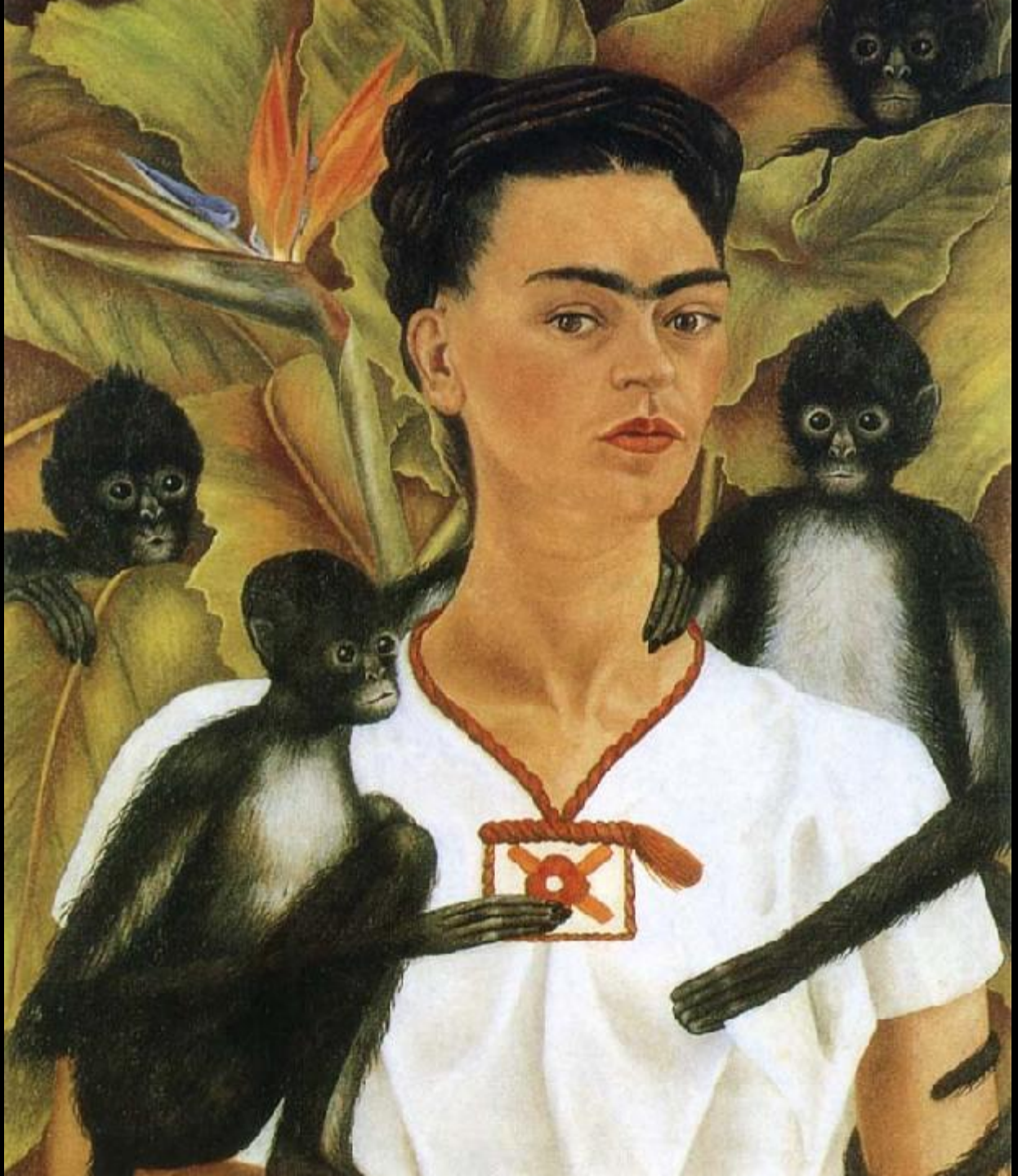
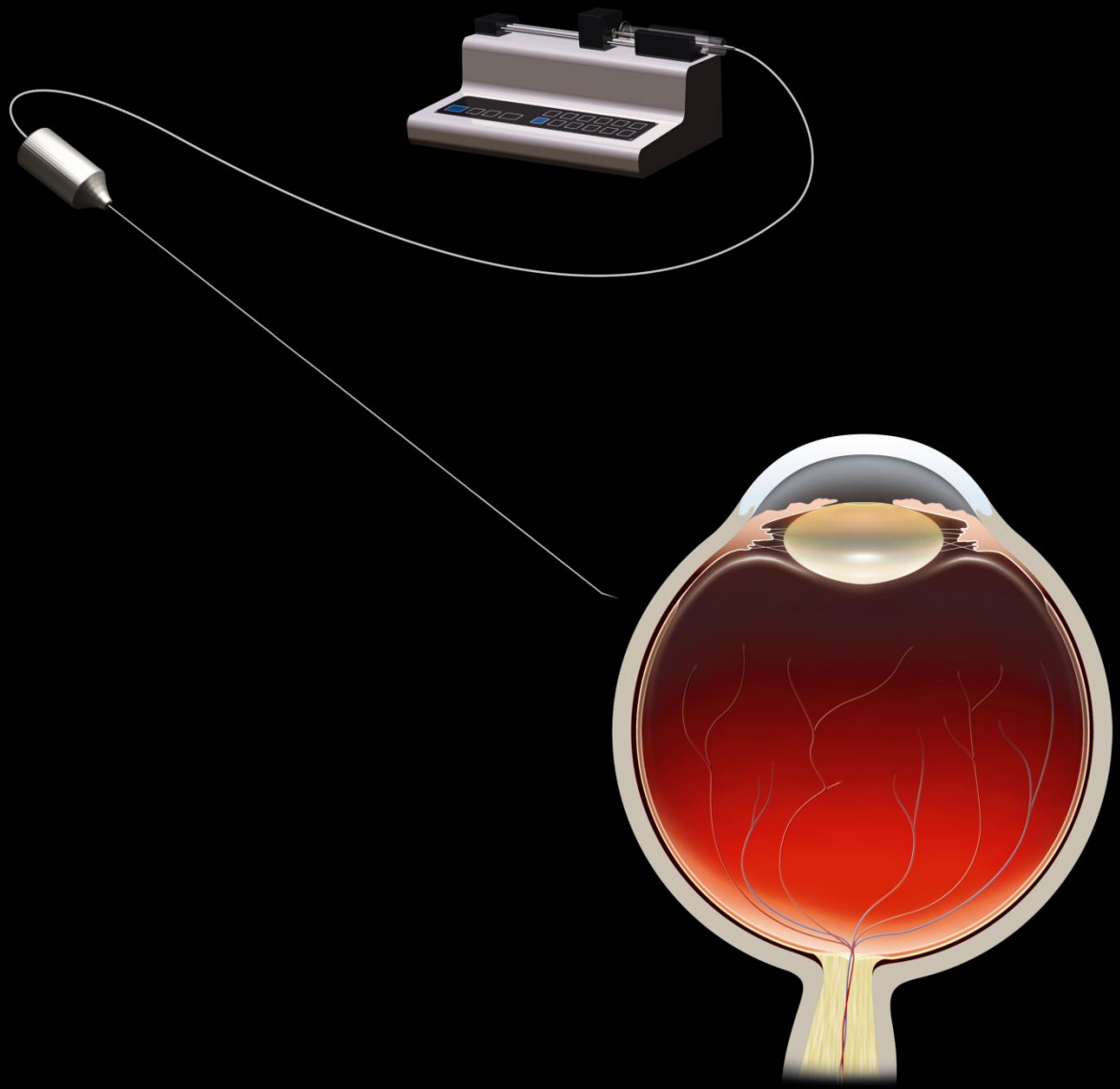
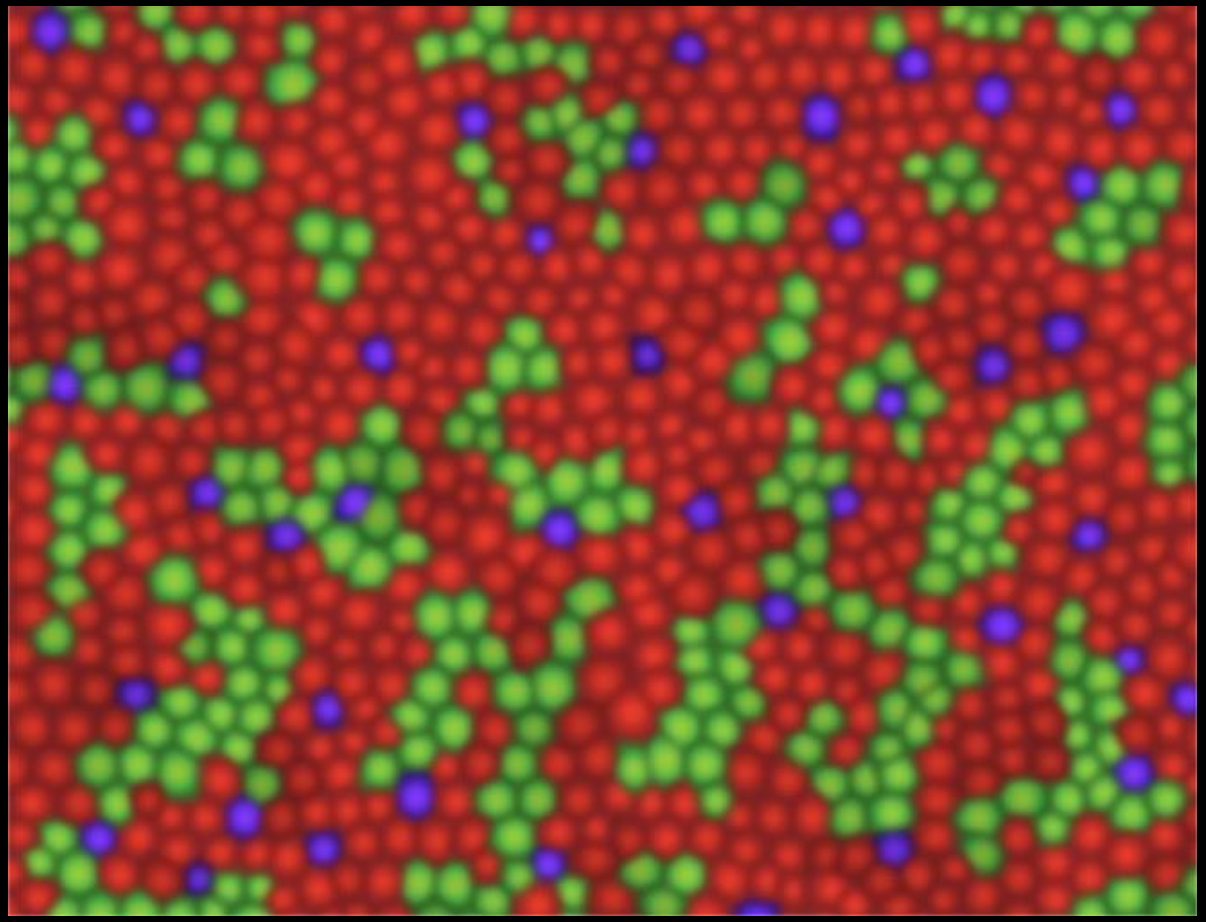
Gene Therapy Approach to curing color blindness



