase of the standard deviation. Now, it is surprised why the mean length of fiber ends and their standard deviation have a different effect on neural responses. In theory, when the mean length of fiber ends keep constant, an increase of the standard deviation leads to a larger

Fig. 8 Effect of the standard deviation of fiber end length on neural responses of triggered nociceptors

difference between the length of multiple fiber ends, so that few and even only one fiber end comes to endure the total interaction force and easily buckles or bends to slide along skin surface. On the contrary, more fibers are involved in contact, more nociceptors will be triggered. As for the mean length of fiber ends, its variation only can shift the distribution pattern of the length of fiber ends, not the distribution shape, herewith, the number of fiber ends in contact is nearly invariable. In this sense, this phenomenon validates the dominant role of fiber ends density in fabric-evoked prickliness and the limited role of diameter of fiber ends.

Conclusions

An analytical model of transduction of cutaneous A δ nociceptor in fabric-evoked prickliness has been developed by introducing the fiber buckling mechanics, skin mechanics and considering the current biophysical and neurological properties of nociceptors. The concept of bioengineering are coupled with established methods in neuroscience, and the model development has been made consistent with the known morphology and physiology of skin tissues and A δ nociceptors. After the model is validated to be capable of capturing the essential properties of experimentally measured frequency responses of cutaneous A δ nociceptor, this model is used to facilitate insight into the relationship between statistical features of fiber ends protruding above fabric surfaces and the neural responses of triggered nociceptors. By the case studies on statistical features of fiber ends, the following conclusions are drawn.

In multiple levels of stimulus-responses processes, this study demonstrates the dominant role of fiber ends density in fabric-evoked prickliness, and provides a neuromechanical explanation for the relationship between physical properties of fiber ends, neural responses of cutaneous A δ nociceptor and the resulting prickliness sensation. The neural responses of triggered nociceptors deceleratingly increase with the spatial density of fiber ends in a power law, and sigmoidally increase with the mean diameter of fiber ends and their standard deviation. It is not clear of the relationship between the mean length of fiber ends and the triggered neural responses, whereas the increasing standard deviation of fiber ends length acceleratingly decreases triggered neural responses by an increasing number of fiber ends in contacts with skin.

There are nonetheless several limitations of this model. For cutaneous A δ nociceptors their constant position beneath skin masks the realistic anatomical changes, while the depth beneath skin may impact nociceptors' sensitivity to pin-prickle stimulus. Moreover, this model is lack of the modulation of central nervous system on the transmitted

external stimulus signal via peripheral nervous system, as determines to some degree the magnitude of perceived prickliness sensation. These deficiencies will be addressed in our future studies.

Acknowledgments The authors would like to acknowledge the project (No. KF0903) and NNSF through project (No. 10872068).

