A. SPECIFIC AIMS

The somatosensory system is the only sensory channel that directly interacts with the objects in the external world. The human hand achieves this interaction by integrating tactile features (like motion direction, texture, force) with the proprioceptive state of the arm (posture of the elbow, shoulder, wrist). During goal-directed actions like grasping a glass sliding from your hands (motion from your palm towards the fingertips, i.e. with respect to the hand) or counter-pulling a leash rightwards on a dog running leftwards with respect to your body (body-centric reference frame), the brain computes the resultant motion direction in respective reference frames from the tactile motion on the hand and the posture of the arm. A reference frame is defined as a point of observation to determine object positions and directions in space. Understanding reference frame transformations of tactile motion is pivotal to our understanding of how the brain generates signals that enable goal-directed actions, yet the theoretical framework and neural mechanisms underlying these computations are yet to be elucidated. We address these gaps through a series of complementary human psychophysical, computational, and monkey neurophysiological studies.

Aim 1: To test that humans perceive tactile motion directions in different reference frames under different postures of the arm. Mathematically, Euler rotation matrices are used to represent reference frame transformations. If the brain perfectly employs these rotations, then we can deterministically calculate the motion information in a given reference frame. In contrast, the brain might not accurately infer the proprioceptive state of the arm or have noise in employing coordinate transformations, leading to probabilistic inference of the resultant motion direction. Previous psychophysical studies have shown interactions of proprioception and tactile features, but have failed to explicitly modulate the reference frames for estimating tactile motion. Additionally, no theoretical framework underlying reference frame—based transformation of tactile motion has been proposed. In our study, human participants will judge the direction of motion on their finger, in two explicitly instructed reference frames, left or right with respect to the center-of-the-body (body-centric) or towards the tip or base of the finger (finger-centric).

We hypothesize that the sequence of proprioceptive transformations and the uncertainty in arm posture systematically deviate how humans perceive tactile motion direction in different reference frames. Confirmation of the expected outcome will demonstrate that the brain has inherent uncertainty in the transformation process, and performs tactile motion transforms sequentially at intermediate joints from the point of stimulation to the point of observation. We will model our data by extending the Euler matrix transformations to a Bayesian inference framework. Our preliminary data show higher discrimination thresholds in the body-centric reference frame, implying sequential inclusion of proprioceptive noise. Additionally, we find posture-dependent biases deviating from ideal Euler transformations. We capture this deviation by modifying the Euler Model with a prior over postures.

Aim 2: Examine the neural correlates underlying coordinate transformation of tactile motion by the upper limb. We will perform a similar behavioral experiment in non-human primates. Neurons in Area 1 of the somatosensory cortex have been shown to encode tactile motion information. However, in those studies, the hand was placed in a fixed position. To our knowledge, no research has shown how the brain integrates proprioceptive signals with the motion information on the skin. Additionally, previous research has shown the task-dependent interaction of spatial touch with proprioception in the parietal cortex. Studies have identified medial intra-parietal area (MIP) to receive proprioceptive inputs and mediate control of goal-directed arm movements and encode for passive arm movements. But no previous work has described the neural basis for reference frame-based transformations of tactile motion signals. We propose to use monkey neurophysiological experiments to examine: (1) how tactile motion coding is modulated by proprioception, and (2) how the brain performs reference frame transformations of tactile motion.

We hypothesize that Area 1 and MIP hierarchically represent variables for tactile motion transformations, where MIP encodes tactile motion signals in different reference frames and Area 1 encodes tactile motion and proprioceptive states independent of the reference frame. To compare findings from humans and monkeys, we will decode neural activity from Area 1 and MIP and compare predicted performance with monkey and human behavior. Successful outcomes will suggest the MIP region as the basis of tactile motion reference frame transformation. Model-free analyses of neural responses for different motion directions, and proprioceptive states will add critical information to our understanding of how the brain performs goal directed actions.

We propose, for the first time, to study how the brain infers tactile motion under posture modulation in different coordinate frames. The knowledge gained from this work can assist in enhancing upper-limb neuro-prosthetics and deep brain stimulators, and may help us better understand the underlying pathologies of sensori-motor disorders (e.g., Parkinson's disease and dystonia).