Frida Kahlo "Self-portrait with Monkeys" (1943), oil on canvas

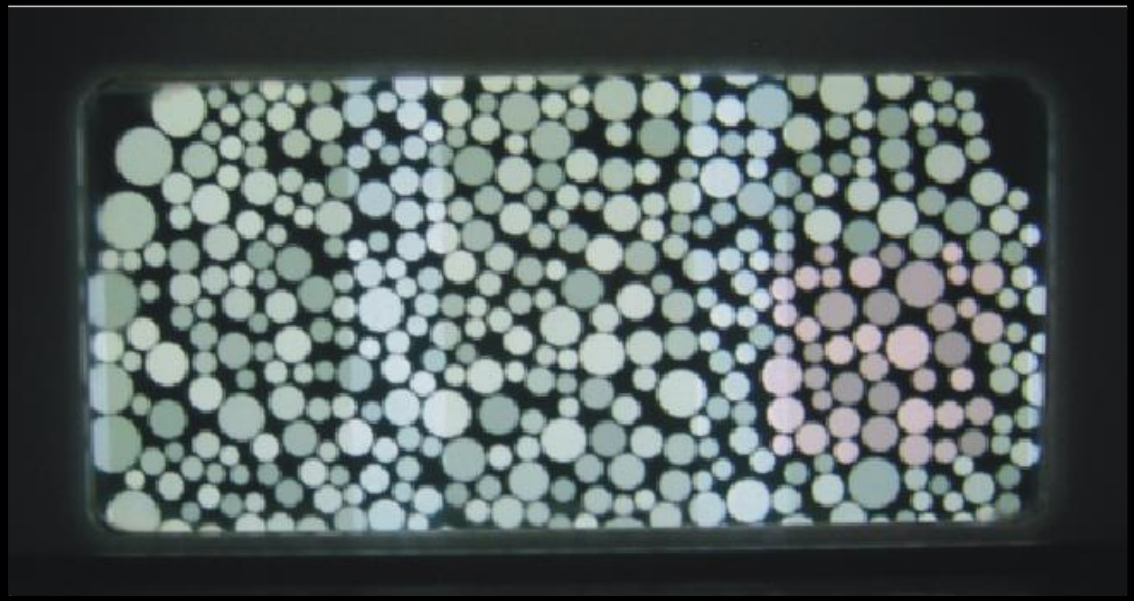

TORRE 6
TOWER 6
AUDITÓRIO
Auditorium
QUADRA DE ESPORTES
SPORTS AREA
RESTAURANTE
RESTAURANT
RECEPÇÃO
RECEPTION

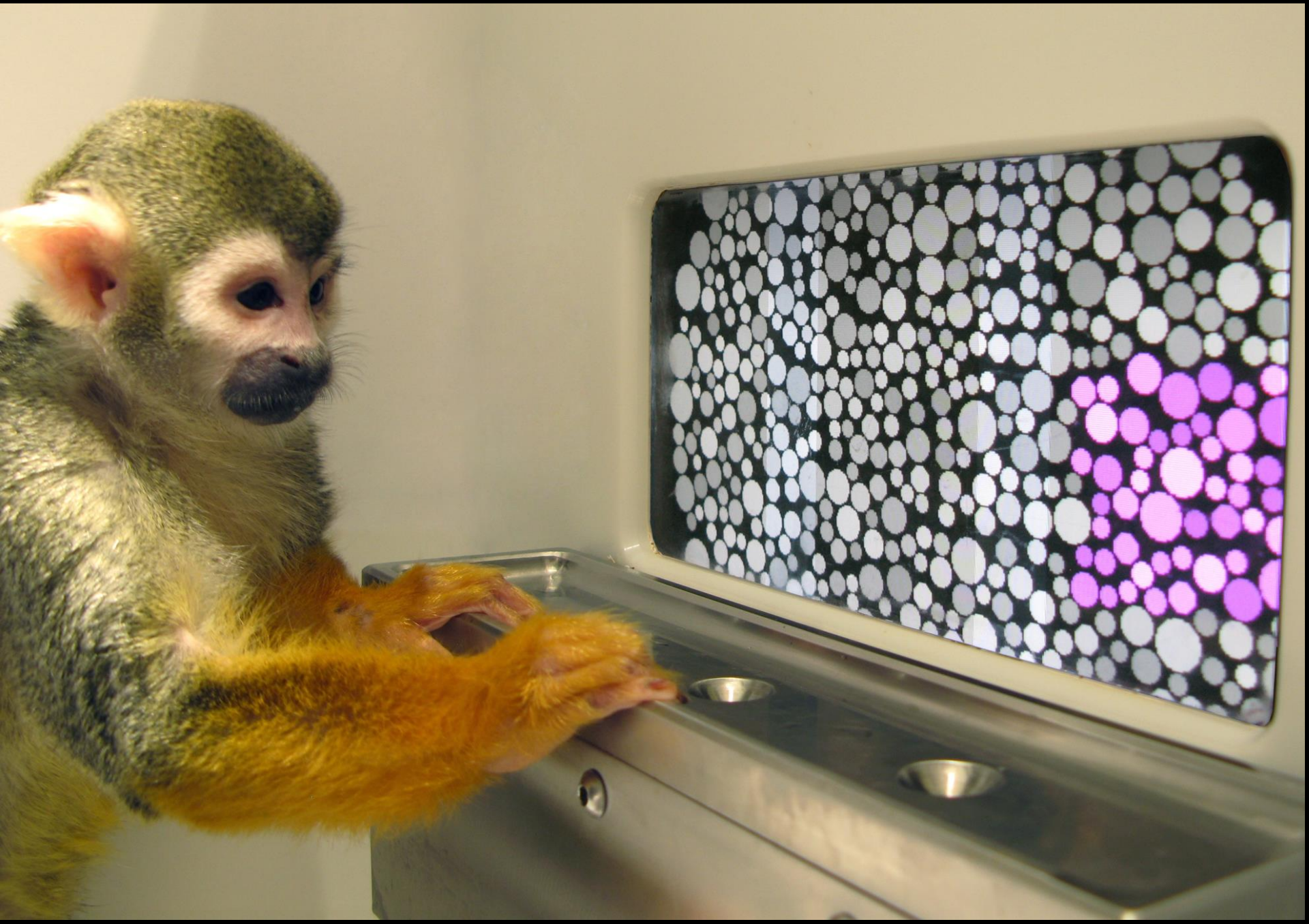


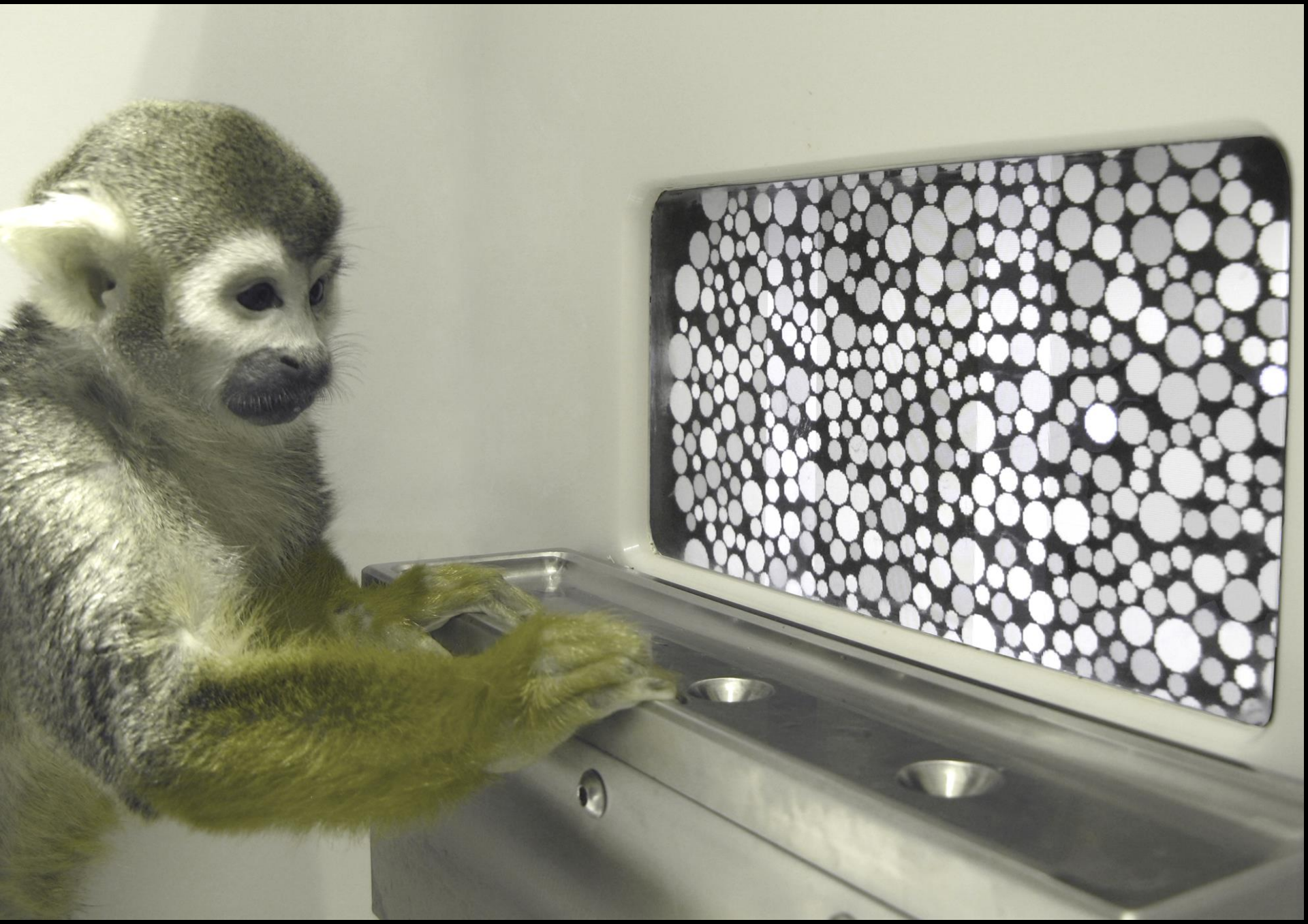


Cambridge color Test

- Developed by Mollon & Regan; Available through Cambridge Research Systems
- Animals are not able to use luminance differences or edge artifacts to make the correct color discriminations.

