**(Brederoo et al., 2019)**

Right and left, big and small: hemispheric laterality of population receptive field properties.

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# Abstract

# Introduction (1065)

The two cerebral hemispheres noticeably play different roles in visual perception despite their close interaction. The how or the why of this lateralization is not clearly understood. Hemispheric lateralization has been thoroughly documented for processing global and local aspects of visual stimuli (A. V. Flevaris & Robertson, 2016), with the right hemisphere exhibiting a global bias and the left hemisphere showing a local preference. These biases for the local/global levels have been established through psychophysical \*\*\*\*(Brederoo et al., 2017, 2019), neuropsychological (\*\*\*\*), electrophysiological, (A. V. Flevaris et al., 2014; Iglesias-Fuster et al., 2014; Jiang & Han, 2005) and functional magnetic resonance -fMRI- (\*\*\*\*) studies. The preferred level for processing at any moment is under attentional control (Kimchi, 2015).

The global/local bias of the right/left hemispheres could be explained in terms of the spatial frequencies (SFs) associated with different levels of a visual stimulus: lower SFs for global and higher SFs for local aspects (A. V. Flevaris & Robertson, 2016). Human psychophysical studies and monkey neuronal recordings show that the primary visual cortex (V1) filters images in different SF channels (De Valois and De Valois 1988), that are passed on to further stages of visual processing. A shift in the tuning of these channels towards higher SFs in the left and towards lower SFs in the right hemisphere could explain local/global lateralization. In support of this, several studies have revealed a bias for lower SFs in the right and higher SPs in the left hemisphere (\*\*\*\*\*). Furthermore, links between global/local attentional selection and SFs have been found (\*\*\*). However, any theory based on these considerations must account for the fact the same aspects of a visual stimulus can be global in one context and local in another (e.g., a tree is global relative to a leaf but local relative to a forest). The role of any SF is no fixed but depends on the context.

The Double Filtering by Frequency (DFF) theory (Robertson & Ivry, 2000) proposes two stages of attentional selection based on SFs, with the two hemispheres differing in how they use SF information. Attention first selects a SF range from the incoming image spectra most suited for the current task, a range symmetrically fed forward to both cerebral hemispheres. In the second stage, the hemispheres diverge in their handling of SFs: the right acting as a relatively low-pass filter and the left acting as a relatively high-pass filter. Thus, the same SFs may be preferred by the different hemispheres as a function of the SF range imposed by the task demands.

Although predictions based on the DFF theory have been confirmed in several experiments (Flevaris et al., 2010; A. Flevaris & Robertson, 2016), it has not been implemented in computational models grounded on the properties of different visual cortical areas. Measuring population receptive fields with fMRI creates an opportunity to develop such models (Dumoulin & Wandell, 2008; Kay, 2017). A population receptive field (pRF) is a quantitative model of the aggregate response of neurons within a fMRI voxel (or cortical vertex). Usually, pRFs estimate the position and size of the visual field (VF) section influencing a voxel (Wandell & Winawer, 2015). Recently, the SF responses of pRFs have also been measured (Aghajari et al., 2020; Aghajari & Ling, 2018; Broderick et al., 2022; Ha et al., 2023; Wiecek et al., 2023) in early visual areas (V1-V3). These studies found that the spatial frequency tuning of a pRF is lower the larger its size. The DFF theory predicts larger sizes and lower SF tuning for homologous sites in the right compared to the left Hemisphere, but only for some visual areas.

Most studies of pRF properties as a function of the VF sector have examined differences between the upperand lower quadrants in V1. No significant right/left differences have been reported in V1 when investigated. One study found slightly smaller pRF sizes in the left compared to the right horizontal quadrants of V2 and V3, and again, no difference in V1 (Silva et al., 2018). The absence of clear laterality for pRF size in early visual cortices does not contradict the DFF theory, which posits a symmetric early stage in both hemispheres. Understandably, the laterality of pRF properties in intermediate or higher-order visual areas has not been well studied, given the difficulty in identifying which sites are homologous across hemispheres for this type of region in which retinotopic maps are less well defined.

