The visualFields package: A tool for analysis and visualization of visual fields

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This paper introduces the R package visualFields, a contributed, open-source software for the analysis of the visual field. The package aims to provide a framework for collaborative research, including data sharing and conventional and novel methods. Single visual field and progression analyses, such as Permutation of Pointwise Linear Regression can be performed with visualFields using simple scripts. The package can be easily customized and it allows the inclusion of custom test locations and different normative values. Here, we demonstrate how to use the visualFields package and discuss its capabilities. The analyses presented here are easy to replicate upon installation of the package, which is freely available for download from the Comprehensive R Archive Network. The relevant R code is shown and commented on. A shift from proprietary to an open-source research platform is an important step towards more direct collaborative research. The visualFields package is part of the Open Perimetry Initiative, which is expected to grow as researchers contribute new routines and datasets.

Introduction

The visualFields R package is an open-source collection of tools for analyzing the visual field. It provides a framework for the development of innovative methods for visualization, statistical analysis, and clinical interpretation of visual field loss and its change over time. The aim of this paper is to introduce and demonstrate the package, which was developed in R, an environment for statistical computing (R Core Team 2012). The R environment is freely available for download in `http://cran.r-project.org/`, and the visualFields package can be found in `http://cran.r-project.org/web/packages/visualFields/index.html` or installed with the command

```
> install.packages( "visualFields" )
```

Interpretation of visual field data requires a large amount of data manipulation and statistical analysis; the visualFields package provides analytical tools for such analyses and visualization tools for their interpretation. In particular, the package contains the implementation of methods for detection and follow-up of glaucoma.

Before introducing the package, we review the present conventions in perimetry and the most common statistical analyses for glaucomatous damage.

Conventions in perimetry

Perimetry is the conventional form of assessment of the visual field, and it has been an important part of vision science and clinical ophthalmology since the middle of the 19th century (Johnson, Wall, & Thompson, 2011). In its original form, kinetic perimetry, physical objects were moved to determine which regions of the visual field could or could not see them, and in time these were replaced with moving virtual objects, such as circular luminance increments. The use of virtual objects allowed the development of static perimetry, in which a stimulus could be flashed on and off to assess visibility at an array of preselected locations. That led to threshold perimetry, in which a range of stimulus intensities is presented to determine the increment threshold. The inverse of such a threshold is called *sensitivity* in psychophysics (Levine & Shefner, 2001). To avoid adapting to the test stimuli,

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this form of static perimetry alternated test locations from trial to trial and was too complex for routine clinical use. In the late 1970s, computer power had evolved enough for automation of static perimetry, which lead to widespread clinical use.

The instruments used for measuring the visual field are called perimeters (Johnson et al., 2011). The most common form of perimetry is the static automated perimetry (also known as standard automated perimetry or "white-on-white" perimetry). The main output is the visual sensitivities at an array of preselected locations. The conventional units of visual sensitivity are decibels of a stimulus's contrast attenuation in relation to the instrument's maximum contrast. In static automated perimetry, the target stimulus is a small circular increment of white light subtending 0.43° of visual angle—the Goldmann size III stimulus (Goldmann, 1999)—presented on a dimmer white background. Newer instruments allow use of very different types of target stimuli, such as sinusoidal stimuli, flicker-defined forms, or moving lines. Given that different perimeters have different types of stimuli, and even different definitions of sensitivity, the decibel scale is instrument dependent (Anderson, 1987; Anderson, Johnson, & Werner, 2011).

Analysis of glaucomatous visual fields

The visual sensitivities at each location returned by any given visual field examination are compared against a reference based on age-corrected normative values derived from large datasets of healthy experienced observers (Flammer, 1986; Heijl, Lindgren, & Olsson, 1987b). Differences from such reference values are called total-deviation (TD) values (Heijl et al., 1987b). In glaucomatous eyes, it is generally assumed that visual loss can be due to two components: a global loss component and a focal loss component (Henson, Artes, & Chauhan, 1999). Moreover, there exist systematic differences in average visual sensitivities among individuals (Hood, Anderson, Wall, Raza, & Kardon, 2009). Therefore, since the assessment of glaucomatous damage relies on evaluation of focal visual field losses, the TD maps are elevated or lowered towards the level of a normative visual field (Heijl et al., 1987b). These corrected maps are called the pattern-deviation (PD) maps. The spatial profile and extent of damage can be shown with a gray scale, on which darker grays represent lower sensitivities, or with probability maps (Heijl, Lindgren, & Olsson, 1987a; Heijl, Lindgren, Olsson, & Åsman, 1989). TD rank curves (also known as Bebie cumulative defect curves) may be used as an alternative analysis to estimate the global loss (Bebie, Flammer, & Bebie, 1989; Funkhouser, 1991). Global summary indices of the visual field such as mean deviation (Heijl et al., 1987b), pattern standard deviation (Heijl et al., 1987b), mean defect (Flammer, 1986), loss variance (Flammer, 1986), and the visual field index (Bengtsson & Heijl, 2008) are used to summarize the depth of defect and its change over time. Two or more global indices may also be used in combination to characterize the stage of disease, as in the Glaucoma Staging System (Brusini & Johnson, 2007; Goldmann, 1999).