B. SIGNIFICANCE

In any direct interaction with objects, humans engage with object surfaces moving on the skin. The spatial properties of these objects are encoded by tactile receptive fields anchored to the skin surface (*Constanzo and Gardner 1980*). To enable manipulations of dynamic objects with the hand, the brain should be able to flexibly switch between object representations in multiple reference frames (*Avillac et. al 2005; McGuire and Sabes 2009; Battaglia-Mayer et. al 2003*). In the somatosensory system, this invariant object representation is mediated by the proprioceptors of the limbs (elbow roll, shoulder pitch, wrist yaw etc.). Previous studies have described how the position of the hand is encoded in multiple reference frames during reaching and grasping (*Caminiti et. al 2017; Piserchia et al. 2017*) but do not address how the motion information on the hand surface is integrated with the position of the hand. The encoding of motion signals impinged on the skin has previously been described but with the hand fixed in one posture (*Pei et. al 2008; 2011*). In the visual system, neural correlates of coordinate transformation are often found to involve gain-field mechanisms (*Anderson et. al 1985; Orban et. al 2021*). But no previous work study has described how the brain infers tactile motion under posture modulation in different reference frames. In this proposal, for the first time, we bridge this gap through a series of complementary human psychophysical, computational, and monkey neurophysiological studies.

The modulation of tactile signals in different reference frames can be illustrated by the following example: when an object slips between our fingers, the object is perceived moving downwards regardless of whether the object is held with the hand in a supinated or pronated position (**Figure 1**). In the pronated position, the object slides from the palm to the fingertips, whereas in the supine position the object slides in the opposite direction. Yet, the motion percept relative to the world is the same in both hand postures. This is resolved if we consider that motion signals on the skin are remapped into a body-centric reference frame that is modulated by proprioception (wrist roll in this example). Now, if the percept was instead inquired with respect to the palm, then we would perceive the motion differently — away from the palm in the pronated posture, and towards the palm in the supinated posture. In other words, we selectively integrate proprioceptive state of the hand with the tactile motion signals in the context of a specific reference frame. It is currently unknown how the brain performs these fundamental transformations.

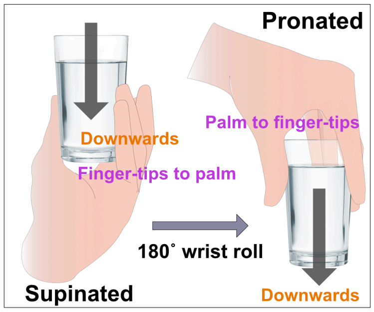

Figure 1: Schematic illustration of an object slipping between the fingers in different postures, but the perceived direction remains the same — downwards.

Theoretically, proprioceptive transformations between the point of stimulation on the skin (e.g., the finger) and the point of observation (e.g., with respect to the elbow, in an elbow-centric reference frame) can be represented by a product of Euler transformation matrices at the intermediate joints. In the example above, these intermediate joints are the finger joints, wrist and the elbow. However, due to inherent noise in sensory channels (*Faisal et. al 2008*), we may not be able to deterministically compute the tactile motion direction. Additionally, due to incorrect internal estimates of the proprioceptive state, we may not be able to perfectly integrate the exact posture of the limbs with motion information on the skin. *Chen et. al (2020)* performed a human psychophysics experiment to study the interaction of tactile motion with the proprioceptive state of the head and arm; they found systematic biases, but their experimental design did not instruct a reference frame. The lack of instruction leaves the reference frame in use open to interpretation by the subject. Hence, the observed biases could actually be explained by the use of a mixture of reference frames, instead of bias relative to a canonical reference frame.

In **Aim 1,** we will test if humans perceive tactile motion direction in different reference frames under different postures of the arm. Participants will perform a two alternative-forced choice task (2-AFC) in which they judge whether a stimulus impinging on their index finger is moving leftwards or rightwards with respect to their body as the elbow is positioned in different postures. Alternatively, the participants will be cued to perform the task in a finger-centric reference frame, judging whether the stimulus is moving towards the tip or the base of the finger. We hypothesize that the sequence of proprioceptive transformations and the uncertainty in arm posture systematically deviate how humans perceive tactile motion direction in different reference frames. The biases from ideal behavior will be observed if there exists a non-uniform prior over different arm postures. Additionally, the sequential application of proprioceptive transformation (if the point of stimulation is on the fingers, then the sequence is from the fingers to the wrist, from the wrist to the elbow and so on) will imply that proprioceptive noise is added in each subsequent transformation leading to increase in discrimination threshold in higher-order reference frames. Our preliminary data support the above predictions. No previous computational framework has been suggested for the underlying transformations. We will quantify our predictions, and capture the uncertainty and biases in human behavior by extending the theoretically ideal Euler matrix transformations to a Bayesian inference framework.