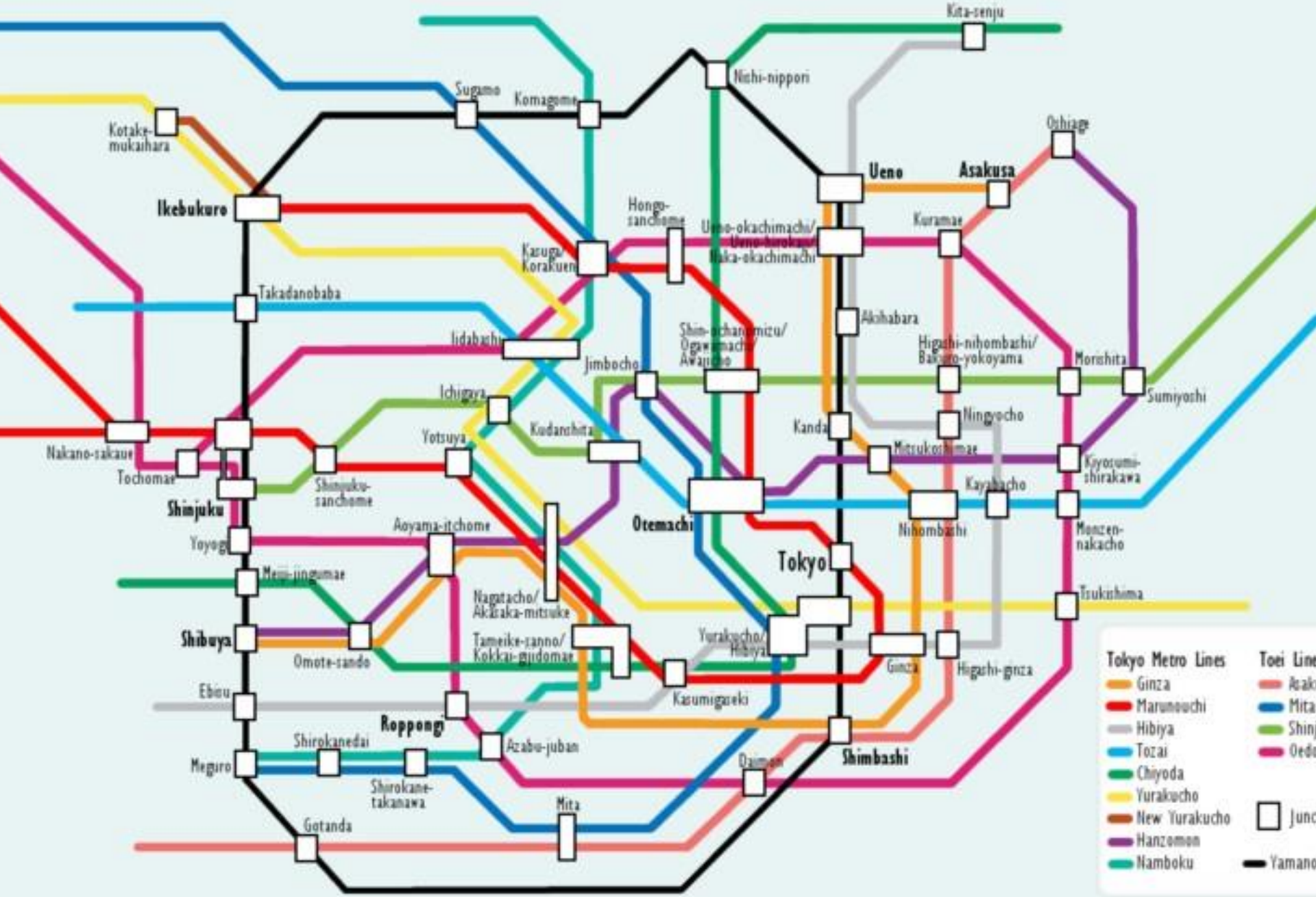


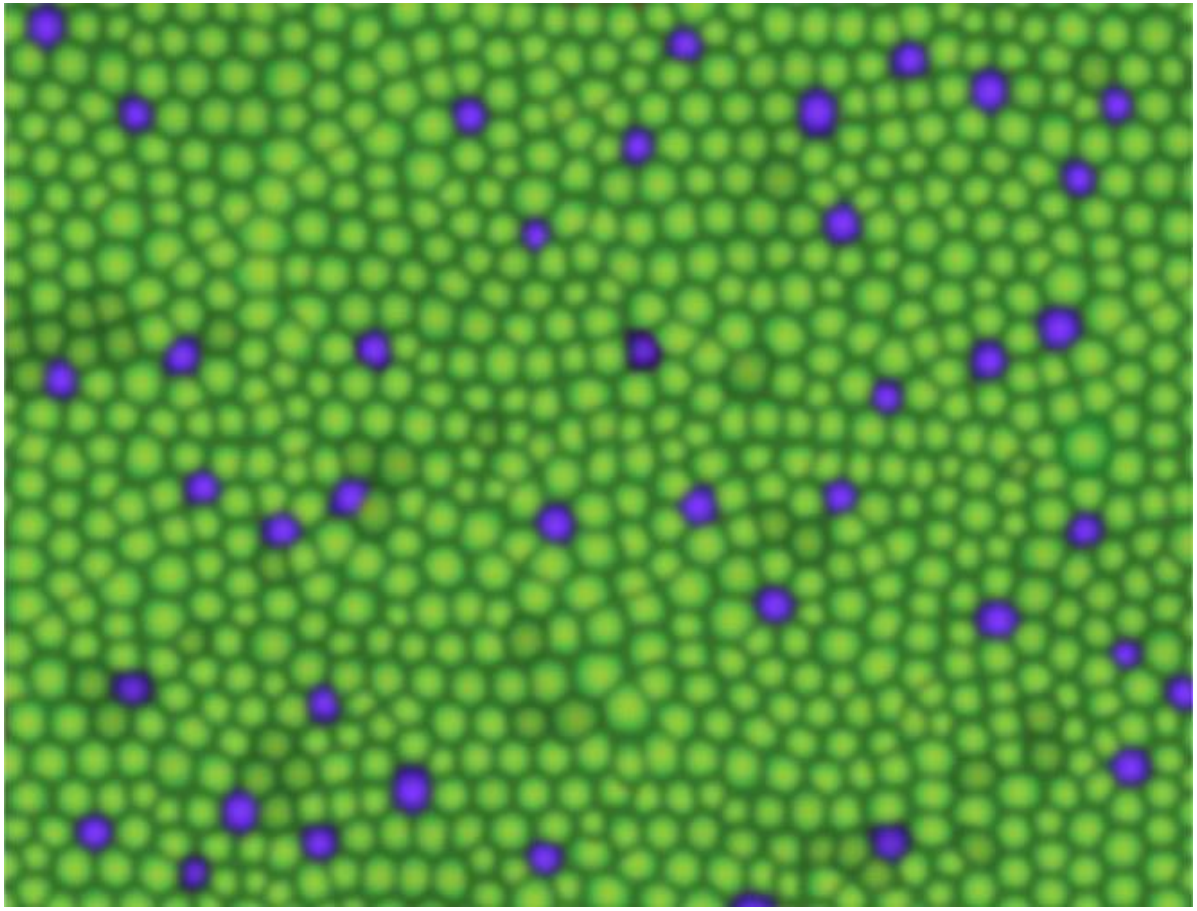





Crayola®
™


Crayola


Kita-senju
Nishi-nippori
Sugamo
Komagome
Kotake-mukaihara
Ikebukuro
Takadanobaba
Iidabashi
Ochiai
Ueno
Asakusa
Hongo-sanchome
Ueno-okachimachi/
Ueno-hirokoji/
Naka-okachimachi
Kuramae
Kasuga/
Korakuen
Akihabara
Shin-ochanomizu/
Ogawamachi/
Awajicho
Higashi-nihombashi/
Bakuro-yokoyama
Jimbocho
Morishita
Sumiyoshi
Ichigaya
Kudanshita
Kanda
Ningyocho
Nakano-sakaue
Tochomae
Yotsuya
Shinjuku-sanchome
Mitsukoshimae
Kiyosumi-shirakawa
Shinjuku
Otemachi
Kayabacho
Nihombashi
Monzen-nakacho
Aoyama-itchome
Yoyogi
Tokyo
Meiji-jingumae
Nagatacho/
Akasaka-mitsuke
Tsukishima
Shibuya
Omote-sando
Tameike-sanno/
Kokkai-gijidomae
Yurakucho/
Hibiya
Ginza
Higashi-ginza
Ebisu
Kasumigaseki
Roppongi
Azabu-juban
Shirokanedai
Meguro
Shirokane-takanawa
Daimon
Shimbashi
Mita
Gotanda
Tokyo Metro Lines
Ginza
Marunouchi
Hibiya
Tozai
Chiyoda
Yurakucho
New Yurakucho
Hanzomon
Namboku
Toei Lines
Asak
Mita
Shinj
Oedo
Junc
Yamano

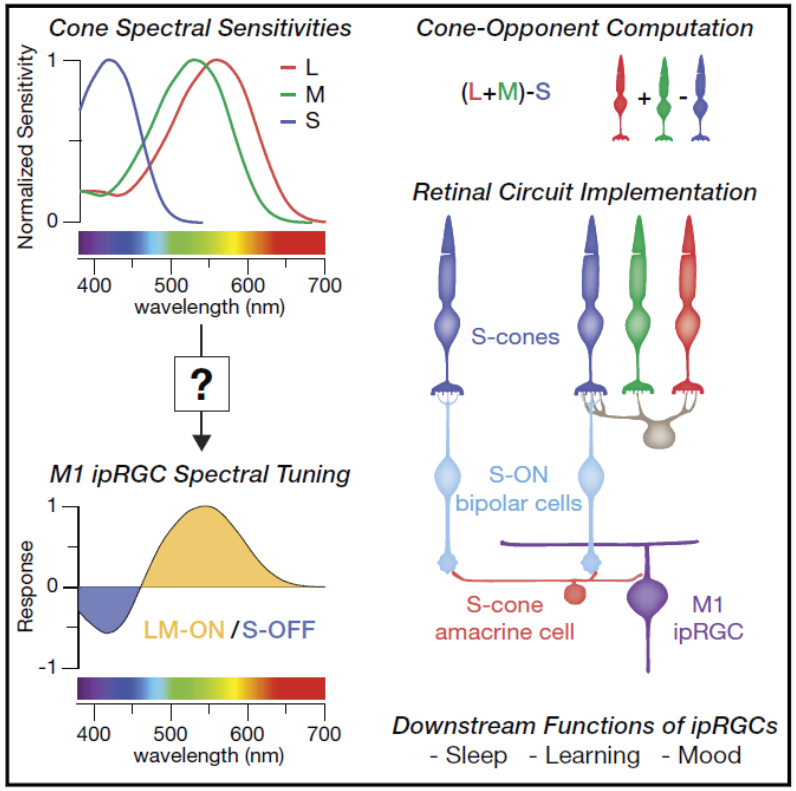


Report

Current Biology

A Color Vision Circuit for Non-Image-Forming Vision in the Primate Retina

Graphical Abstract



Authors

Sara S. Patterson,
James A. Kuchenbecker,
James R. Anderson, Maureen Neitz,
Jay Neitz

Correspondence

jneitz@uw.edu

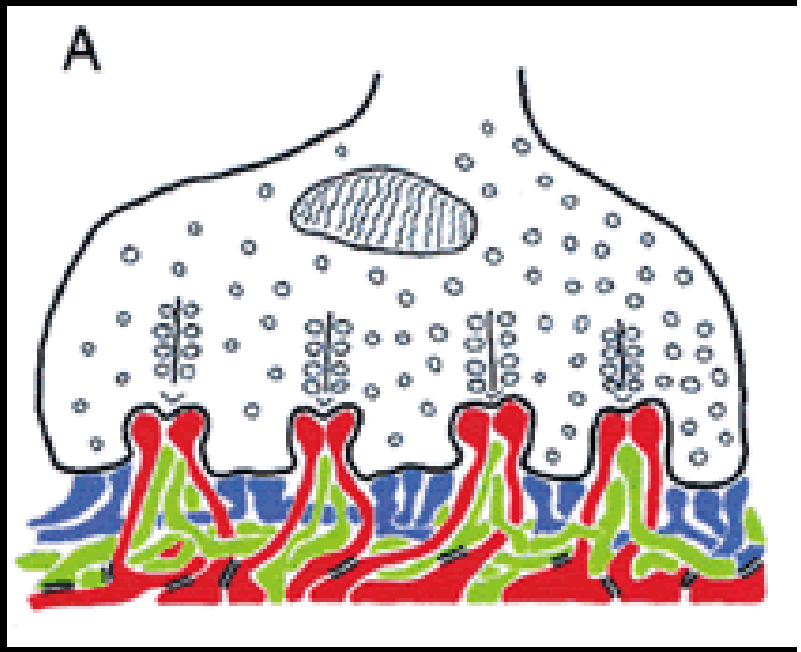
In Brief

Patterson et al. identify a new amacrine cell type in the primate retina with "blue" S-cone circuit input and targeted output to intrinsically photosensitive retinal ganglion cells (ipRGCs). This circuit may contribute to the effects of short-wavelength light on ipRGC downstream non-image-forming visual functions such as sleep, mood, and learning.