Different perimeters use different analytical methods and normative reference values. Software programs for clinical analysis of visual field data are proprietary and it is not always clear how calculations are performed, how such normative reference values were constituted, or what were the underlying assumptions in the mathematical models and statistical methods. Sometimes, the methods used by a particular vendor are not completely disclosed or described with enough precision.

Fortunately, some vendors allow exporting data from their perimeters in different formats, including the Humphrey Field Analyzers (HFA; Carl Zeiss Meditec Inc., Dublin, CA), the Octopus family of perimeters (Haag-Streit AG, Koeniz-Berne, Switzerland), and the Heidelberg Edge Perimeter (Heidelberg Engineering, Heidelberg, Germany). Yet, each research lab has its own software, conventions, and routines for the management and analysis of visual fields. In addition, over the last three decades, many research groups have proposed alternatives to static automated perimetry that attempt to detect glaucomatous damage earlier or to improve correspondence with structural measures (Anderson, 2006). These developments have created a need for new statistical approaches for data analysis. It would be ideal to have a conventional, yet highly adaptable, open-source platform for developing mathematical and statistical methods and for data sharing. This would help create a more efficient collaborative research that may not be possible with the constraints of proprietary software.

The visualFields package and the R project

The package visualFields has been designed to make research on visual field data easier and as reproducible as possible through an open-source platform. The package includes a set of tools for the generation of normative reference values from control subjects and the generation of TD and PD values, and corresponding probability maps from such normative values. It also contains tools to compute global indices, graph visual field data, perform progression analysis, and more.

The package visualFields was entirely developed under the open-source statistical language R, which is a widely used environment for data analysis in multidisciplinary research. More than 4,300 contributed packages can be found at `http://www.CRAN.r-project.org/` and 610 packages at `http://www.bioconductor.org/` (as part of a project dedicated at providing tools for the analysis and comprehension of high-throughput genomic data). The R program can be installed and run in any computer with Windows, Mac, or Linux operating systems. Only elementary programming experience is necessary for implementation of powerful, sophisticated applications. As with any language, mastering R takes a greater effort than just writing scripts using existing functions.

In the remainder of this paper, technical aspects are briefly described in Methods, some examples of the functionality of visualFields are shown in Results, and the state of version 0.3 of visualFields, developed in R 2.15.2 and available as Supplemental Material, is outlined in the Discussion.

Methods

In addition to methods and functions to manipulate and display visual field data, visualFields contains normative values obtained for static automated perimetry (SAP) with the Goldmann size III stimulus presented with the 24–2 pattern of locations using the SITA-Standard strategy. The control subjects whose data were used for the generation of the normative values were from a prospective longitudinal study conducted at two sites: Bloomington, Indiana University (IU) and New York City, State University of New York (SUNY). Subjects were recruited who had no known eye disease, best corrected visual acuity of 20/20 or better, or 20/30 over age 70 years, spherical equivalent within −6 to +2 diopters (D), cylinder correction within 3 D, clear ocular media, and intraocular pressure <21 mm Hg. Subjects were excluded if they had a history of intraocular surgery (except uncomplicated cataract surgery), a first-degree relative with glaucoma, narrow angles, peripheral anterior synechiae, abnormal optic disc or fundus appearance, or were using medications known to affect vision. All fields were examined visually for evidence of eyelid or lens artifact and reliability criteria were set at no more than 20% of false positives, false negatives, or fixation losses. The study was conducted following the tenets of the Declaration of Helsinki. Written informed consent was obtained from each participant before testing and after explaining the procedure and goals of the experiment. The protocol was approved by the Institutional Review Boards of the Indiana University and of the SUNY State College of Optometry.

From a dataset of 337 visual fields for 100 eyes of 100 control subjects, 60 visual fields were removed that did not pass the reliability criteria and 14 that had clear eyelid or lens artifact. The remaining dataset consisted of 263 visits (1 to 7 visits) for 91 eyes of 91 control subjects. All subjects had previous experience with perimetry. The median number of visits (and interquartile interval) was 2 (2–4), the median follow-up time was 1 month (0–4). The median age was 61 (56–67) years old, ranging from 42 to 85 years.

