Deriving Bilateral Lower Limb Kinematics from Cortical Population Activity During Bipedal Primate Locomotion

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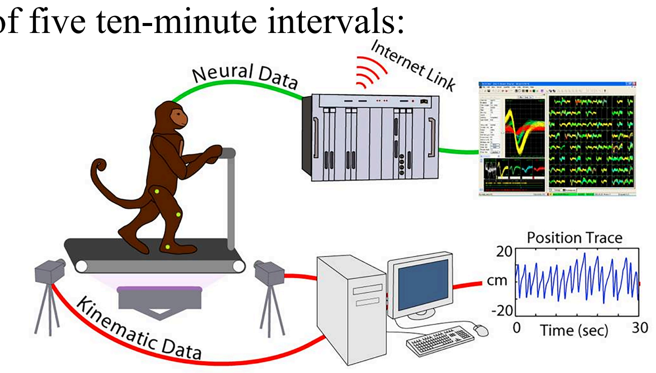
Introduction

Loss of lower limb control is a common outcome of both spinal cord injury and neurodegenerative diseases. Brain-machine interfaces (BMIs) offer a potential solution to aid or restore locomotion by using neural activity to drive an external, artificial actuator such as a leg prosthesis or exoskeleton. While upper limb BMIs have been demonstrated with success in both primate models and humans, however, the feasibility of a lower limb BMI remains to be seen.[1] This is in part because locomotion poses a challenge for existing BMIs due to its decentralized source of control; there are significant spinal and cerebellar contributions that cannot be reconstructed from a cortically-implanted microelectrode array.

Despite this limitation, initial research was able to extract single-leg kinematics from cortical activity.[2] This study expands on that work to look at both legs simultaneously, with goals being to 1) build models of leg movement based on modulations in primary motor (M1) and primary somatosensory (S1) cortices, and 2) quantify changes in neural activity across walking direction and phase of gait.

Experimental Setup

- Two female rhesus macaques were trained to walk bipedally on a treadmill.
- Cameras on both sides of the treadmill captured leg position by tracking high-contrast fluorescent markers on hip, knee, and ankle locations.
- 32- and 64-electrode chronic microwire arrays implanted in left and right M1 and S1 were used to collect firing data from 490 total units.
- Each trial session consisted of five ten-minute intervals:
  - Stationary
  - Forward (12.5 cm/s)
  - Forward (25 cm/s)
  - Backward (12.5 cm/s)
  - Backward (25 cm/s)



Neural Encoding and Decoding

Multilinear regression was used to model firing rate $\boldsymbol{F}$ of each single unit n over time as a function of the x- and y-axis movement ($\boldsymbol{x}$ and $\boldsymbol{y}$) of both legs:

$$\boldsymbol{F}_n = \alpha_{nL}\boldsymbol{x}_L + \beta_{nL}\boldsymbol{y}_L + \alpha_{nR}\boldsymbol{x}_R + \beta_{nR}\boldsymbol{y}_R + \mathbf{C}$$

Tuning depth for neuron n with respect to each leg was calculated as:

$$T_L = \sqrt{\alpha_L{}^2 + \beta_L{}^2} \quad , \quad T_R = \sqrt{\alpha_R{}^2 + \beta_R}^2$$

describing the relative strengths of each leg in predicting firing rate.

Decoding neural activity into leg position was done with a Wiener filter:

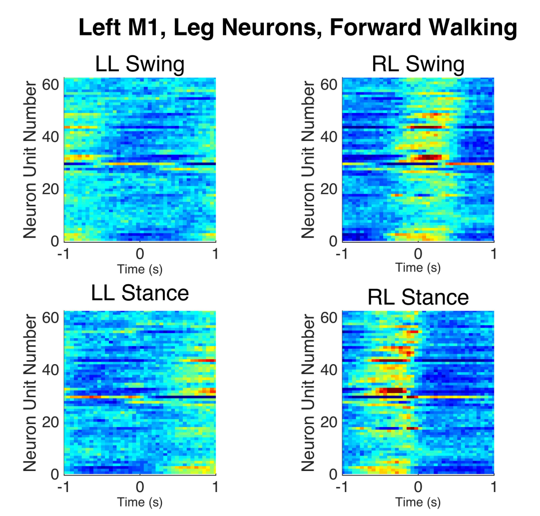
$$P(t) = b + \sum_{i=1}^{N}\sum_{j=-5}^{0} w_{ij}n_i[t - j\tau] + \varepsilon(t)$$