The computational framework and human psychophysical reports form the basis for evaluating the neural mechanisms underlying tactile motion transformations. Previous research (Pei et. al 2008; 2011) has demonstrated that neurons in Area 1 encode tactile motion, but this study was performed with the hand in a fixed posture. Another study (*Kim et. al 2015*) showed that neural activity in Area 1 is modulated by the change in proprioceptive state of both simulated and non-simulated fingers. This study, like *Chen et. al (2002)*, did not explicitly instruct a reference frame, hence the modulation could have originated from an assumed reference frame. Further, human psychophysical studies have reported how proprioception affects tactile localization in different reference frames (*Badde et. al 2015*; *Azañón et. al 2015*). However, how the brain integrates tactile motion signals with the proprioceptive state of the hand in different reference frames is yet to be elucidated. Are proprioceptive inputs integrated with tactile motion direction representations in Area 1 in a goal-directed manner? Alternatively, are tactile motion signals anchored to a skin-based reference frame in Area 1, and transformed only in the parietal cortex? Neurons in the medial intra-parietal area (MIP) receive arm, shoulder and neck proprioceptive inputs from both the Dorsal Cochlear Nucleus (DCN) and primary somatosensory cortex (*Prevosto et. al 2011*). Rostral MIP is also shown to mediate control of goal-directed arm movements via its connections with frontal lobe motor areas (*Johnson et al. 1996*; *Rizzolatti et al. 1998*) and encode for passive arm movements (*Burbaud et al. 1991*). In **Aim 2**, we will perform a series of monkey electrophysiological studies to find the neural correlates underlying coordinate transformation of tactile motion by the upper limb. Specifically, we address (1) how are the tactile motion representations in somatosensory cortex modulated by the proprioceptive state of the arm, and (2) what is the neural substrate underlying the decision readout of the resultant motion direction based on the reference frame. We hypothesize that Area 1 and MIP hierarchically represent variables for tactile motion transformations, with MIP encoding tactile motion signals in different reference frames and Area 1 encoding tactile motion and proprioceptive states independent of the reference frame. We will perform a motion discrimination task with monkeys in multiple reference frames, similar to the human psychophysical task in Aim 1, while we simultaneously record from Area 1 and the MIP area. If the decision is read out from MIP, then the same linear decoder will be able to predict behavior in the two reference frames with the same shared weights (*Sasaki et. al 2020*). Additionally, in model-free analyses of single-unit and population recordings in Area 1, we will study how tactile tuning functions are modulated by change in proprioceptive states. Our experimental design allows us to tear apart neural activity originating from the change in proprioceptive state and from the instructed reference frame. This investigation will elucidate the neural circuitry between Area 1 and MIP that is utilized in tactile motion transformations.

Taken together, these experiments will examine, for the first time, the reference frame transformations of motion information on the skin during upper limb proprioception using a series of human psychophysical, computational modeling and electrophysiological non-human primate experiments. The knowledge gained from this work can assist in enhancing prosthetics, and may help us better understand the underlying pathologies of sensori-motor disorders.

C. APPROACH

C.1. General Experimental Methods for Aim 1

Human subjects: Psychophysics will be the main methodology used to measure human behavior in Aim 1. All subjects will be healthy adult volunteers (age 18-65).

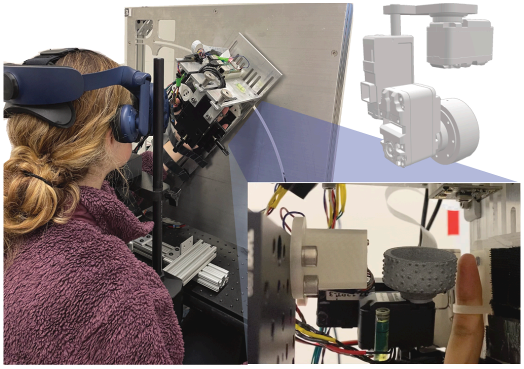

Figure 2: A participant performing the experiment. A zoomed-in view of the tactile stimulator impinging motion direction on the finger (bottom-right). A 3D model of the tactile stimulator (top-right).