The methods used for the derivation of the normative values were as described by Heijl et al. (1987b). A linear model was obtained by weighted simple linear regression to model normal sensitivity decay with age at each location, and two-dimensional quadratic fits to smooth out noise in slopes and intercepts estimated at each location of the visual field. The weights were the inverse of the number of visits per subject, so that all subjects made the same contribution to the linear regression. The use of a linear age model and of polynomial fits to account for eccentricity effects has been justified by observations in healthy control subjects (Heijl et al., 1987a, 1987b). TD and PD values were derived and empiric probability maps (Heijl et al., 1989) obtained using percentiles 0.5, 1, 5, and 95. Standard deviations of TD and PD, necessary for the derivation of global indices such as mean deviation and pattern standard deviation, were also smoothed using two-dimensional quadratic fits (Heijl et al., 1987b). Further details about the derivation of the normative values can be found elsewhere (Heijl et al., 1987a, 1987b, 1989). We obtained our normative values with tools that are already part of visualFields using the script constructnv.r available as Supplemental Material.

As an example to demonstrate the visualFields package, we selected the right eye of a patient with glaucoma who participated in the Bloomington longitudinal study and underwent 27 examinations with static automated perimetry and the 24–2 test pattern (SITA standard) from 1997 to 2012. For the study, subjects were recruited who were undergoing treatment for glaucoma, best corrected visual acuity of 20/20 or better, or 20/30 over age 70 years, spherical equivalent within −6 to +2 D, cylinder correction within 3 D, clear ocular media, and current intraocular pressure <30 mm Hg. Patients were excluded if they had an ocular or systemic disease known to affect the visual field (other than glaucoma), history of intraocular surgery (except uncomplicated cataract surgery or glaucoma surgery), narrow angles, peripheral anterior synechiae, abnormal optic disc or fundus appearance (other than consistent with glaucoma), or were using medications known to affect vision. Diagnosis of glaucoma was made by the

treating clinician after a complete ophthalmic examination including medical history. At the first visit, the patient was 64 years old (the date of birth was modified by a small random amount to preserve confidentiality). The visual fields for this subject are included as a default example in visualFields. The name of the variable in the package is `vf91016right`. The left eye is also included in the package, `vf91016left`.

The same patient underwent another form of perimetry, named contrast sensitivity perimetry (CSP; Harwerth et al., 2002). CSP was based on a different type of stimulus tested on an alternative array of locations and whose size is dependent on eccentricity (Horner, Dul, Swanson, Liu, & Tran, in press). The testing locations were based on retinal nerve fiber layer projections rather than a regular pattern of locations, and there was a greater emphasis on testing the macula than in the 24–2 grid. The properties of this type of perimetry for control subjects are still under study, and the normative values made available with visualFields are experimental. Two single visual field printouts were generated with visualFields: one for SAP and one for CSP less than 3 months apart from each other.

In addition, Permutation-of-Pointwise-Linear-Regression (PoPLR; O'Leary, Chauhan, & Artes, 2012) analysis was performed with visualFields on the example eye. The PoPLR analysis returns a single overall *p*-value for the null hypothesis that there is no deterioration in the visual field. This *p*-value is determined through random re-ordering (permutation) of the individual patient's visual field sequence and is therefore individualized to a particular patient's data. More in detail, for the visual-field sequence, simple linear regression is obtained at each location and the *p*-values for the statistical tests that the slope equals zero combined into a single *S*-value using Fisher's method (see details in O'Leary et al., 2012). Then, the visual-field sequence is repeatedly permuted and *S*-values obtained. The aforementioned overall *p*-value that there is no deterioration is obtained by comparing the *S*-value for the true temporal visual field sequence against the histogram of *S*-values obtained for the permuted sequences.

All printouts are replicable with visualFields after loading it with the command

```
> library( visualFields )
```

A list of all functions available in visualFields, and help with examples on how to use them, can be obtained by typing

```
> help( visualFields )
```

and clicking "Index" at the bottom of the help page.

Results

Four examples of visual field analysis are shown along with the corresponding code used for their generation: two single visual field analyses (see Figures 1 and 2) and two PoPLR analyses (see Figures 3 and 4). The single visual field analyses were based on normative values obtained with visualFields. Exhaustive validation of the normative values was out of the scope of this manuscript, but a preliminary comparison was done between mean deviations (MD) from HFA against MD obtained with visualFields with 2,934 visual fields of 129 healthy controls and 140 patients with glaucoma from the SUNY and IU longitudinal studies. Agreement was good, with 95% limits of agreement from −0.5 to 0.2 decibels (dB). The 95% limits of agreement were calculated too for the visual field index. These were from −2.2% to 2.5%.

Single visual field analysis

Figure 1 shows a printout for a single visual field analysis for SAP. This figure can be obtained by typing the command

```
> vflayout( vf91016right[27,] )
```

This and the following printouts can be saved as a portable document format (.pdf) file by adding the argument filename = <path/name.pdf> to the call. For instance,

```
>vflayout(vf91016right[27,],filename=
  "Figure01.pdf")
```

saves a pdf file in the working directory.