Several large databases of pRF have been made publicly available (Benson et al., 2018; Himmelberg et al., 2021, 2023), covering broad expanses of the cortex, which makes testing the laterality of pRF properties in intermediate or higher-order visual areas possible. To examine right/left differences in pRF size and eccentricity range, three strategies branded here as "anatomical", "homotopic", and "retinotopic" can be used. The goal is to compare homologous cortical sites, but as mentioned before, defining "homologous" presents difficulties, especially for higher-order visually responsive areas. Future studies should examine the laterality of SF tuning, which were not measured in the above-mentioned databases.

Our anatomical strategy measures the differences in pRF properties in the HCP\_LR space (\*\*\*), where cortical surfaces are approximately symmetric across the left and right hemispheres. This symmetry means that when vertex order is considered, those with the same rank in both hemispheres are roughly homologous (<https://osf.io/k89fh/wiki/Surface/>). Thus, pRF size and eccentricity for corresponding left and right vertices could be subtracted. This straightforward approach allows rough visualization of asymmetries across the whole cortex. The shortcoming is that the homology of left/right vertices is only approximate, and the wrong pair of vertices may be compared. Any mismatch could be mitigated by smoothing the pRF parameter maps over the cortex to enhance correspondence across hemispheres and individuals, although with a loss in map resolution.

The homotopic approach compares cortical patches with the strongest anatomical or functional connectivity between the two hemispheres, a connection indicating they probably work together. Therefore, lateralization of pRF properties can be examined with a parcellation based on resting-state or task-related fMRI connectivity that identifies pairs of homotopic cortical areas. One such parcellation has been recently reported (Yan et al., 2023). The drawback of this method is that the region sizes used in the parcellation limit its resolution.

The retinotopic strategy uses pRF positions within the retinotopic map of homologous cortical regions to decide which vertices must be compared. For cortical areas with nonoverlapping left/right VF coverage (i.e., V1), vertices are compared if their pRF centers are symmetrically placed across the vertical meridian in the VF. For cortical areas with overlapping left/right VF coverage (e.g., LO2), vertices are compared if their pRF centers are close in the VF. This strategy is theoretically sound but could suffer from errors in pRF center estimation. All the methods would suffer from errors in pRF size estimation, which seems to some degree unavoidable (Lage-castellanos et al., 2020).

This aim of this study is to determine if there are systematic differences in the properties of pRFs between left and right hemispheres in intermediate and higher-order visual areas and, if they exist, discuss how to frame a computational implementation of the DFF theory. For this goal, we will compare the results of applying the strategies outlined above to three large databases of pRF data and perform simulations in neural networks.

# Materials and methods

## Data used

Three databases were used: The HCP 7T retinotopic study with adult 181 participants (Benson et al., 2018); the NYU retinotopic study with 50 adult participants (Himmelberg et al., 2021), and the Stanford retinotopic study with 24 adults and 25 child participants (Himmelberg et al., 2023). The first database was already in fs\_LR\_32 space, whereas the maps from the other two studies were transformed in the HCP workbench program to fs\_LR\_32 space as decribed in \*\*\*\*\*. The pRF models were filtered according to the variance explained at each cortical vertex, retaining only vertices with R2 above 0.1.

The fitting of pRF models is accomplished in two stages \*\*\*: a first course search at predefined values in a mesh; and a second more exhaustive search based on a non-linear fit. When the histograms of pRF size and eccentricity of all databases are compared, it is evident that estimates are concentrated around the values of the original mesh (see Supplementary Figure 1). We therefore will treat size and eccentricity as ordinal dependent variables in the statistical analyses.

## Whole-cortex anatomical laterality tests

In fs\_LR\_32 space, where surfaces are approximately symmetric across the left and right hemispheres This symmetry means that a vertex with a specific number in one Hemisphere will refer to roughly homologous areas in the other Hemisphere (https://osf.io/k89fh/wiki/Surface/). Given this approximate symmetry, we subtracted the values of the right from the left Hemisphere for each vertex number. We then performed Wilcoxon signed rank tests across individuals using the null hypothesis of equal medians in the two hemispheres. The probabilities of rejecting the null hypothesis across vertices were used to calculate a threshold using the Benjamini (\*\*\*) nonparametric false discovery rate (FDR) correction for multiple comparisons. The number of vertices surviving these thresholds within the t maps were counted for the ROIs defined by (Sereno et al., 2022) and (Glasser et al., 2016) surface atlases, separately for negative values (right>left) and positive values (left>right). This procedure was performed with unsmoothed maps and also with maps smoothed with the -cifti-smoothing command in the HCP workbench program applied using a Gaussian kernels of 2 and 5 mm.