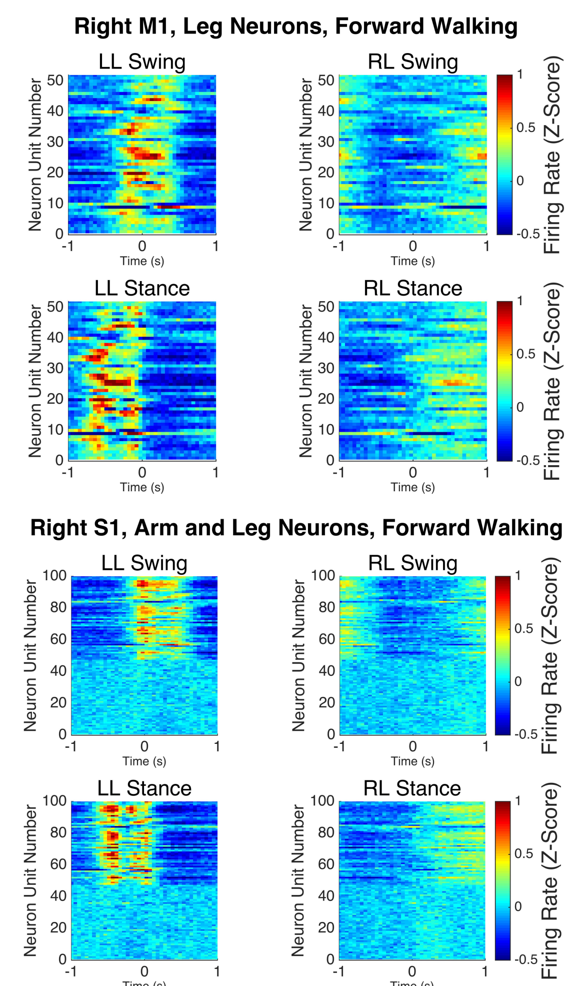
where N = total number of neurons, j = tap number (only past information was used), τ = bin size (50 ms), b = bias, and ε = residual error. Five taps (250 ms) of total firing data before time t were used to predict location at time t.

Goodness of fit was calculated using Pearson's correlation coefficient:

$$R(X,\hat{X}) = \frac{cov(X,\hat{X})}{\sigma_X\sigma_{\hat{X}}}$$

Results: Neural Firing Rate



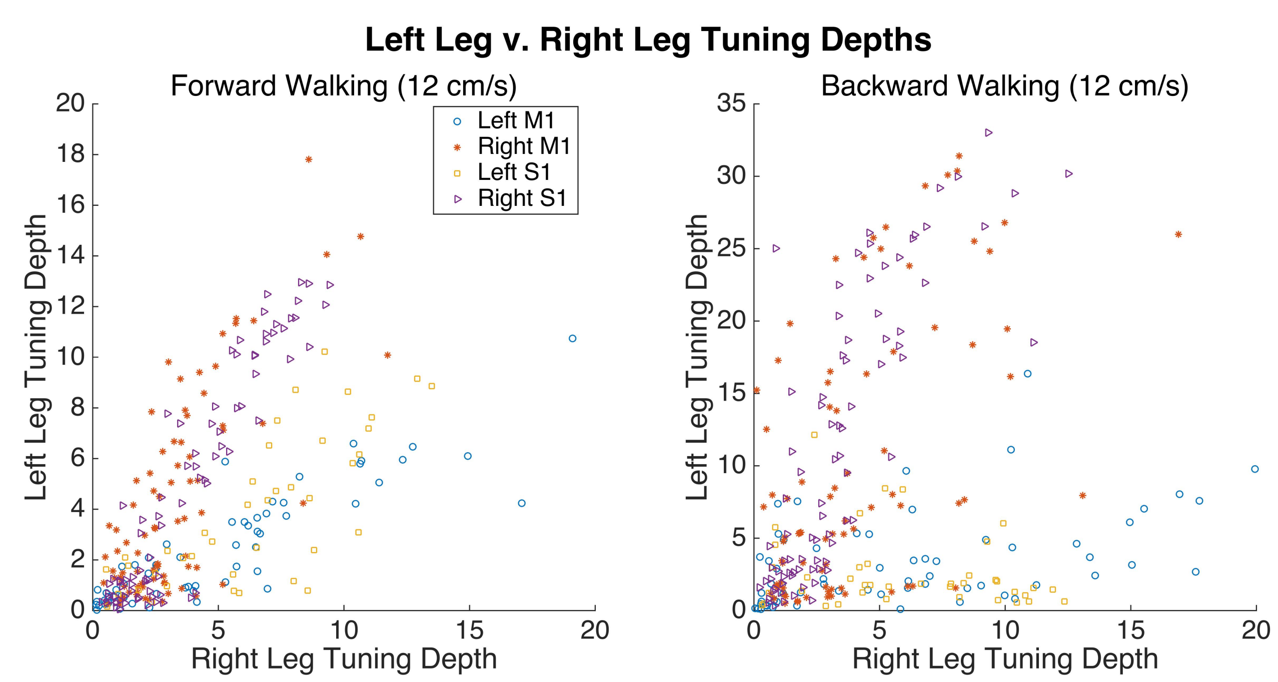


Periodicity of firing

- Primarily observed among leg representation neurons
- Increased activity aligned with contralateral swing
- Depressed during ipsilateral swing

Neural activity patterns

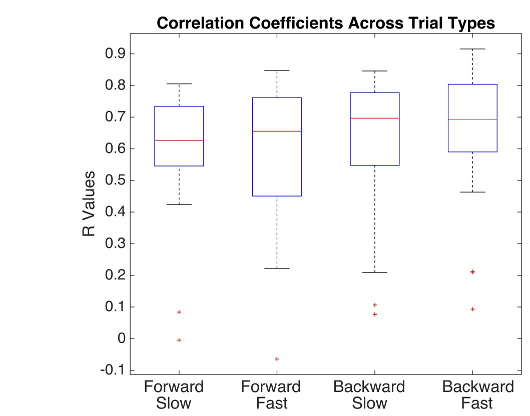
- Arm representation neurons (bottom half of right S1 plots) showed significantly less evident periodicity across all brain regions
- Z-scores were calculated over entire trial condition
- Similar patterns were observed across all walking conditions



Tuning depths from linear regression model of firing rate

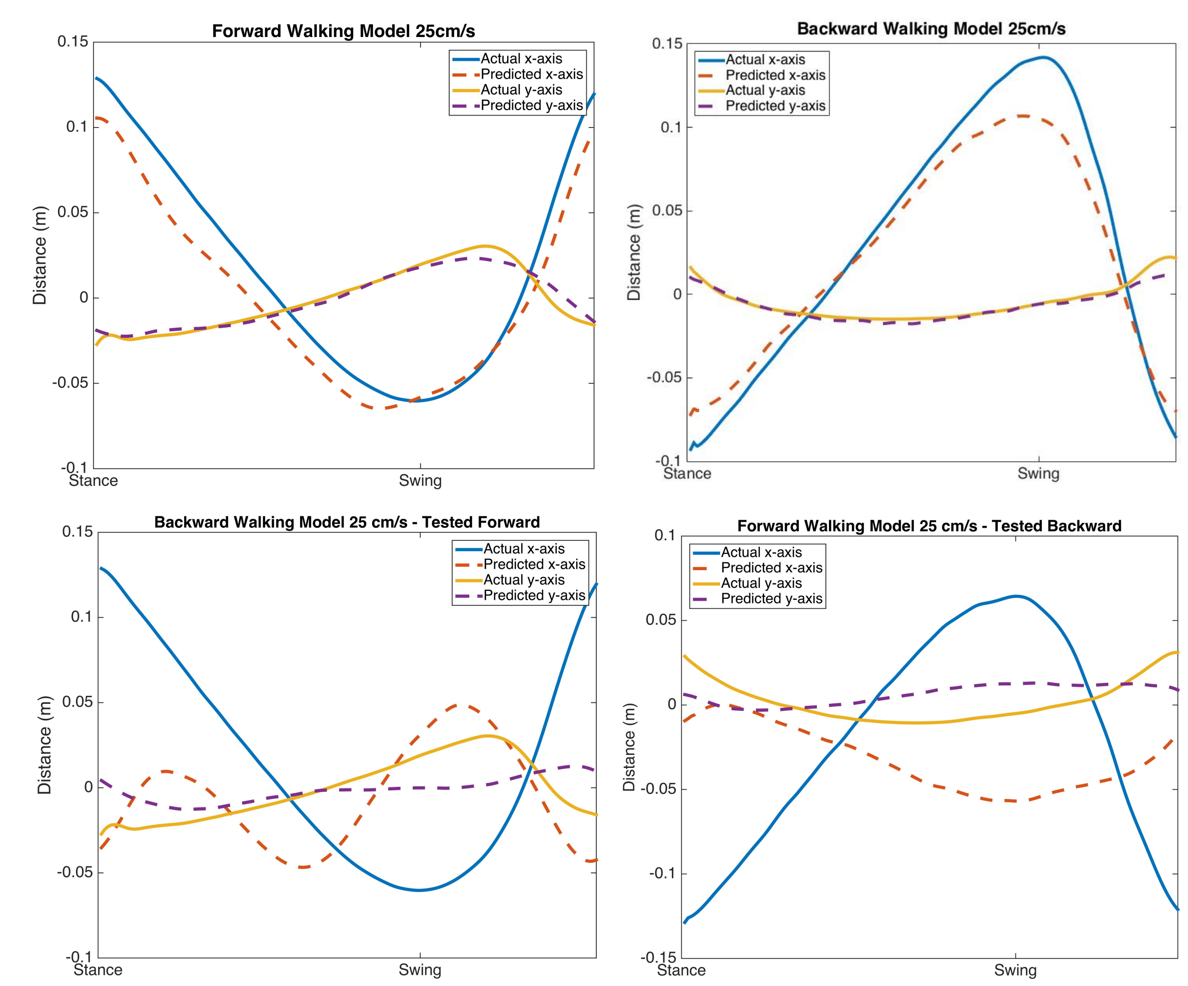
- Contralateral leg position correlates more strongly with neural firing rates during backward walking compared to forward
- Arm representation neurons tend to have weaker lateral preference
- May indicate larger cortical influence on controlling backward walking