There are five main elements in the printout. The first element, on top left, is the subject-test information. It contains (de-identified) information about the subject and visit, as well as the global indices for the examination (Bengtsson & Heijl, 2008; Heijl et al., 1987b). The global indices mean sensitivity (MS in the printout in Figure 1), MD, and pattern standard deviation can be calculated with

```
> vfstats( vf91016right[27,] )
```

The visual field index can be obtained with

```
> vfindex( vf91016right[27,] )
```

And the general height with

```
> ghpostd( tdval( vf91016right[27,] ) )
```

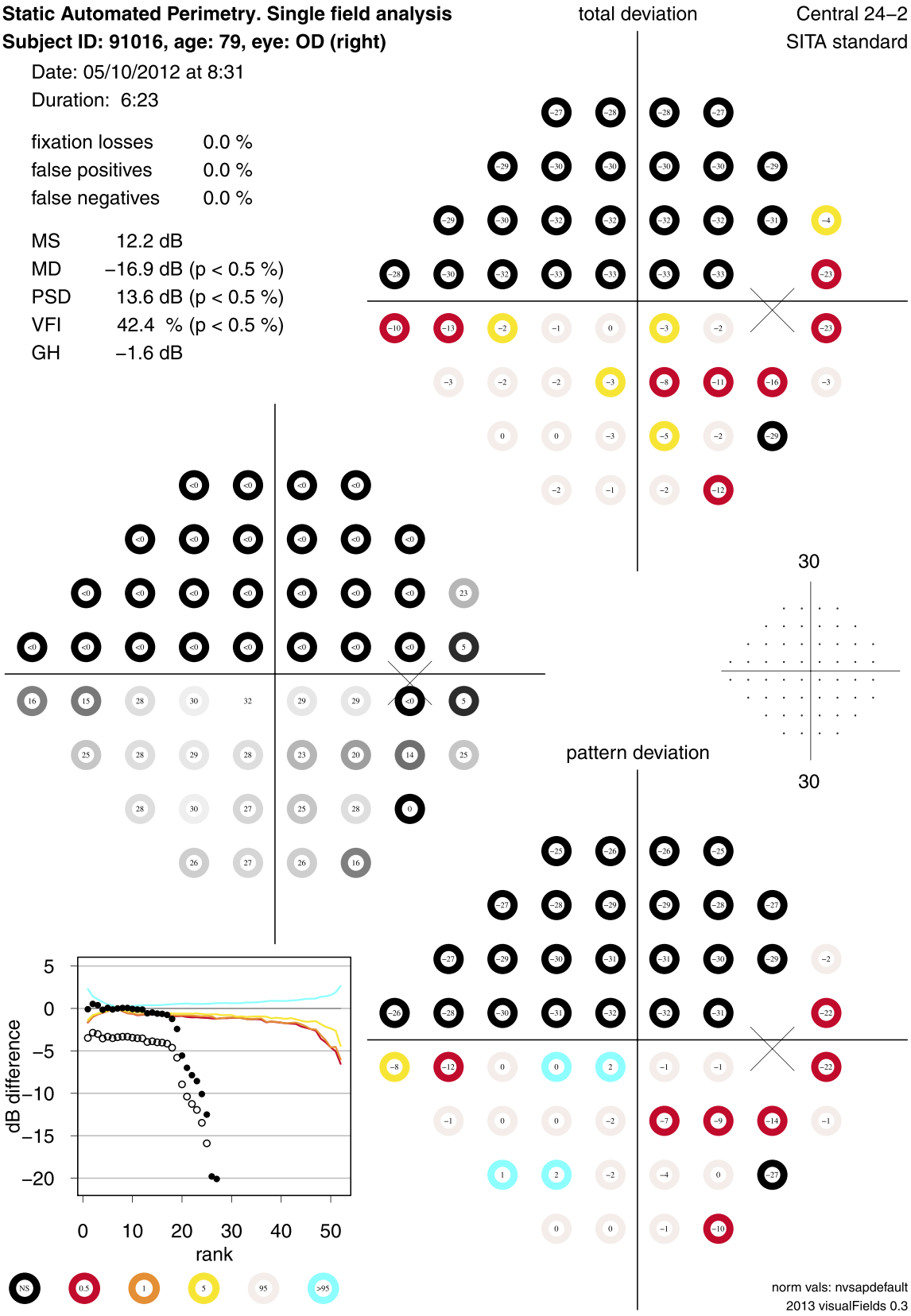

Figure 1. visualFields printout for a single SAP visual-field analysis.