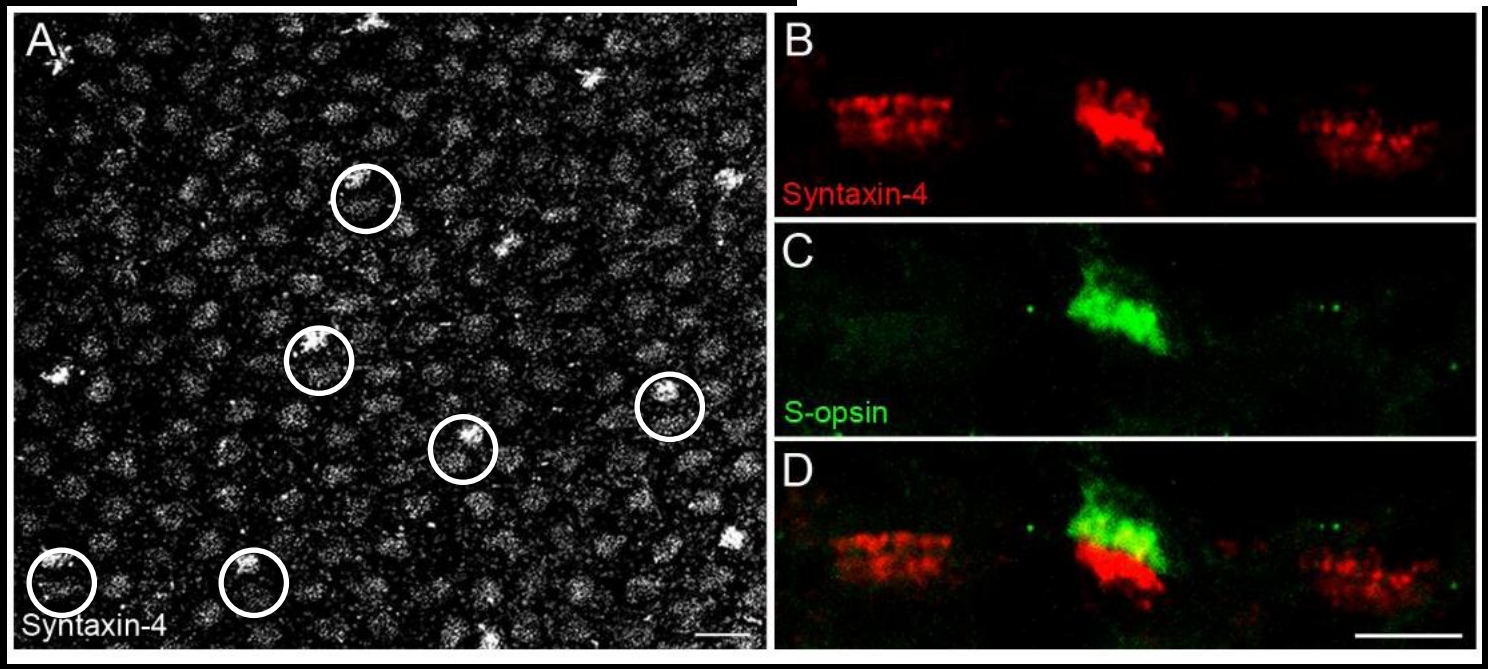
Specialized synaptic pathway for chromatic signals beneath S-cone photoreceptors is common to human, Old and New World primates

Christian Puller, Michael B. Manookin, Maureen Neitz, and Jay Neitz*

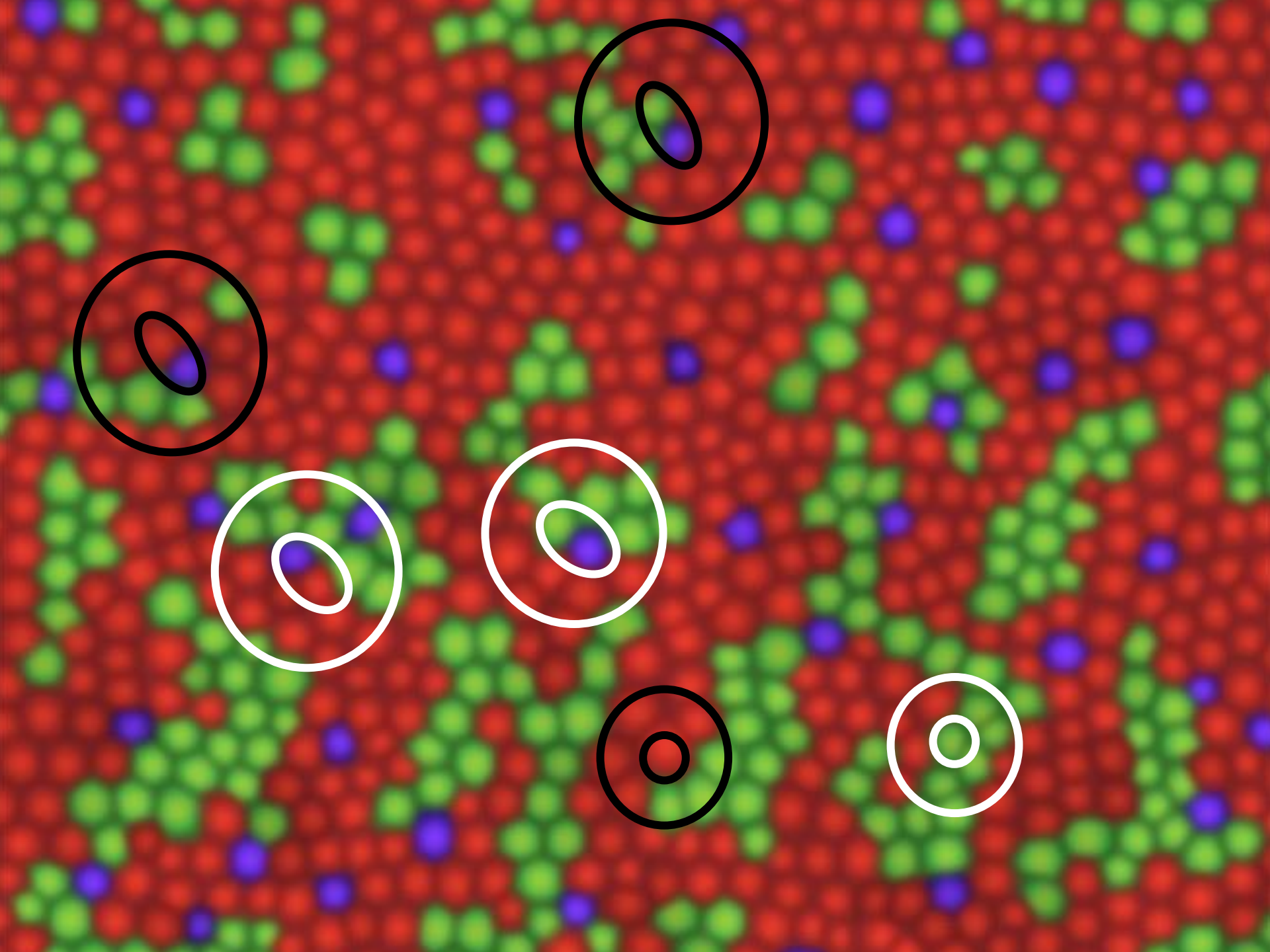
Department of Ophthalmology, University of Washington, Seattle, Washington 98109, USA
**Corresponding author: jneitz@uw.edu*

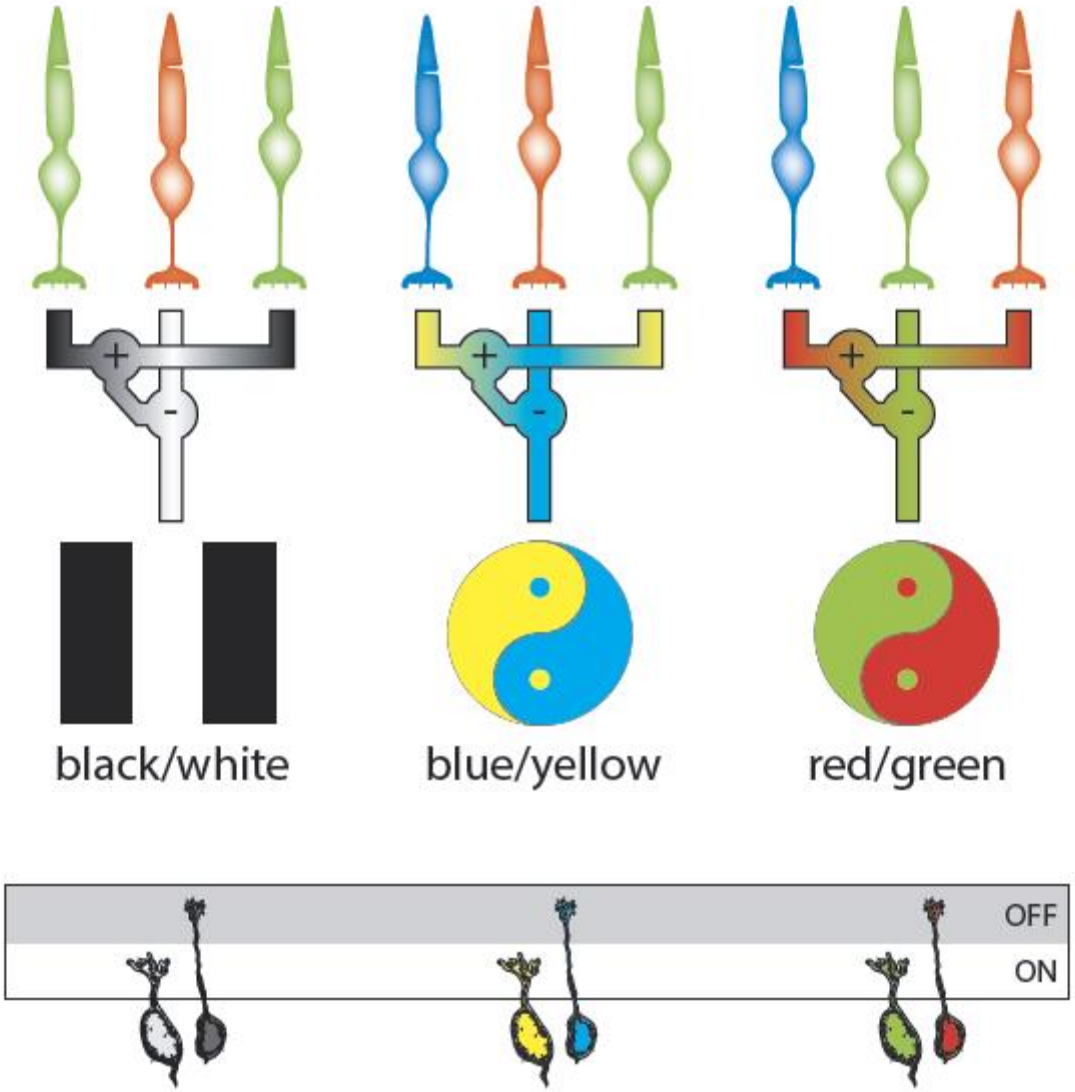


Puller C, Haverkamp S, Neitz M, Neitz J (2014) Synaptic elements for GABAergic feed-forward signaling between HII horizontal cells and blue cone bipolar cells are enriched beneath primate S-cones. PLoS ONE