## Laterality tests for homotopic cortical areas

## Retinotopically based laterality tests

All vertices' size and eccentricity values, for one ROI at a time, were submitted to a mixed effect ordinal regression, using Hemisphere (left vs. right) as an independent fixed effect, with the participant as a random effect. The following formula was used in the R ordinal package (https://cran.r-project.org/web/packages/ordinal/index.html):

hemisphere + (1 | participant)

SIZE vs ECCENTRICITY??

## Visual field coverage maps

SMOOTH MAPS? USE METRIC SMOOTH

OBTAIN MAXIMUM VALUE AT EACH POINT?

BOOTSTRAP?

Coverage defines VF sites that evoke a response from the cortical vertices within a ROI by conjoining the pRFs locations and size estimates. Here, coverage was estimated separately for the left and right hemispheres using methods described before (Amano et al., 2009). For each vertex in the ROI, we calculated the pRF Gaussian envelope and projected it onto a matrix of \*\* X \*\* pixels, representing \*\* x \*\* degrees of visual angle. A map was built with the highest value of all the envelopes overlapping at each VF site. The pRFs were randomly sampled with replacement 100 times, and the mean of the resulting maps was taken as a final robust estimate for the map in each ROI in all participants. The map from the right was flipped in the horizontal axis to allow direct comparison of coverage across hemispheres. These maps ranged from 0 to 1. The maps from all the individuals from one Hemisphere were stacked upon one another, and then stacked on top of those from the other to produce a 3D matrix.

We tested differences in coverage between the two hemispheres for each ROI using the iMap4 toolbox (Lao et al., 2017). Each entry in the 3D matrix described above was used as the dependent variable and modeled in a mass univariate linear mixed model (LMM) according to the following equation:

hemisphere + (1 | participant)

The LMMs at each pixel were fit by maximum likelihood (ML) using the fitlme function from the Statistics Toolbox™, Matlab 2022b. The subsequent analysis was in two steps. First, the original parametric statistical values from the LMMs were thresholded at a given p-value, which in different iterations was 0.05, 0.1, and 0.2. This step was repeated after 1000 random permutations of the maps from the two hemispheres. For the original and permuted data, the cluster mass was obtained by summing the contrast coefficient values of the LMM within each cluster. An empirical distribution of these cluster mass measures was obtained from the permuted values. The cluster mass of the original clusters was then compared with the observed distribution, accepting as significant clusters in the p<0.05 rightmost tail. This non-parametric procedure allowed us to correct the type-1 error inflation due to multiple comparisons inherent to the mass univariate nature of the coverage map statistical tests.

Sonia Poltoratski & Grllspector

Visual field coverage. Visual field coverage density plots for each visual region in Fig. 5 and Supplementary Fig. 8 were generated first for each participant, and then averaged across participants. Created using a custom Matlab bootstrapping procedure, these density plots represent the proportion of pRFs in a region that overlap with each point in the visual field. Overlap is determined using a binary circular pRF at the estimated center, and with a radius of 2 × pRF size (2σ/√n32), which captures ~86% of the total volume of the CSS pRF. This metric does not account for the Gaussian profile of individual pRFs, but allows for greater interpretability when combining data across pRFs and participants. For each participant and ROI, density plots were generated by taking 1000 bootstrap samples of 80% of voxels with replacement. Each voxel was represented with a circular binary mask as described above, and coverage was computed by calculating the mean density across voxels for each bootstrap draw. The average of these bootstrapped images is taken as the density coverage for each participant. Participant-wise metrics, like FWHM area and center-of-mass (Fig. 5, Supplementary Fig. 9), are computed from these images. Averages across participant-wise images are taken as overall coverage density summaries (Fig. 5, Supplementary Fig. 8); no rescaling or normalization is done, such that plotting colors retain meaningful quantitative information about pRF coverage across the visual field.

## Relationship with task fMRI?

## Relationship with individual characteristics?

# Discussion

Summary of results

Problem with group atlases, need for individually defined ROIs

To directly test DFF we need spatial frequency properties of pRFs. However prior work has shown that preferred SPF increases with size and with eccentricy in V1 to V3.