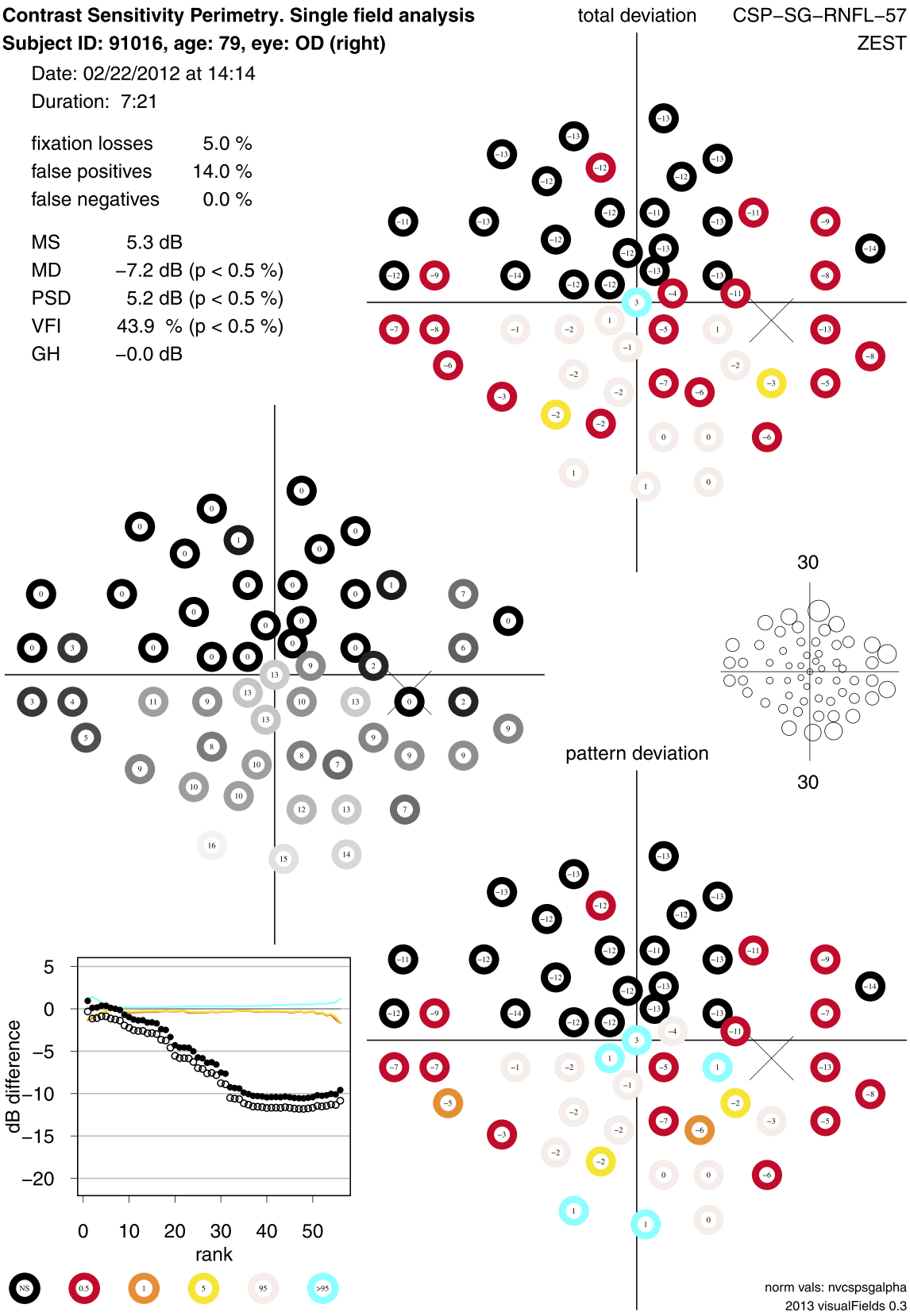

Figure 2. visualFields printout for a single CSP visual-field analysis.