***Tactile Stimulator*:** A dotted cylindrical drum (32mm diameter) is used to provide tactile stimulation on the finger (**Figure 2, bottom and top right**). Dots are half-spheres with a radius of 2mm and the minimum surface distance between dots is 5mm (*McIntyre et. al 2012*). The cylindrical drum will be aligned over the center of the distal phalange of D2 (upper portion of the index finger) of the left hand. This region of the hand has the highest innervation of mechanoreceptors (*Smith et. al 2002*), hence provides the greatest sensitivity to different tactile motion directions. We will ensure that the drum does not run over the edges of the finger to prevent any edge effects. Additionally, rotation will be initialized before the drum contacts the finger surface to prevent cues about stimulus orientation. The stimulus will spin at 85 mm/s (*McIntyre et. al 2012*) in one of 20 directions spanning 360˚ space for a maximum of 2 seconds duration, calibrated to indent 1.5 mm into the skin surface.

Experimental Setup: The subject's head will be stabilized by a chin and forehead rest. The left arm will be strapped into the rig and all fingers will be immobilized using grips to restrict any movement. The subjects will

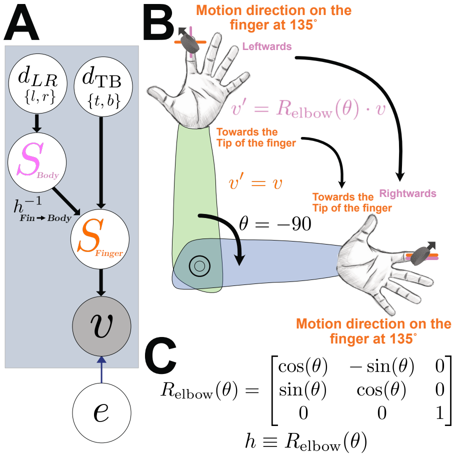

Figure 3: (**A**) Bayesian generative model for the experiment. (**B***)* The forearm moving between two example postures, perceived direction (v') and the ideal responses (or decisions) in the finger-centric (TB) reference frame (*orange)* and body-centric (LR) reference frame (*pink*), when the stimulus is moving at 135˚. (**C**) Example Euler matrix for rotation around the elbow.

wear a virtual reality (VR) headset while performing the task. The VR headset blocks any visual information about the position of the arm or the orientation of the tactile stimuli. Additionally, we will use the VR headset to provide cues about the instructed reference frame. To meet the data requirements for the computational analysis at individual subject level (Section C.3. *Stimuli and Task*), we designed an in-house rig that allows automatic positioning of the arm with high reliability (**Figure 2**; proprioceptive error: ±1˚).

Computational Analysis: A Bayesian ideal observer model will be built based on a generative model of the psychophysical task (**Figure 3A,B**) to make quantitative predictions that can be compared to behavior. The model will be fitted to the data to explore the biases compared to mathematically ideal rotations (**Figure 3C**). Additionally, we will use the variance parameter fitted to the data to find how subjects' discrimination sensitivity changes across reference frames (**Figure 5C**). The decision variables in the model represent the decisions that the brain makes about the motion direction of the wheel. Here, $d_{\textbf{RF}}$ *(*decision in a **R**eference **F**rame) denotes the subject's decision about whether the stimulus is moving **l**eft or **r**ight in the body-centric reference frame ($d_{\textbf{LR}}$) or towards the **t**ip or **b**ase of the stimulated finger in the finger-centric reference frame ($d_{\textbf{TB}}$). The inferred state variables represent what the brain believes about the current state of environmental parameters, where $S_{\textbf{body}}$ denotes the perceived direction of motion in the body-centric reference frame, and $S_{\textbf{finger}}$ denotes the direction of motion in the finger-centric reference frame. Finally, the sensory observation 'v' represents the state variable observed through our sensory organs, namely the motion direction on the skin of Digit 2 in our task. 'e' represents the experimentally presented stimulus. Further, h represents the Euler Matrix Transformation from the finger-centric to the body-centric reference frame. In this task, h is equivalent to rotation at the elbow (**Figure 3C**). The transformation can further be generalized to other reference frames as a product of rotation matrices. Hence, this model can be generalized to scenarios wherein tactile motion is perceived under multiple limb transformations.