And this is how red-green color vision evolved in primates




+
-
black/white
blue/yellow
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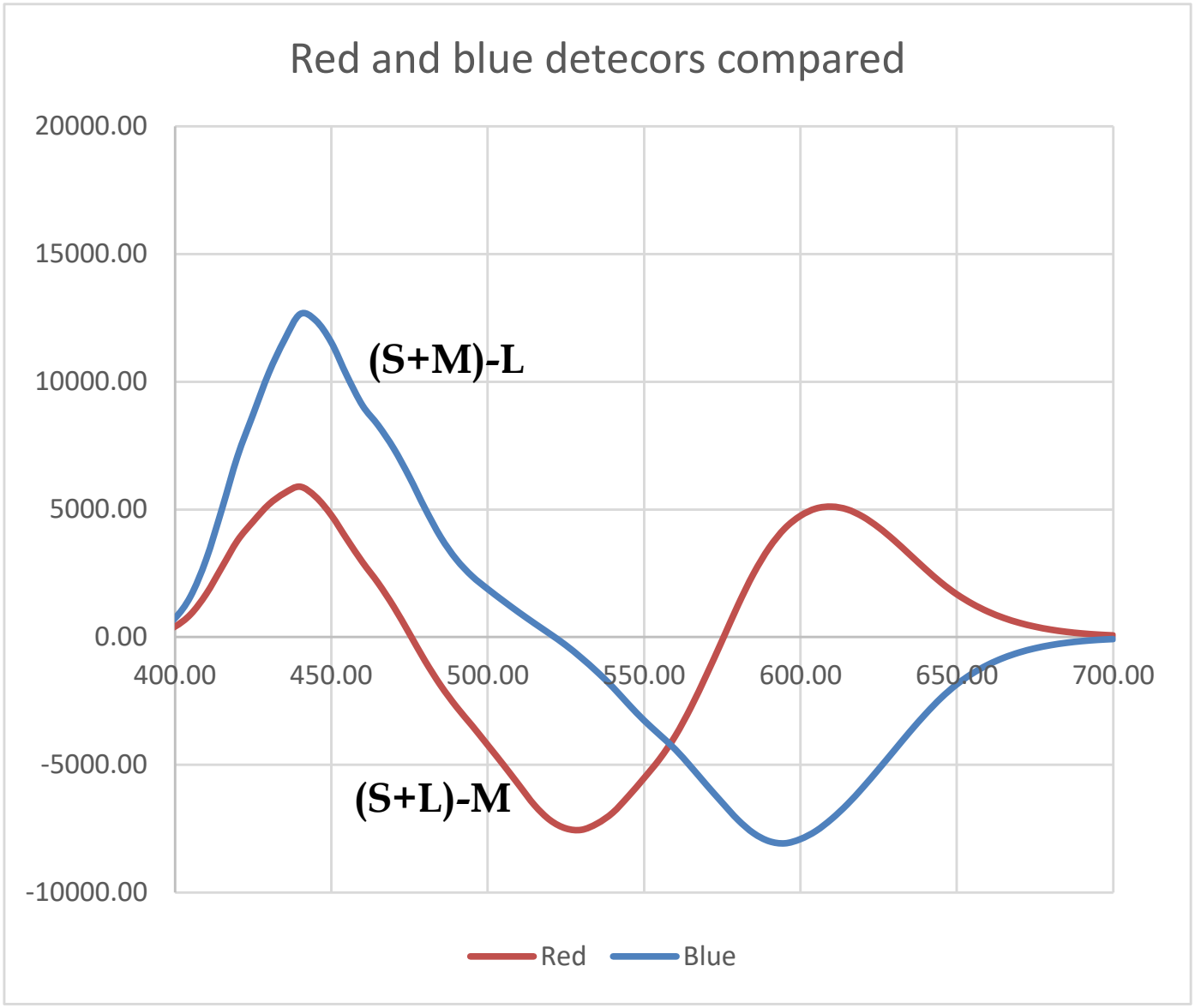
OFF
ON


Red and blue detecors compared
20000.00
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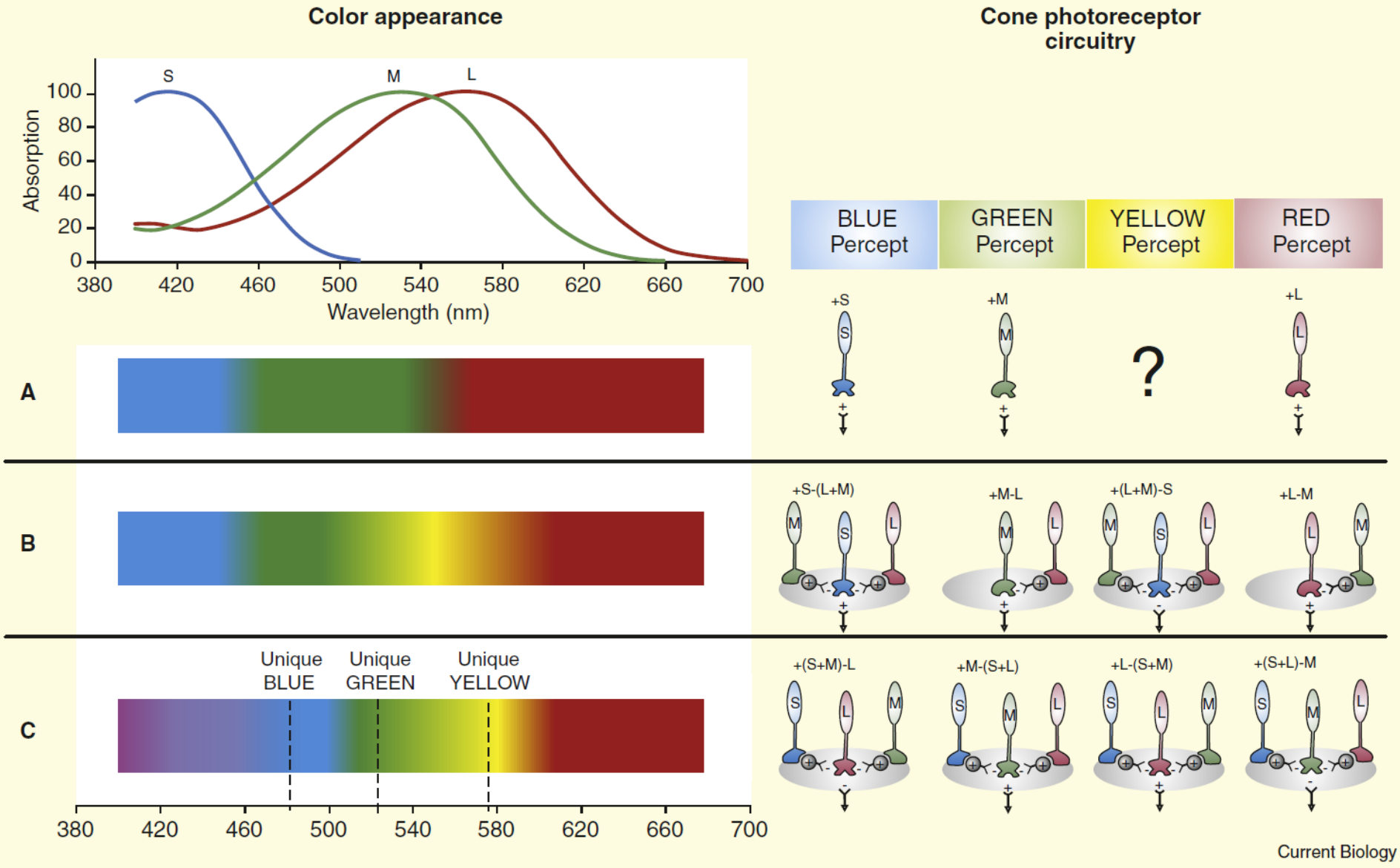
(S+M)-L
(S+L)-M
Red
Blue



Neitz, J., & Neitz, M. (2008). Colour vision: the wonder of hue. Current Biology

Neurobiological hypothesis of color appearance and hue perception

Brian P. Schmidt,[1] Maureen Neitz,[2] and Jay Neitz[2,*]

[1]*Graduate Program in Neurobiology and Behavior, University of Washington, Seattle, Washington 98109, USA*
[2]*Department of Ophthalmology, University of Washington, Seattle, Washington 98109, USA*
**Corresponding author: jneitz@uw.edu*

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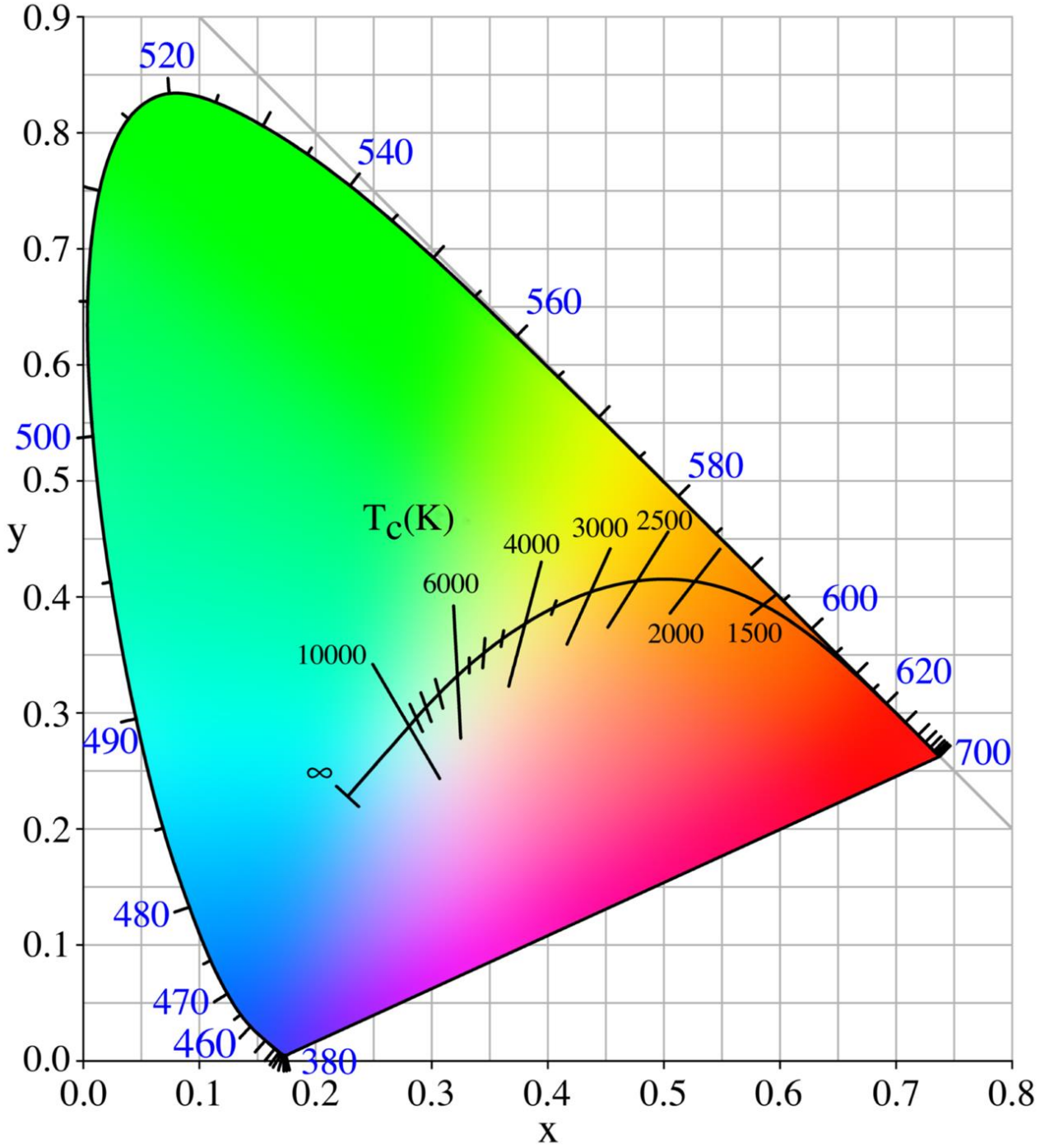
posted January 13, 2014 (Doc. ID 198757); published February 12, 2014

De Valois and De Valois [Vis. Res. **33**, 1053 (1993)] showed that to explain hue appearance, S-cone signals have to be combined with M versus L opponent signals in two different ways to produce red–green and yellow–blue axes, respectively. Recently, it has been shown that color appearance is normal for individuals with genetic mutations that block S-cone input to blue-ON ganglion cells. This is inconsistent with the De Valois hypothesis in which S-opponent konio-geniculate signals are combined with L-M signals at a third processing stage in cortex. Instead, here we show that color appearance, including individual differences never explained before, are predicted by a model in which S-cone signals are combined with L versus M signals in the outer retina.