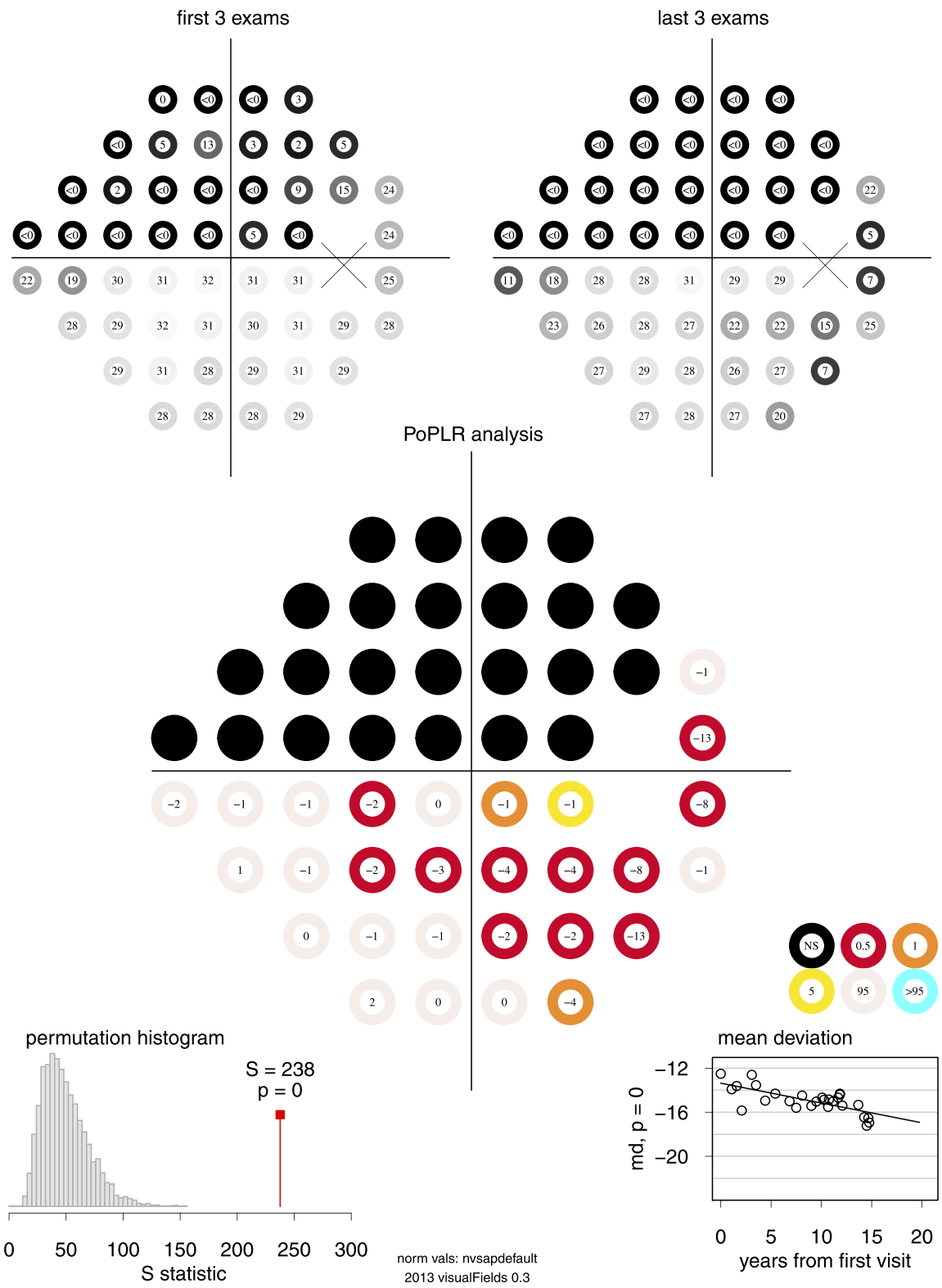

Figure 3. visualFields printout for a PoPLR progression analysis.