Rigor and reproducibility: The experiment will recruit 12-15 human participants to have a large enough sample to identify possible outliers in behavior. For characterization of any deviations from ideal behavior within a single subject, we will perform a total of ~3000 trials per subject (detailed in *C.3. Stimuli and Task*).

C.2. General Experimental Methods for Aim 2

Animal preparation: Experiments will be performed with rhesus macaques (Macaca mulatta) prepared by surgically implanting a head holding device and a recording chamber. Animals will be trained by operant conditioning with water or juice as a reward.

Multi-electrode recordings: We will record simultaneously from Area 1 and medial intra-parietal area (MIP) using high-density linear electrode arrays. We will use Neuropixel probes for non-human primates (10mm, 1024 channels) to record from area 1 and area MIP. Data will be acquired by a Neuroprobe system and OpenEphys software**.** We will extract signals from well-isolated single units, as well as multi-unit clusters.

Apparatus and Experimental setup: Animals' hand will be immobilized on a setup similar to the human apparatus. To ensure the comfort of the animal, the monkey will have their forelimb placed laterally from the body (**Figure 4,** ***left***). Accordingly, the monkeys will perform two tasks cued via a colored fixation cross: away or towards the center-of-the body (in a body-centric reference frame) and tip or base with respect to the finger (finger-centric reference frame). To reduce the duration of the entire experiment, the monkey will have the arm situated in only three proprioceptive states. The tactile stimulator is similar in design to the apparatus described in Aim 1, but with a cylindrical dotted drum of diameter 10mm to accommodate the monkey's finger-pad dimensions.

Animals will perform the task as per the timeline described in **Figure 4 (right)**. In each session, after positioning the electrode arrays in MIP and Area 1, we will conduct preliminary tests of neural response properties. To identify single units in area 1, we will manually stroke different regions on the hand skin surface to identify the somatotopic location corresponding to the receptive field (RF). Recordings will be obtained from neurons that meet the following criteria: (1) the neuron responds to cutaneous stimulation; (2) the RF of the

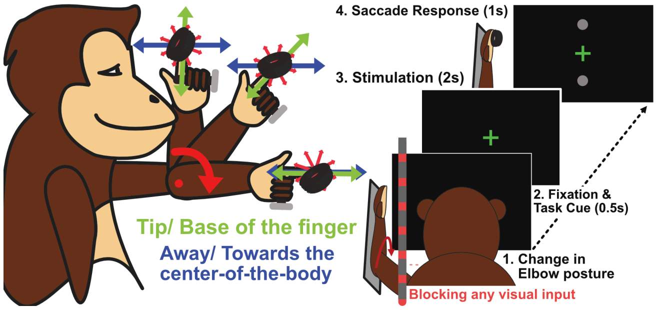

Figure 4: Schematic illustration of the task design for non-human primates in two reference frames *(left)*. Task timeline for the monkey experiment (*right*): (1) first the elbow posture is changed to one of the three postures, followed by (2) a colored fixation cross, cueing the reference frame the task will be performed in. Once the subject maintains fixation for 500ms, (3) the rotating stimulus drum is impinged on the finger for 2 seconds. After the stimulus is lifted, (4) the monkey performs a saccade corresponding to the two responses in the respective reference frame within 1 second of the stimulus delivery to receive a reward.

neuron includes at least one of the distal finger pads on digits 2–5 (3) the stimulator array can be positioned so that the RF of the neuron is centered on the array. We will select neurons irrespective of whether they respond to joint manipulation or not. For MIP, we will record from any neuron that can be isolated; there will be no selection criteria based on response properties other than the receptive field location. Subsequently, we will record from MIP and Area 1 while the animal performs the motion discrimination task in the two reference frames. We expect to need ~10 repetitions of each unique task condition per session to have sufficient data for analysis. With 2 reference frames, 3 proprioceptive states, and ten motion directions, this will require 600 trials. Unlike the human psychophysical task above, motion directions will only span 180˚ on the skin surface. This is done to limit the number of trials per session. After a block of motion discrimination trials, we will conduct another block of trials in which the animal simply maintains fixation while we "replay" the different conditions from previous motion discrimination trials in that session. These replay trials will allow us to examine neural responses, especially in MIP, to the task conditions while the animal is actively performing the task vs. when the animal is passively observing tactile stimulation and change in proprioceptive state.