References

- Adriaensen H, Gybels J, Handwerker HO et al (1983) Response properties of thin myelinated (A-delta) fibers in human skin nerves. *J Neurophysiol* 49(1):111–122
- Burgess PR, Perl ER (1973) Cutaneous mechanoreceptors and nociceptors. In: Iggo A (ed) *Handbook of sensory physiology, somatosensory system*. Springer, New York
- De Boos AG, Naylor GR, Slota IJ et al (2002) The effect of the diameter characteristics of the fibre ends on the skin comfort and handle of knitted wool fabrics. *Wool Technol Sheep Breed* 50(2):110–120
- Garell PC, McGillis SLB, Greenspan JD (1996) Mechanical response properties of nociceptors innervating feline hairy skin. *J Neurophysiol* 75(3):1177–1189
- Garnsworthy PK, Gully RL, Kenins P et al (1988) Identification of the physical stimulus and the neural basis of fabric-evoked prickle. *J Neurophysiol* 59(4):1083–1097
- Gentle MJ, Tilston V, McKeegan DE (2001) Mechanothermal nociceptors in the scaly skin of the chicken leg. *Neuroscience* 106(3):643–652
- Goransson LG, Mellgren SI, Lindal S et al (2004) The effect of age and gender on epidermal nerve fiber density. *Neurology* 62(5):774–777
- Güçlü B, Bolanowski SJ (2002) Modeling population responses of rapidly-adapting mechanoreceptive fibers. *J Comput Neurosci* 12(3):201–218
- Hansen N, Klein T, Magerl W et al (2007) Psychophysical evidence for long-term potentiation of C-fiber and A-fiber pathways in humans by analysis of pain descriptors. *J Neurophysiol* 97(3):2559–2663
- Holt JR, Corey DP (2000) Two mechanisms for transducer adaptation in vertebrate hair cells. *PANS* 97(22):11730–11735
- Hu J, Li Y, Hu J (2010a) The mechanics of buckling fiber in relation to fabric-evoked prickliness—a theory model of single fiber prickling in human skin. *J Text Inst* (accepted)
- Hu J, Li Y, Hu JY (2010b) Neuromechanical representation of fabric-evoked prickle: spatial and probability integration. *Fibers Polym* 11(5):790–797
- Izhikevich EM (2004) Which model to use for cortical spiking neurons? *IEEE Trans Neural Netw* 15(5):1063–1070
- Jachowicz J, McMullen R, Prettypaul D (2007) Indentometric analysis of in vivo skin and comparison with artificial skin models. *Skin Res Technol* 13(3):299–309
- Johnson KL (1985) *Contact mechanics*. The Press Syndicate of the University of Cambridge, London
- Johnson KO, Hsiao SS, Yashioka T (2002) Neural coding and the basic law of psychophysics. *Neuroscientist* 8(2):111–121
- Karagueuzian HS, Katzung BG (1982) Voltage-clamp studies of transient inward current and mechanical oscillations induced by ouabain in ferret papillary muscle. *J Physiol* 327(1):255–271
- Khalsa PS, Ge W (2004) Encoding of tensile stress and strain during stretch by muscle mechano-nociceptors. *Muscle Nerve* 30(2):216–224
- Khalsa PS, Zhang C, Qin YX (2000) Encoding of location and intensity of noxious indentation into rat skin by spatial populations of cutaneous mechano-nociceptors. *J Neurophysiol* 83(5):3049–3061
- LaMotte RH, Shimada SG, Green BG et al (2009) Pruritic and nociceptive sensations and dysesthesias from a spicule of cowhage. *J Neurophysiol* 101(3):1430–1443
- Lauria G, Holland N, Hauer P et al (1999) Epidermal innervation changes with aging, topographic location, and in sensory neuropathy. *J Neurol Sci* 164:172–178
- Li Y (2001) The science of clothing comfort. *Text Prog* 31(1/2):1–135
- Lumpkin EA, Caterina MJ (2007) Mechanisms of sensory transduction in the skin. *Nature* 445(7130):858–865
- Naylor GRS (1992a) The relationship between the fibre diameter distributions of wool top, fibre ends and yarn surface fibres. *Wool Technol Sheep Breed* 40(2):40–43
- Naylor GRS (1992b) The role of coarse fibres in fabric prickle using blended acrylic fibres of different diameters. *Wool Technol Sheep Breed* 40(1):14–18
- Naylor GRS (1996) The coarse fibre component and fibre end diameter characteristics of Australian Wool tops. *J Text Inst* 87(2):265–273
- Naylor GRS (2010) Fabric-evoked prickle in worsted spun single jersey fabrics, Part IV: extension from wool to Optim(TM) fine fiber. *Text Res J* 80(6):537–547
- Naylor GRS, Phillips DG (1997) Fabric-evoked prickle in worsted spun single jersey fabrics. Part II. The role of fiber length, yarn count, and fabric cover factor. *Text Res J* 67(5):354–358
- Naylor GRS, Veitch CJ, Mayfield RJ et al (1992) Fabric-evoked Prickle. *Text Res J* 62:487–493
- Naylor GRS, Phillips DG, Veitch CJ (1995) The relative importance of mean diameter and coefficient of variation of sale lots in determining the potential skin comfort of wool fabrics. *Wool Technol Sheep Breed* 43(1):69–82
- Naylor GRS, Phillips DG, Veitch CJ et al (1997) Fabric-evoked prickle in worsted spun single jersey fabrics. Part I the role of fiber end diameter characteristics. *Text Res J* 67(4):288–295
- Roberts WM, Rutherford MA (2008) Linear and nonlinear processing in hair cells. *J Exp Biol* 211(11):1775–1780
- Siemens J, Zhou S, Piskowski R et al (2006) Spider toxins activate the capsaicin receptor to produce inflammatory pain. *Nature* 444(7116):208–212
- Slugg RM, Meyer RA, Campbell JN (2000) Response of cutaneous A- and C-fiber nociceptors in the monkey to controlled-force stimuli. *J Neurophysiol* 83(4):2179–2191
- Veitch CJ, Naylor GRS (1992) The mechanics of fibre buckling in relation to fabric-evoked prickle. *Wool Technol Sheep Breed* 40(1):31–34
- Zheng Z, LaMotte RH, Grigg P (2002) Comparison of responses to tensile and compressive stimuli in C-mechanosensitive nociceptors in rat hairy skin. *Somatosens Mot Res* 19(1):109–113