Results: Kinematic Predictions



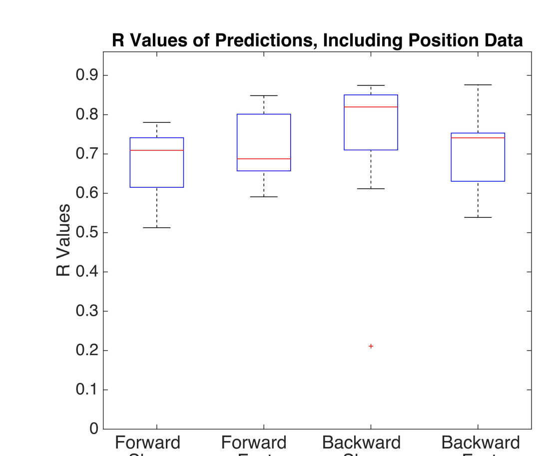
R value across trial types

- Measure of correlation between predicted and actual kinematics
- One subject exhibited larger R values during backward walking
- Small difference between trials over all subject data



Wiener filter decoding of neural activity to ankle position

- High correlation between real-time predictions and actual leg position across all walking types
- Significant error when applying a trained model to a different walking condition



Including contralateral position data in predictive model

- X- and y-axis location of opposite leg was included in building predictive model
- Global increase in correlation between prediction and real data is seen, along with a smaller overall variance

Conclusions

- Statistically significant increase in M1 and S1 firing and evident periodicity during walking indicate cortical representation/control.
- Neurons within area of cortex known to contain leg representation exhibit obvious periodicity of firing during walking, primarily aligned with the onset of contralateral swing.
- Cortical neurons become more highly correlated with contralateral leg motion during backward walking.
- Control of non-stereotyped movements, even if periodic, may undergo a shift from central pattern generator to cortical influence.
- Bilateral leg position can be extracted using linear predictive models from cortical neuron firing.
- Despite similarities in neural firing cycles, predictive models for kinematics are not generalizable across walking directions.

[1] Moran, Daniel W., and Andrew B. Schwartz. "Motor cortical activity during drawing movements: population representation during spiral tracing." *Journal of neurophysiology* 82.5 (1999): 2693-2704.

[2] Fitzsimmons, Nathan A. et al. "Extracting Kinematic Parameters for Monkey Bipedal Walking from Cortical Neuronal Ensemble Activity." *Frontiers in Integrative Neuroscience* 3 (2009): 3.