Rigor and reproducibility: We plan to perform 15-20 sessions while simultaneously recording from area 1 and MIP. This should yield at least 400-600 single units per area as well as ~1000 multi-unit recordings per area. Two macaques will be used as per the standards of the field; if the results are not reproducible, additional animals will be studied.

C.3. Aim 1: To test that humans perceive tactile motion directions in different reference frames under different postures of the arm.

Background/rationale: In this aim we describe the underlying computational framework for inferring tactile motion in different coordinate frames. Previous studies have demonstrated biases in human tactile reports as a function of proprioceptive state (*Rinker and Craig 1994; Chen et. al 2020*), but their task design assumed a reference frame for the task. The subjects were not explicitly instructed to perform the task in a reference frame. In such a scenario, biases can alternatively be explained by the use of a mixture of reference frames. Hence, explicit instruction of reference frames is crucial to associate perceptual biases with proprioceptive modulation, disentangling biases originating from proprioception or an assumed reference frame. Our experiment design allows us tease apart systematic deviations arising separately from proprioceptive modulation or the choice of reference frame. The goal of this experiment is to determine whether the brain can compute motion direction on the skin by selectively integrating the proprioceptive state of the hand with tactile motion signals in the context of a specific reference frame. We will explore this question by asking subjects to judge the direction of motion in two reference frames: body-centric and finger-centric as the arm is rotated around the elbow to different proprioceptive states.

Hypothesis: We hypothesize that sequence of proprioceptive transformations and the uncertainty in arm posture systematically deviate how humans perceive tactile motion direction in different reference frames. Subjects' psychophysical report will be modeled using the Bayesian generative model described above (Section *C.1 Computational Analysis*). Deviation from ideal Euler matrix transformations will be measured in each posture and reference frame. Discrimination thresholds predicted by the model fits will be used to calculate the additional proprioceptive noise in one reference frame over the other.

Stimuli and task: Participants will perform the task under five proprioceptive states and two reference frames. The proprioceptive state will change back and forth between five elbow rotations (**Figure 5A, inset**). The subjects will not be informed that the arm will be switching between a limited number of postures. Trials with random arm positions will be interleaved to project a pseudo-random distribution of arm postures. The participants will respond verbally: left/ right in the body-centric task and towards the tip/ base of the finger in the finger-centric reference frame. On each trial, the arm will be rotated around the elbow and the subject will be cued with a colored ellipse (500ms) to perform the task either in the body-centric reference frame or the finger-centric reference frame. Then, a rotating cylindrical drum will be impinged on the index finger. 300 trials will be distributed across 20 motion directions spanning 360˚ for each combination of proprioceptive state and reference frame, resulting in a total of 3000 (300x5x2) trials per subject. These trials will be distributed across 4-5 sessions and breaks will be given to subjects as needed to limit the impact of fatigue on performance.

Data analysis: Tactile motion report psychometric functions (**Figure 5A,B**) will be fit with a Bayesian generative model (Section *C.2 Computational Analysis*). The model will also be used to calculate biases and psychophysical discrimination threshold for each subject to note deviations from ideal behavior.