(Aghajari et al., 2020)

(Wiecek et al., 2023)

(Aghajari & Ling, 2018)

(Ha et al., 2023)

(Broderick et al., 2022)

# Results

## Whole cortex vertex-wise laterality tests

### Size

### Eccentricity

## Roi-based analysis

### Size

### Eccentricity

### Size vs Eccentricity

## Visual field coverage maps

## Relationship with task fMRI?

## Relationship with individual characteristics?

# Discussion

Summary of results

Problem with group atlases, need for individually defined ROIs

# References

Aghajari, S., & Ling, S. (2018). Efficient Mapping of Spatial Frequency Sensitivity in Human Visual Cortex. *Journal of Vision*, *18*(10), 252. https://doi.org/10.1167/18.10.252

Aghajari, S., Vinke, L. N., & Ling, S. (2020). Population spatial frequency tuning in human early visual cortex. *Journal of Neurophysiology*, *123*(2), 773–785. https://doi.org/10.1152/jn.00291.2019

Amano, K., Wandell, B. A., & Dumoulin, S. O. (2009). Visual Field Maps, Population Receptive Field Sizes, and Visual Field Coverage in the Human MT+ Complex. In *Journal of Neurophysiology* (Vol. 102, Issue 5). https://doi.org/10.1152/jn.00102.2009

Benson, N. C., Jamison, K. W., Arcaro, M. J., Vu, A. T., Glasser, M. F., Coalson, T. S., Van Essen, D. C., Yacoub, E., Ugurbil, K., Winawer, J., & Kay, K. (2018). The Human Connectome Project 7 Tesla retinotopy dataset: Description and population receptive field analysis. *Journal of Vision*, *18*(13), 23. https://doi.org/10.1167/18.13.23

Brederoo, S. G., Nieuwenstein, M. R., Cornelissen, F. W., & Lorist, M. M. (2019). Reproducibility of visual-field asymmetries: Nine replication studies investigating lateralization of visual information processing. *Cortex*, *111*, 100–126. https://doi.org/10.1016/j.cortex.2018.10.021

Brederoo, S. G., Nieuwenstein, M. R., Lorist, M. M., & Cornelissen, F. W. (2017). Hemispheric specialization for global and local processing: A direct comparison of linguistic and non-linguistic stimuli. *Brain and Cognition*, *119*(December 2016), 10–16. https://doi.org/10.1016/j.bandc.2017.09.005

Broderick, W. F., Simoncelli, E. P., & Winawer, J. (2022). Mapping spatial frequency preferences across human primary visual cortex. *Journal of Vision*, *22*(4), 3. https://doi.org/10.1167/jov.22.4.3

Dumoulin, S. O., & Wandell, B. A. (2008). Population receptive field estimates in human visual cortex. *NeuroImage*, *39*(2), 647–660. https://doi.org/10.1016/j.neuroimage.2007.09.034

Flevaris, A. V., Bentin, S., & Robertson, L. C. (2010). Local or global? Attentional selection of spatial frequencies binds shapes to hierarchical levels. *Psychological Science*, *21*(3), 424–431. https://doi.org/10.1177/0956797609359909

Flevaris, A. V., Martínez, A., & Hillyard, S. A. (2014). Attending to global versus local stimulus features modulates neural processing of low versus high spatial frequencies: An analysis with event-related brain potentials. *Frontiers in Psychology*, *5*(April), 1–11. https://doi.org/10.3389/fpsyg.2014.00277

Flevaris, A. V., & Robertson, L. C. (2016). Spatial frequency selection and integration of global and local information in visual processing: A selective review and tribute to Shlomo Bentin. *Neuropsychologia*, *83*, 192–200. https://doi.org/10.1016/j.neuropsychologia.2015.10.024

Flevaris, A. v, & Robertson, L. C. (2016). Spatial frequency selection and integration of global and local information in visual processing: A selective review and tribute to Shlomo Bentin. *Neuropsychologia*, *83*, 192–200. https://doi.org/10.1016/j.neuropsychologia.2015.10.024

Glasser, M. F., Coalson, T. S., Robinson, E. C., Hacker, C. D., Harwell, J., Yacoub, E., Ugurbil, K., Andersson, J., Beckmann, C. F., Jenkinson, M., Smith, S. M., & Van Essen, D. C. (2016). A multi-modal parcellation of human cerebral cortex. *Nature*, *536*(7615), 171–178. https://doi.org/10.1038/nature18933