OCIS codes: (330.0330) Vision, color, and visual optics; (330.1720) Color vision; (330.4060) Vision modeling.
http://dx.doi.org/10.1364/JOSAA.31.00A195


0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
y
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
x
520
540
560
580
600
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700
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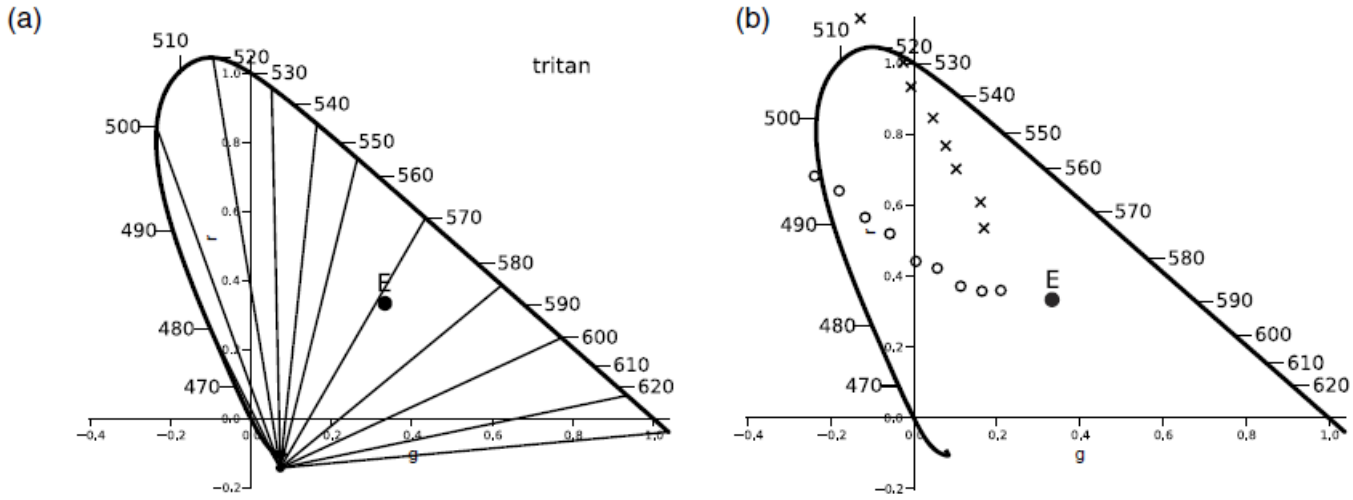
490
480
470
460
380
T_c(K)
10000
6000
4000
3000
2500
2000
1500
∞


(a)
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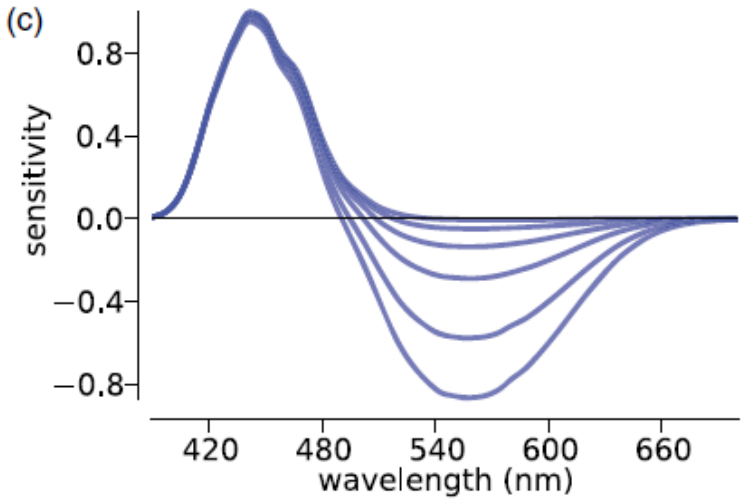
g
(b)
E


(c)
sensitivity
0.8
0.4
0.0
−0.4
−0.8
420
480
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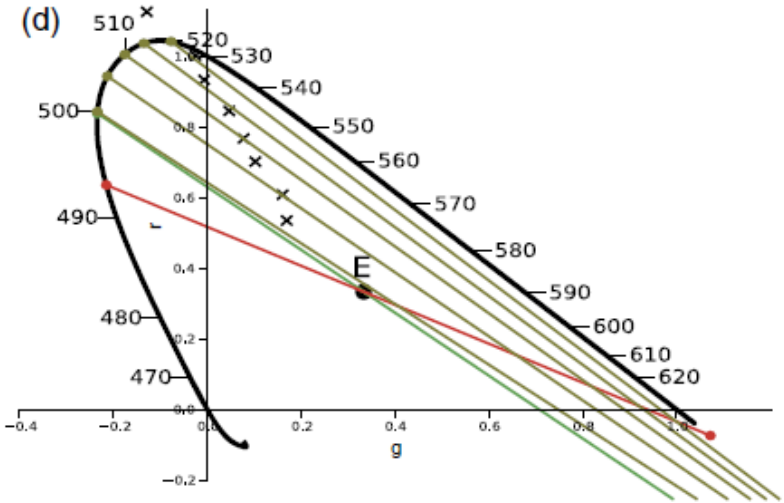
600
660
wavelength (nm)


(d)
510
520
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E
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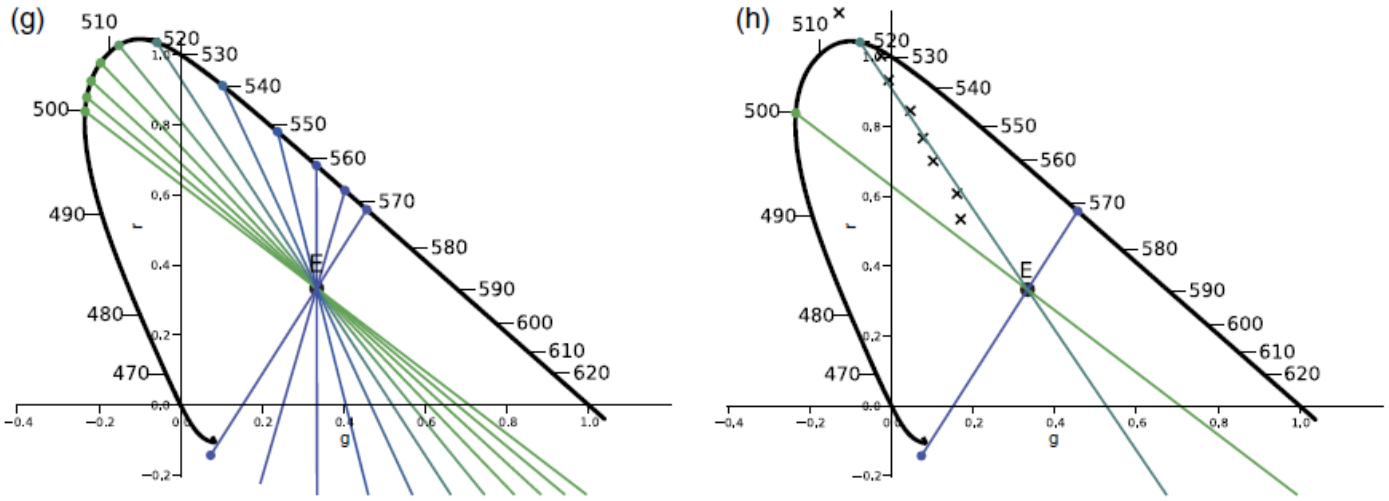
g
−0.4
−0.2
0.2
0.4
0.6
−0.2


(g)
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g
(h)
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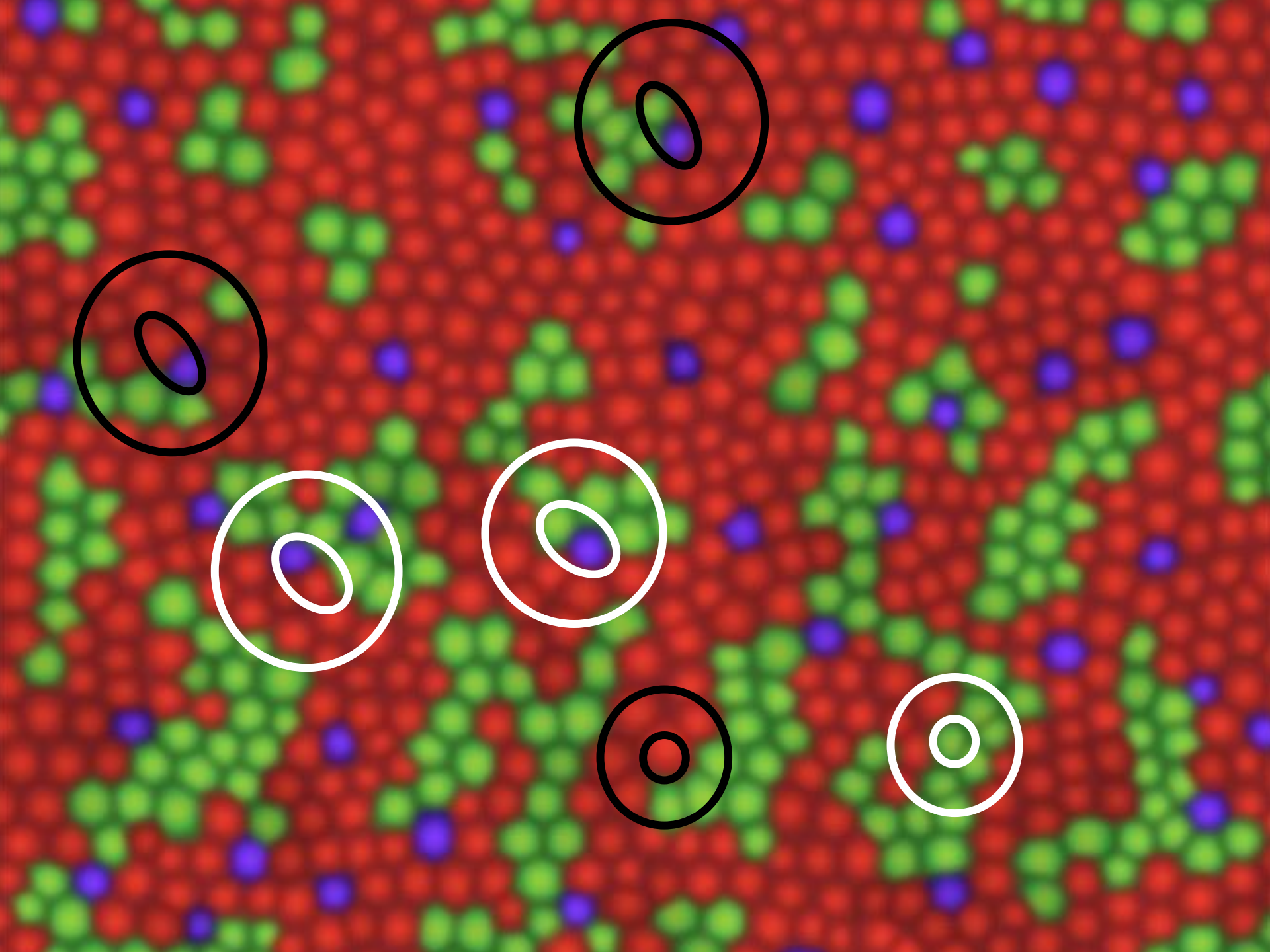
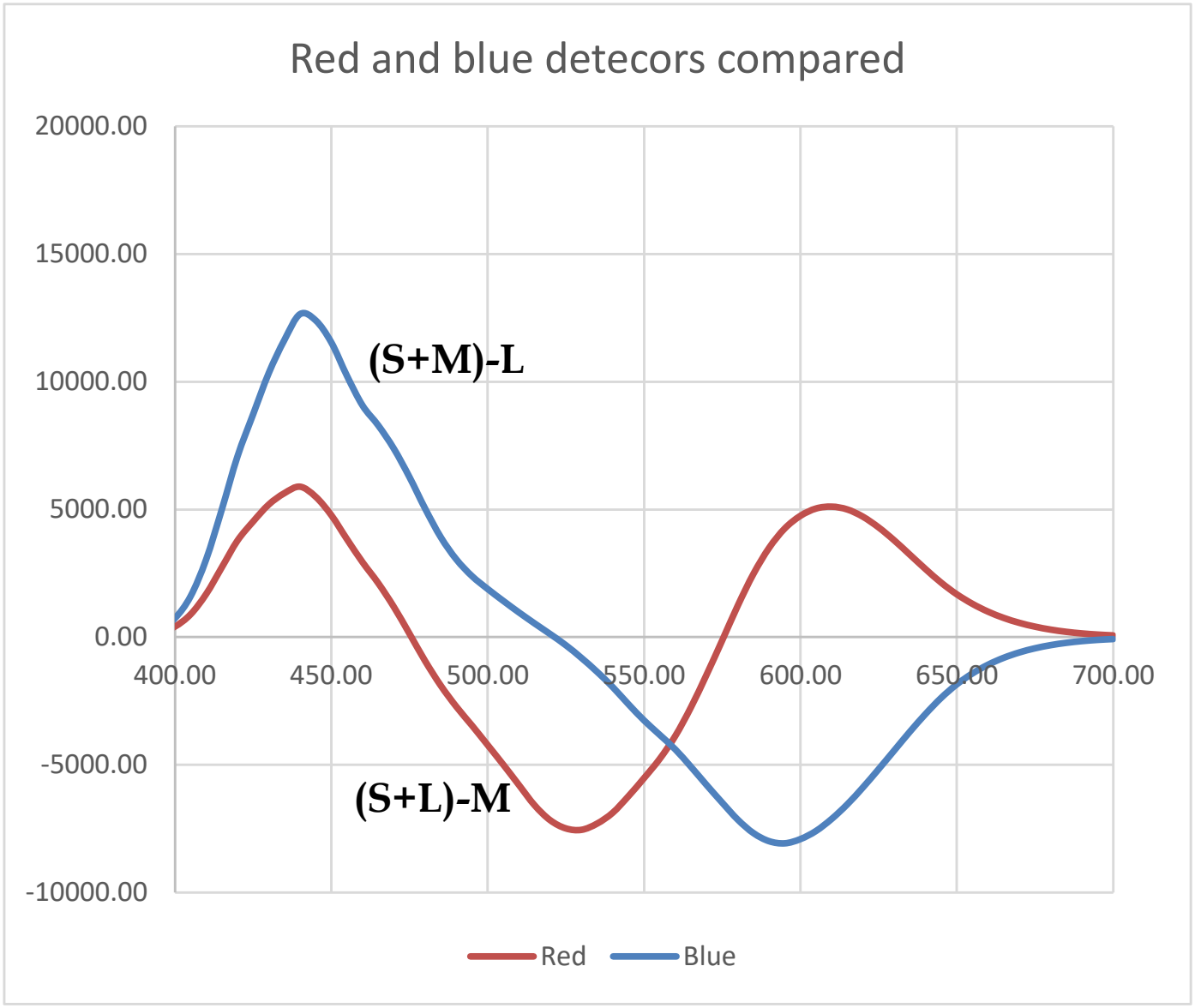
480
470
E
r
g