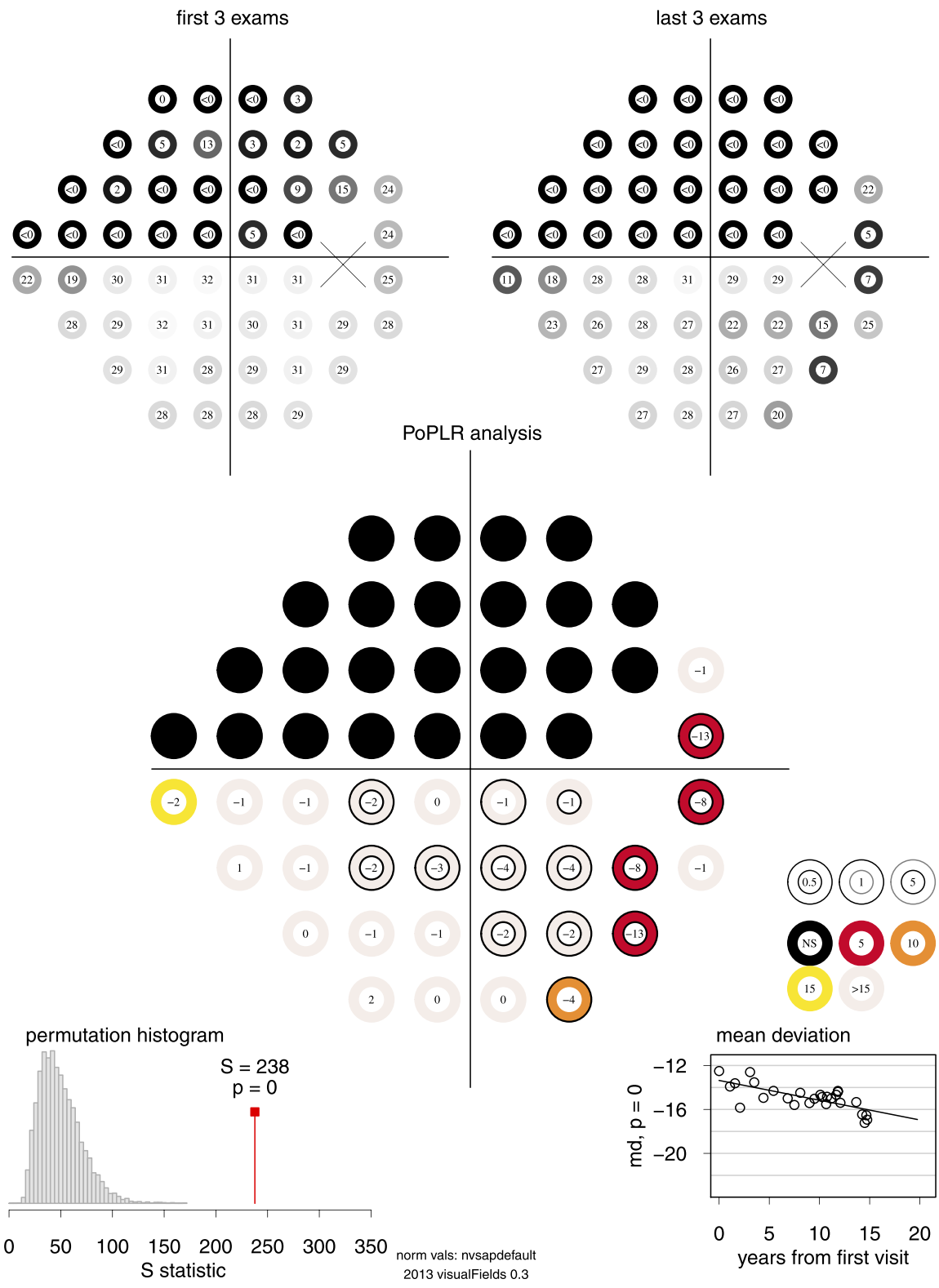

Figure 4. visualFields alternative printout for a PoPLR progression analysis.

The second element, below the subject-test information, is the sensitivity plot. It shows the sensitivity values at each location superposed on a gray-scale plot. The third and fourth elements, on the top right and bottom right of the page, respectively, are the TD and the PD plots. They show the TD and PD values superposed on a color-coded probability map. The TD and PD values can be calculated, respectively, with

```
> td91016right <- tdval( vf91016right[27,] )
> pd91016right <- pdval( td91016right )
```

and their corresponding probability categories with

```
> tdp91016right <- tdpmap( td91016right )
> pdp91016right <- pdpmap( pd91016right )
```

The sensitivity, TD, and PD plots can be obtained with the function vfplot. The different plots are obtained by modifying the argument plotType. Thus,

```
> vfplot( vf91016right[27,], plotType =
  "vf", newWindow = TRUE )
> vfplot( vf91016right[27,], plotType =
  "td", newWindow = TRUE )
> vfplot( vf91016right[27,], plotType =
  "pd", newWindow = TRUE )
```

A color coding was adopted following a traffic-light type of coding (Wall, Johnson, Kardon, & Crabb, 2009), but the "green light" demarking within-normal limit points was substituted by a pale-cream color. There are two other categories: "no sensitivity" category represented in black and above normal limits represented by a light-blue color. Notice that all locations in black will have a probability category of 0.5. The inclusion of the latest category is useful to identify locations that seem "too sensitive" and can be used to identify artifacts, statistical or not, such as a large false-positive rate or, in PD maps, a potential overestimation of global loss.

The fifth element, on the bottom left of the page, is the Bebie TD-rank difference plot. It shows the difference between the Bebie TD rank curve (Bebie et al., 1989) for the subject's TD plot and the mean normal Bebie TD rank curve, along with confidence limits. The TD-rank-curve graph can be plotted with

```
> tdr <- tdrank( td91016right )
> bebie( tdr )
```

The rest of the elements give details about the pattern of locations and presentation strategy (on top right), the normative values and the version of the visualFields package used (see bottom right), the legend for the color coding for the probability maps (bottom left), and a stimulus-location map with the locations and relative size of the stimulus at each location (middle right).

Figure 2 shows an example of a single visual-field analysis for CSP. The stimulus sizes vary at each location as can be seen in the stimulus-location map. To replicate the figure, we first need to change the normative values to be used by the visualFields package from the default ones to the CSP ones. This is achieved with the command

```
> setnv( "nvcspsgalpha" )
```

Notice that the name of the variable ends in "alpha", to remark that these normative values are just experimental. Once we have set the new normative values, Figure 2 can be obtained with

```
> vflayout( vf91016csp1vf )
```

To go back to the default normative values, type

```
> setnv( "nvsapdefault" )
```

Progression analysis with PoPLR

In addition to single visual field printouts for analysis, progression analyses such as PoPLR are available in visualFields. Figure 3 shows a printout of the PoPLR analysis for the same subject and eye as the single field analyses in Figures 1 and 2. Figure 3 can be replicated using visualFields by executing the command

```
> vflayout_poplr( vf91016right )
```

There are five main elements in the printout. The first and second elements, on top left and top right, respectively, show the sensitivity plots of the average values over the first three (left) and last three (right) visits considered in the analysis. Although it is possible that over the period of three visits there will be some progression, averaging reduces substantially test–retest variability. And, as long as there is enough separation between the first three visits and the last three, these graphs will show change (if there is any) more reliably than single visual fields would. The generation of these two graphs is made through the multipurpose function vfplotloc, and some data processing and analysis are necessary. The commented R script firstlastvisits.r (in the Supplemental Material) generates these two graphs.