Ha, J., Broderick, W., Kay, K., & Winawer, J. (2023). Spatial Frequency Maps in Human Visual Cortex: A Replication and Extension. *Journal of Vision*, *23*(9), 5624. https://doi.org/10.1167/jov.23.9.5624

Himmelberg, M. M., Kurzawski, J. W., Benson, N. C., Pelli, D. G., Carrasco, M., & Winawer, J. (2021). NeuroImage Cross-dataset reproducibility of human retinotopic maps. *NeuroImage*, *244*(May), 118609. https://doi.org/10.1016/j.neuroimage.2021.118609

Himmelberg, M. M., Tünçok, E., Gomez, J., Grill-Spector, K., Carrasco, M., & Winawer, J. (2023). Comparing retinotopic maps of children and adults reveals a late-stage change in how V1 samples the visual field. *Nature Communications*, *14*(1), 1561. https://doi.org/10.1038/s41467-023-37280-8

Iglesias-Fuster, J., Santos-Rodríguez, Y., Trujillo-Barreto, N., & Valdés-Sosa, M. J. (2014). Asynchronous presentation of global and local information reveals effects of attention on brain electrical activity specific to each level. *Frontiers in Psychology*, *5*(OCT), 1–14. https://doi.org/10.3389/fpsyg.2014.01570

Jiang, Y., & Han, S. (2005). Neural mechanisms of global/local processing of bilateral visual inputs: An ERP study. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, *116*(6), 1444–1454. https://doi.org/10.1016/j.clinph.2005.02.014

Kay, K. N. (2017). Principles for models of neural information processing. *NeuroImage*, *August*, 1–9. https://doi.org/10.1016/j.neuroimage.2017.08.016

Kimchi, R. (2015). The perception of hierarchical structure. *Oxford Handbook of Perceptual Organization*, 129–149. https://doi.org/10.1093/oxfordhb/9780199686858.013.025

Lage-castellanos, A., Valente, G., Senden, M., Harvey, B. M., & Lage-castellanos, A. (2020). *Investigating the Reliability of Population Receptive Field Size Estimates Using fMRI*. *14*(July), 1–17. https://doi.org/10.3389/fnins.2020.00825

Lao, J., Miellet, S., Pernet, C., Sokhn, N., & Caldara, R. (2017). iMap4: An open source toolbox for the statistical fixation mapping of eye movement data with linear mixed modeling. *Behavior Research Methods*, *49*(2), 559–575. https://doi.org/10.3758/s13428-016-0737-x

Robertson, L. C., & Ivry, R. (2000). Hemispheric asymmetries: Attention to visual and auditory primitives. *Current Directions in Psychological Science*, *9*(2), 59–63. https://doi.org/10.1111/1467-8721.00061

Sereno, M. I., Sood, M. R., & Huang, R.-S. (2022). Topological Maps and Brain Computations From Low to High. *Frontiers in Systems Neuroscience*, *16*, 787737. https://doi.org/10.3389/fnsys.2022.787737

Silva, M. F., Brascamp, J. W., Ferreira, S., Castelo-Branco, M., Dumoulin, S. O., & Harvey, B. M. (2018). Radial asymmetries in population receptive field size and cortical magnification factor in early visual cortex. *NeuroImage*, *167*, 41–52. https://doi.org/10.1016/j.neuroimage.2017.11.021

Wandell, B. A., & Winawer, J. (2015). Computational neuroimaging and population receptive fields. *Trends in Cognitive Sciences*, *19*(6), 349–357. https://doi.org/10.1016/j.tics.2015.03.009

Wiecek, E., Ramirez, L. D., Klimova, M., & Ling, S. (2023). Characterizing the relationship between population spatial frequency tuning and receptive field size. *Journal of Vision*, *23*(9), 5437. https://doi.org/10.1167/jov.23.9.5437

Yan, X., Kong, R., Xue, A., Yang, Q., Orban, C., An, L., Holmes, A. J., Qian, X., Chen, J., Zuo, X.-N., Zhou, J. H., Fortier, M. V., Tan, A. P., Gluckman, P., Chong, Y. S., Meaney, M. J., Bzdok, D., Eickhoff, S. B., & Yeo, B. T. T. (2023). Homotopic local-global parcellation of the human cerebral cortex from resting-state functional connectivity. *NeuroImage*, *273*, 120010. https://doi.org/10.1016/j.neuroimage.2023.120010

# Supplementary material