Red and blue detecors compared
20000.00
15000.00
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400.00
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550.00
600.00
650.00
700.00
(S+M)-L
(S+L)-M
Red
Blue

The dimensionality of color vision in carriers of anomalous trichromacy

Gabriele Jordan — Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, UK

Samir S. Deeb — Departments of Medicine and Genome Sciences, University of Washington, Seattle, USA

Jenny M. Bosten — Department of Experimental Psychology, University of Cambridge, Cambridge, UK

J. D. Mollon — Department of Experimental Psychology, University of Cambridge, Cambridge, UK

Some 12% of women are carriers of the mild, X-linked forms of color vision deficiencies called "anomalous trichromacy." Owing to random X chromosome inactivation, their retinae must contain four classes of cone rather than the normal three; and it has previously been speculated that these female carriers might be tetrachromatic, capable of discriminating spectral stimuli that are indistinguishable to the normal trichromat. However, the existing evidence is sparse and inconclusive. Here, we address the question using (a) a forced-choice version of the Rayleigh test, (b) a test using multidimensional scaling to reveal directly the dimensionality of the participants' color space, and (c) molecular genetic analyses to estimate the X-linked cone peak sensitivities of a selected sample of strong candidates for tetrachromacy. Our results suggest that most carriers of color anomaly do not exhibit four-dimensional color vision, and so we believe that anomalous trichromacy is unlikely to be maintained by an advantage to the carriers in discriminating colors. However, 1 of 24 obligate carriers of deuteranomaly exhibited tetrachromatic behavior on all our tests; this participant has three well-separated cone photopigments in the long-wave spectral region in addition to her short-wave cone. We assess the likelihood that behavioral tetrachromacy exists in the human population.

A 64 year-old woman was referred to us who claims to have congenital red-green color blindness in one eye and normal color vision in the other

Summary

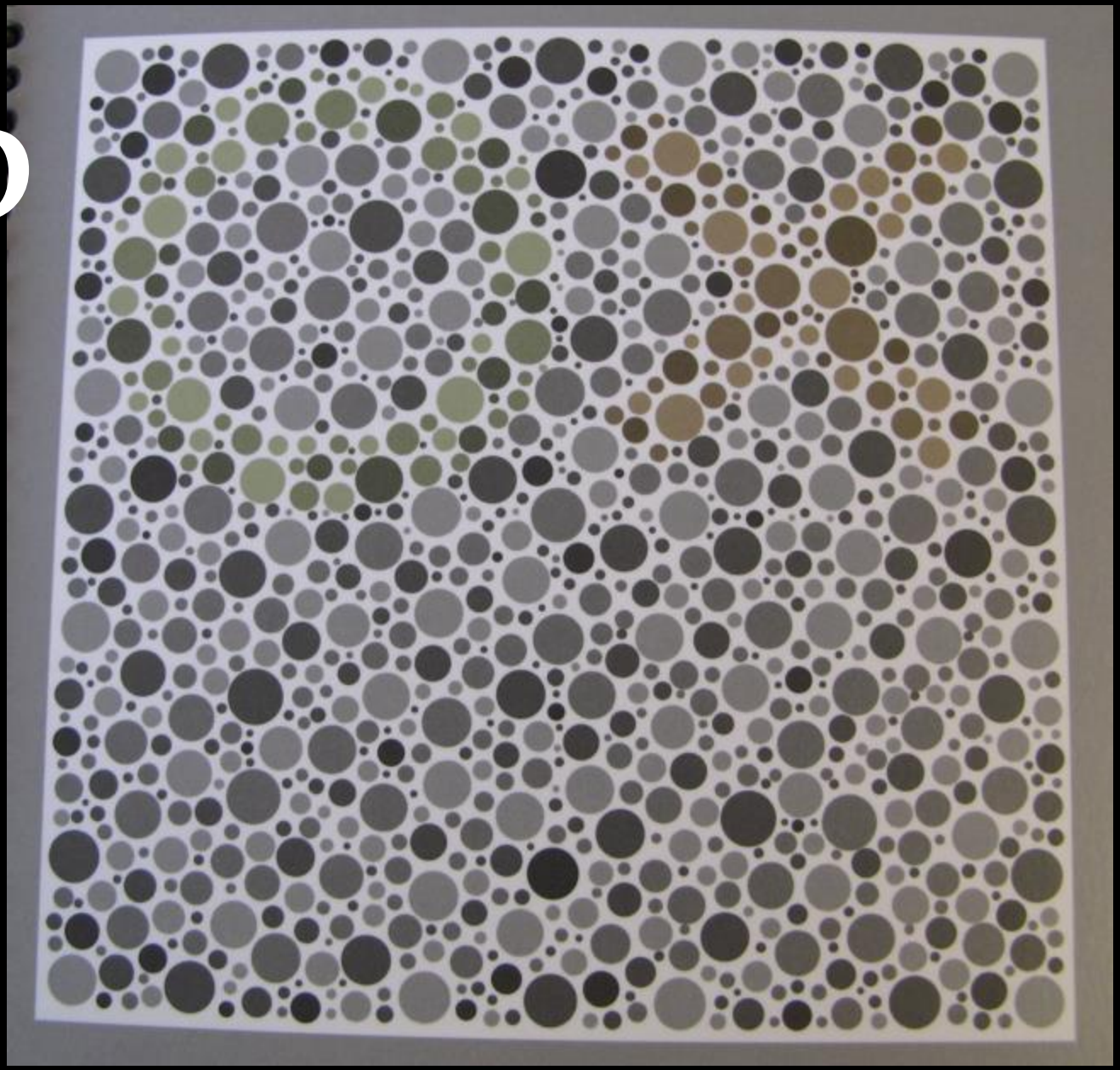
In 303 mothers of colour-blind sons, both eyes were tested with pseudoisochromatic plates and with the anomaloscope. Two hundred thirty healthy normal and 56 colour-blind males served as controls. In good agreement with the expected proportion of homozygotes in our sample, 17 colour-blind mothers were detected. Eight others had difficulty reading pseudoisochromatic plates and were conspicuous at the anomaloscope. In these, both eyes were affected to a very similar, moderate degree. Monocular disturbances of colour vision were not observed in the entire series. Our data suggest that (1) in most (if not all) of the carriers with colour vision impairment, there is no complete lack of normal retina cones, and (2) the proportion of defective retina cones is remarkably similar in both eyes of individual heterozygotes.

The latter observation may indicate that at the time of X-differentiation there is a common primordial cell pool for both retinas.

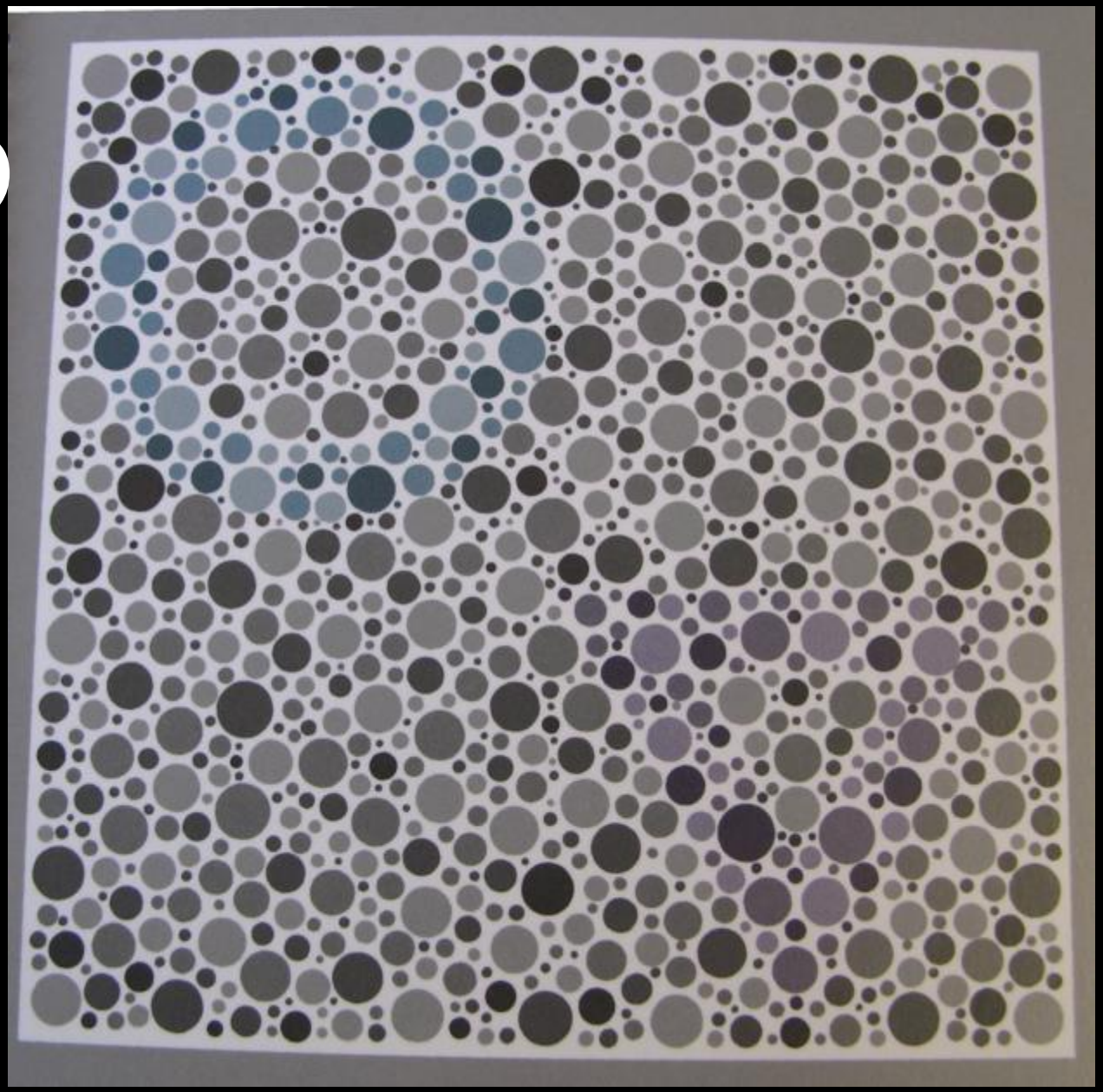
OD	OS
20/25 F E L O P Z D	20/25 F E L O P Z D
20/20 D E F P O T - C	20/20 D - - P O T - C