The third element, in the center of the printout, is the PoPLR plot, which consists of the pointwise slopes estimated (in decibels per decade) and the probability categories obtained using permutation analysis. The

locations for which no stimulus was responded to in the last three exams are shown in black. The PoPLR analysis can be conducted with

```
> plr <- poplr( vf91016right )
```

and the plot PoPLR plot can be obtained with

```
> vfplot_poplr( plr$sl, plr$pval,
  plr$vfdata, newWindow = TRUE )
```

The fourth element, on the bottom left, is the histogram of *S*-values obtained for the permuted sequences from the PoPLR analysis (O'Leary et al., 2012), which can be generated with

```
> hist_poplr( plr$scomb_obs,
  plr$pcomb_obs,
  plr$scomb )
```

Notice that with this call, the shape of the histogram varies slightly from that in Figure 3. This is due to the random nature of the permutation analysis, for which a different set of random permutations is generated every time, leading to slightly different histograms. The fifth element, on the bottom right, is a typical MD rate-of-change analysis using simple linear regression over time, which can be generated with

```
> md <- vfstats( vf91016right )$mtdev
> progols( vf91016right$tdate, md )
```

Different, more experimental visualizations for the PoPLR analysis, as that shown in Figure 4, have been implemented in visualFields. Figure 4 can be replicated with

```
> vflayout_poplr( vf91016right,
  imparedVision = 13,
colorMapType = "blind",
  ringMapType = "pval" )
```

The main difference between both figures, apart from the PoPLR histogram, is on the PoPLR graph in the center of the printouts. The traffic-light-type color code now represents different categories for the estimated number of years in which this subject will become visually impaired. Visual impairment was set at 13 since locations with sensitivities around this value can be considered as severely damaged (Wall, Woodward, Doyle, & Artes, 2009). The estimate of number of years to visual impairment is based on the estimated slopes by pointwise linear regression and the sensitivities of the last examination in the visual field sequence (see Figure 1). The NS category represents the locations for which no stimulus was responded to in the last three exams as in Figure 3. In this visualization, the probability categories are coded with concentric rings, and only four categories were considered: below 0.5%, between 0.5% and 1%, between 1% and 5%, and above 5%.

Discussion

The R package visualFields is a platform-independent, highly flexible framework for collaborative research in the analysis of visual fields. It contains tools and settings that are easy to customize for the generation and use of normative values for different datasets, different stimulus sizes and shapes, and different perimeters and presentation algorithms.

We presented (as Supplemental Material) the script used to generate normative values from a dataset of controls tested using the SAP 24–2 SITA standard, constructnv.r. The same script could be used for a dataset of controls tested with the size V stimulus or with CSP perimetry (as demonstrated in Figure 2). The generated normative values critically depend on the two-dimensional quadratic fit used to obtain the age linear model and the normal variability at each location (Heijl et al., 1987b) that accounts for eccentricity effect (Heijl et al., 1987a). For other types of perimetry, such as frequency-doubling perimetry, for which the eccentricity effect is different than for the size III stimulus (Anderson et al., 2005), we may want to use other smoothing functions or none at all. This can be used by setting the argument smooth to FALSE in the function ageLinearModel, if no smoothing is required, or creating a custom smoothing function in R and specifying it with the argument smoothFunction. Other settings for the generation of the normative values can also be modified fairly easily. For instance, the number and color code of the probability categories used in TD and PD maps can be changed by modifying the cutoffs and red, green, and blue values in the variable pmapsettings in constructnv.r, for example, to match the "continuous" probability coding by Wall et al. (2009).

In addition to normative values for SAP 24–2 SITA standard and the Goldmann size III stimulus, the package includes normative values for the SAP 10–2 SITA standard along with the normative dataset (Shafi, Swanson, & Dul, 2011; Wyatt, Dul, & Swanson, 2007) used for their generation.

The intention of this package is not to replace well-tested, commercially available stand-alone software or software included with the perimeters. Rather, visualFields is sought to be an environment for experimentation and research, and as such it needs to be free and open for anybody to use, scrutinize, and

improve upon. We welcome anybody who wishes to contribute to visualFields with their work. The package can work in conjunction with the Open Perimetry Interface (also developed in R), a set of functions that can be used to control perimeters after obtaining the appropriate libraries from the vendors (Turpin, Artes, & McKendrick, 2012).

Keywords: visual field, perimetry, software, open source, statistics

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