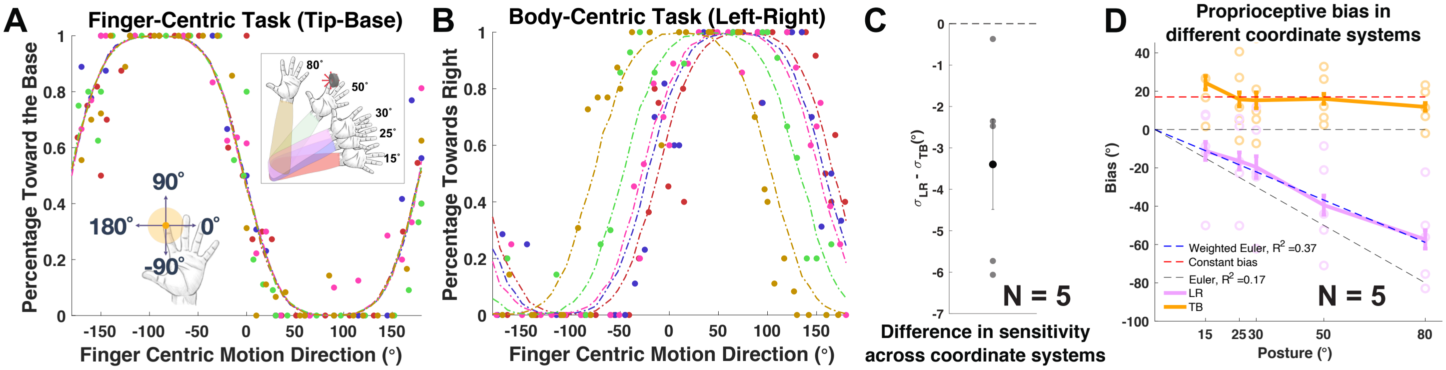

Figure 5: **(A, B)** Psychometric curves for single subject responses (dot scatter) in the finger-centric reference frame (*left)* and center-of-body reference frame (*right),* along with the model fit (dashed-line) given by Euler-matrix based Bayesian generative model. Line color representsS the posture of the hand at various elbow rotations (*inset).* Motion direction on the hand is given in the finger-centric reference frame (*inset).* **(C)** Difference in sensitivity of perceived motion in body-centric v/s skin-centric reference frame. Negative difference in $\sigma_{\mathbf{LR}} - \sigma_{\mathbf{TB}}$ implies subjects are more sensitive to perceived motion in the skin-reference frame (N =5). **(D)** Bias in perceived tactile motion direction as a function of proprioceptive state in different reference frames. There is a posture-dependent bias only in the body-centric reference frame (N=5). Black dotted lines show prediction from the Euler model.

Preliminary Results, potential outcomes and interpretations: We have collected data from 5 human subjects. The psychometric curve of one subject's responses in two reference frames along with the model fit given by the Euler matrix-based generative model is shown in **Figure 5A,B**. These results show that the computational model fits the data well in the finger-centric reference frame. The preliminary data also show deviations in report only in the body-centric reference frame (Quantified in **Figure 5D**). Systematic change of this bias with posture implies that human subjects incorporate a prior belief over proprioceptive states in their tactile motion reports, hence deviating from ideal Euler Matrix rotations (**Figure 5D**, *Weighted Euler model*). This prior could originate from different muscle tension forces in different postures or because of spatial position of the arm. More importantly, we found that this prior biases the perception only when humans require the proprioceptive state of the arm in the decision-making process. This will demonstrate, that tactile motion report is biased by the proprioceptive state only when it is required to compute the resultant motion direction i.e. in the body-centric reference frame. Alternatively, if additional data does not reveal any proprioceptive bias, it would demonstrate that subjects ideally employ Euler matrix transformations, and will suggest that previous research on tactile motion perceptual biases (*Chen et. al 2020*) emerged from an assumed reference frame and not as a function of proprioception. Further, the discrimination threshold (inverse of steepness of the psychometric curve) in the finger-centric reference frame is lower than the body-centric reference frame (**Figure 5C**). This implies that the noise introduced via the proprioceptive signals decreases the sensitivity of perceived motion in the body-centric reference frame. If additional data demonstrates that the discrimination thresholds across the two reference frames are similar, that would suggest simultaneous representation of tactile motion under different reference frames, rather than sequential. In either case, these results will be an important advance in our understanding of how tactile motion perception is selectively mediated by the proprioceptors of the hand under different reference frames.

Potential problems and alternative solutions: Correctly communicating the reference frames for the two tasks is of utmost importance. Any confusion in understanding the reference frame will show up as additional biases in the psychometric curves. To limit this possibility, we will conduct a preliminary session in which the subjects will perform the experiment with coarse motion direction stimuli. The results of the preliminary session will be examined for extreme deviations before participants are followed up for future sessions.

C.4. <u>Aim 2: Examine the neural correlates underlying coordinate transformation of tactile motion by the upper limb.</u>

Background/ Rationale: At the neural level, tactile motion representations can be transformed by posture in Area 1 of the somatosensory cortex, and mediated by a task-dependent control signal from the parietal region. Alternatively, the tactile motion representations in Area 1 can be fixed independent of the posture and relayed to the parietal cortex where it is integrated with the proprioceptive state in a context-dependent manner. The goal of this aim is to address these aspects of the neural circuitry underlying tactile motion transformation by answering the following questions: (1) How is the tactile motion representation in somatosensory cortex modulated by the proprioceptive state of the arm? (2) What is the neural substrate underlying the decision readout of the resultant motion direction based on the reference frame?

