様式３

論　文　内　容　の　要　旨

氏　名　（　竹内遼介　）	
論文題名	Functional microarchitecture and neuronal connectivity rule in areas V1 and V4 of the macaque visual cortex (サル大脳皮質V1野およびV4野における微小機能構築と細胞間結合)

論文内容の要旨

Understanding of functional organization and neural circuitry within a submillimeter cortical space is crucial to uncover the neural basis of cortical computation. In the rodent cerebral cortices, excitatory neurons are not randomly connected; they form a well-defined network based on their functional (connection between the similarly tuned neurons) or topographic specificity (connection between the neighboring neurons). Because of the diversity in anatomical properties of neurons such as dendritic shape and size across species and cortical areas, it is still uncertain how these connection rules are applied to early and late visual processing stages in the primate visual cortex. Here, I examined response profiles of neurons whose location was specified at microscale spatial resolution to understand the rule of microscale functional organization and functional connectivity.

Using 2-photon calcium imaging technique, I recorded responses of neurons in the primary visual cortex (V1) and a middle-stage cortical area (V4) to natural movie stimuli, which allowed us to investigate response profiles without a prior assumption for the neuron's preferred visual features. The functional similarity between neighboring (< 300 μm) neurons was evaluated by correlation of responses to the naturalistic movie (signal correlation). For assessing how an individual neuron had a unique response profile compared to a population of neighboring neurons, I computed "local uniqueness index" of cells (LUI). The LUI of individual cells was computed from the average of signal correlations weighted by cellular distance. A high LUI value indicates that a neuron exhibits response characteristics of a neuron different from those of neighboring neurons. This analysis allowed us to assess the tightness of clustering of neurons with similar response characteristics in a local region. Functional connectivity was examined by computing noise correlation. It is the correlation of response variability across trials between neurons, and can be an indicator of shared inputs and mutual connections.

LUIs were highly diverse among individual neurons both in V1 and V4, suggesting the existence of heterogeneity in the degree of functional clustering of neurons within each of these cortical areas. The median value of local uniqueness was significantly higher in V4 than in V1. Thus, V1 neurons are overall functionally more organized than V4 neurons. Both in V1 and V4, signal correlation, rather than cellar distance, explained the variance of noise correlation for the site populated by neurons with high LUIs. In contrast, the cellular distance accounted for noise correlation for the site where neurons with low LUIs were abundant. Regardless of V1 or V4, functional specificity is an essential factor for determining neural connection in a heterogeneous population (i.e., high LUI regions), whereas topographic specificity is more dominant in determining connectivity for a homogeneous population (i.e., low LUI regions).

I conclude that micro-scale functional organization of a cortical area is related to the connection specificity of its constituent neurons. Anatomically, the concept of potential synapse among neighboring neurons suggests the geometry of neurons are highly related to the potential for their plasticity. Weak functional clustering can cause variation of information flow in local population. Thus, the heterogeneous, but precisely wired microcircuit in higher cortical areas can probably be the substrate of experience dependence association.

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論文審査の結果の要旨及び担当者

氏　　名　（　　竹内遼介　　）			
	（職）		氏　　名
論文審査担当者	主 査	教授	藤田一郎
	副 査	教授	大澤五住
	副 査	教授	北澤茂
	副 査	教授	八木健

論文審査の結果の要旨

本研究はサルの側頭葉視覚経路の初段 V1 野と中段 V4 野における神経回路の構成規則の解明を行った．個々のニューロンがどのような規則に基づき配置・配線されているかを知ることは，脳が行っている情報処理メカニズムを知る上で重要な手がかりである．ニューロンは，非常に狭い領域内において一定の規則にしたがって特異的なシナプス結合を形成し，同一領野の，数百マイクロメーター以内の非常に限られた領域の中にも複数のサブネットワークが存在する．本研究では二光子カルシウムイメージング法を鎮痛不動化したサルの V1 野および V4 野のニューロンに適用した．個々のニューロンの空間配置とその自然動画刺激に対する応答特性を解析することで，この２領野の微細領域における結合規則，また個々のニューロンの配置戦略の違いを示唆する結果を得た．V4 野においては，V1 野と比べ近傍ニューロン同士の応答類似性が低く，結合の機能特異性はより優位になっていることがわかった．また，同一の視覚皮質領野においても，機能特異的な結合は，より近傍ニューロン同士の応答類似性が低い場合に優位となる傾向があった．このことから，視覚皮質において機能的集合と結合ルールは互いに関連し，トレードオフの関係であることが示唆された．これらの結果は，視覚皮質における階層的処理の基盤となる神経回路構成の理解を大きく進めたものとして、博士号に値するものと判断する。