Hypothesis: We hypothesize that Area 1 and MIP hierarchically represent variables for tactile motion transformations, with MIP encoding tactile motion signals in different reference frames and Area 1 encoding tactile motion and proprioceptive states independent of the reference frame.

Tuning-curve based data analysis: We will measure the tuning curves for MIP and Area 1 neurons as a function of tactile motion direction and proprioceptive state of the arm under different reference frames. If a neuron in Area 1 represents the motion in skin coordinates, then its tuning curve will have the same shape independent of the proprioceptive state of the arm or the reference frame the task is performed in. If a neuron encodes for the proprioceptive state independent of the reference frame, the shape of its tuning curve will systematically change in specific predictable ways e.g. through gain-field (*Andersen et. al 1985)*, or shifts in tuning curves. Modulation of neural activity by proprioceptive state can imply reference frame-based coding or a joint coding of proprioception and tactile motion. To tease apart these two conditions we will use a decoding-based analysis.

Decoding-based data analysis: Tactile motion in different reference frames might not be represented explicitly in single unit responses. Thus, we will also use population decoding to map neural responses to monkey behavior. This approach will address whether linearly decodable information about the perceived motion can be represented in area MIP in both the finger-centric and body-centric reference frames. The weights of such a linear decoder would be able to predict monkey responses in both reference frames. Alternatively, a linear decoder that can only predict perceived tactile motion in one reference frame will need a different set of weights for each reference frame. We expect that the population activity in Area 1 will belong to this category.

Expected Results, potential outcomes and interpretations: A linear decoder will be used to classify tactile motion in each reference frame. Each neuron will have a decoding weight computed with the Fisher Linear Discriminant. We will match the proportion of choices reported by the decoder with the monkey behavioral reports in either reference frame. If MIP flexibly encodes tactile motion information in multiple reference frames then a single linear decoder with shared weights across reference frames will show performance similar to that of the behavioral report. We will perform a similar analysis for the neurons recorded from Area 1. Multiple possibilities of neural circuitry can emerge depending on the observed results. First, neurons in Area 1 might receive a control signal to integrate the proprioceptive state of the arm depending on the reference frame. Then, this information will be relayed to MIP, where the decision is read out. This would appear as a reference frame-dependent change in the tuning function of Area 1 neurons. In the finger-centric task, no modulation of activity based on posture will be observed. On the other hand, population activity would systematically change with posture in the body-centric task. In this scenario, both the Area 1 and MIP-based linear decoders would be able to predict behavior in either reference frame. Second, the proprioceptive information and the tactile information might integrate in the parietal cortex in a context-dependent manner. In this case, the tuning function of Area 1 neurons will be invariant to proprioceptive modulation or the instructed reference frame. Additionally, only the MIP-based linear decoder will be able to predict behavior in either reference frame. If the Area 1-based linear decoder is able to predict behavior in one of the two reference frames, that would imply that the representation of tactile motion is anchored to a canonical reference frame in Area 1. Third, the tuning function of Area 1 neurons might be invariant to the reference frame of the task and yet jointly code for both tactile motion and posture. This would appear as changes in tuning function of Area 1 neurons. However, an Area 1-based linear decoder would not be able to predict behavior in either of the two reference frames.

Potential Problems and alternate solutions: It might be difficult for the monkey to learn to flexibly switch between reference frame. We will first train the monkeys to perform the task in only one reference frame. After the monkey successfully learns it, we will train the monkey on the other reference frame. Additionally, we will initiate training with highly discernible trials (orthogonal to the discrimination boundary) and eventually move towards less discernible trials (aligned around the discrimination boundary).

Summary: In this project, we propose a set of carefully designed psychophysical experiments, accompanied by a Bayesian generative model to test behavioral biases in human reports, and neurophysiological studies that elucidate the neural circuitry underlying tactile motion transformations. This project will introduce a computational framework that tears apart the biases originating from proprioception and the instructed reference frame. Further, by studying the coordinated activity between Area 1 and MIP, we will illustrate how the brain generates signals that enable goal-directed actions underlying these fundamental transformations. This project also has clinical implications for various diseases that affect the haptic sensori-motor system.

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REVIEW

Preliminary scores: 4/6(3)/3