Uncorrected Visual Acuity

OD
OS



OD
OS



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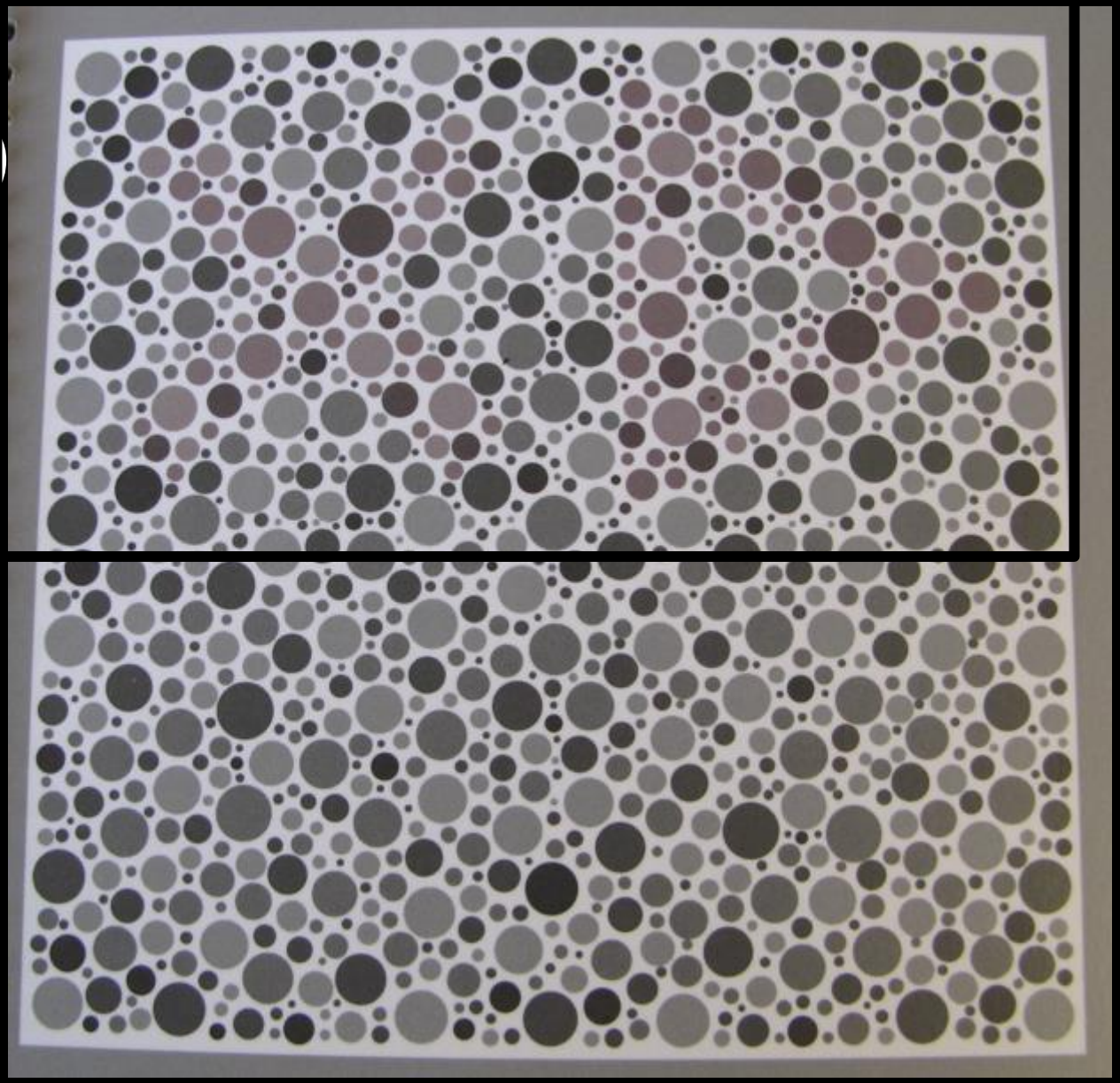

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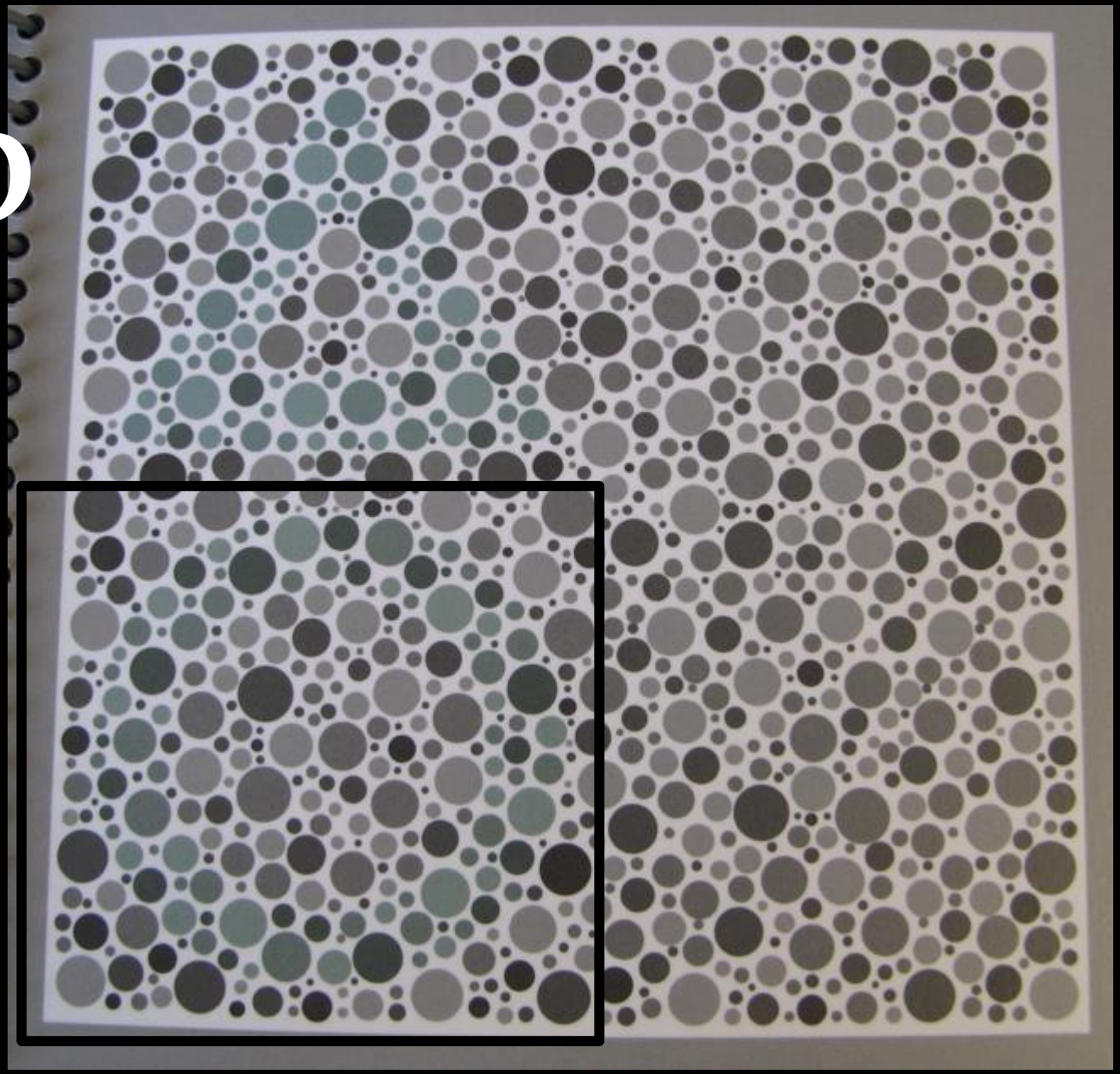

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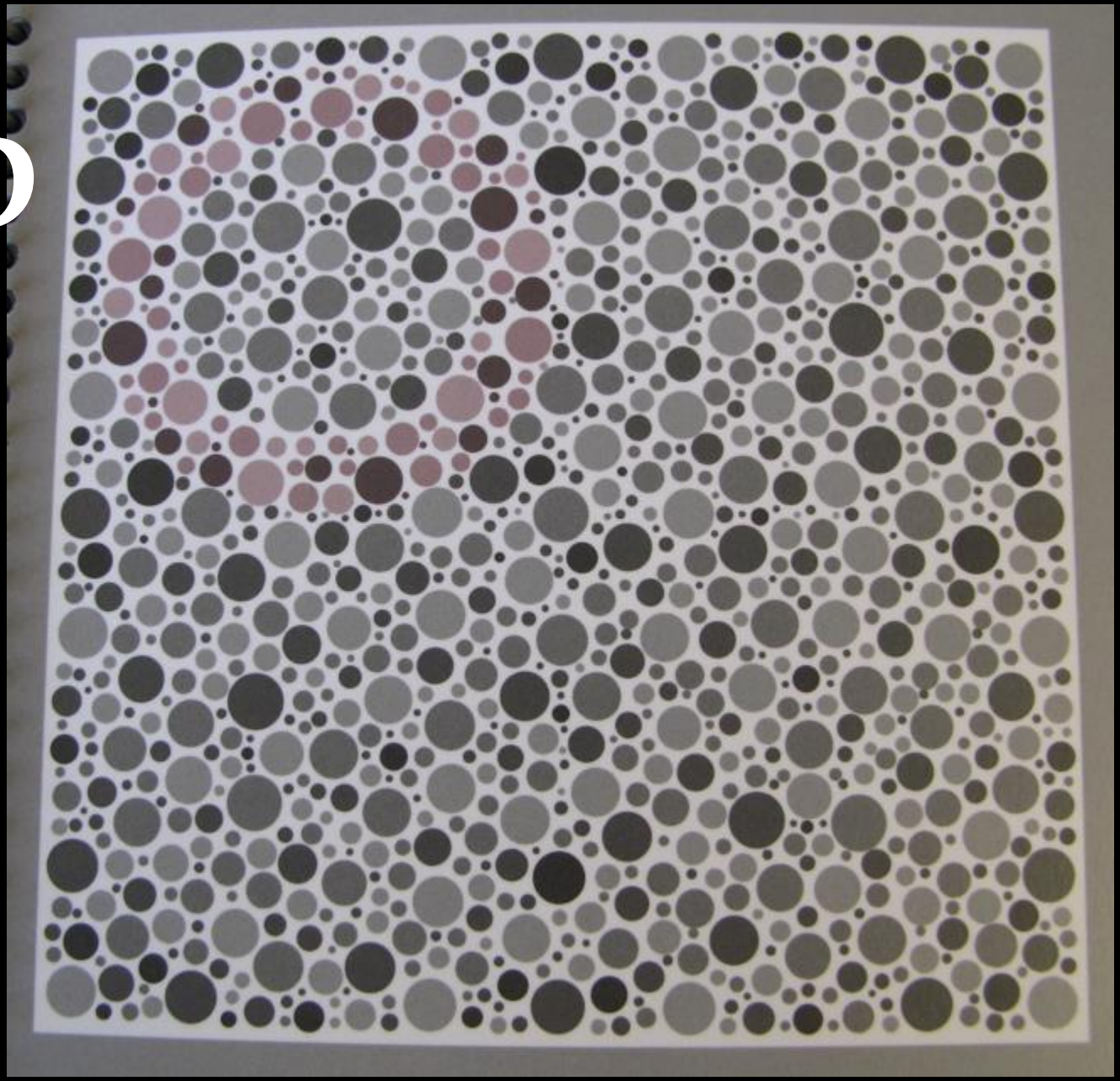

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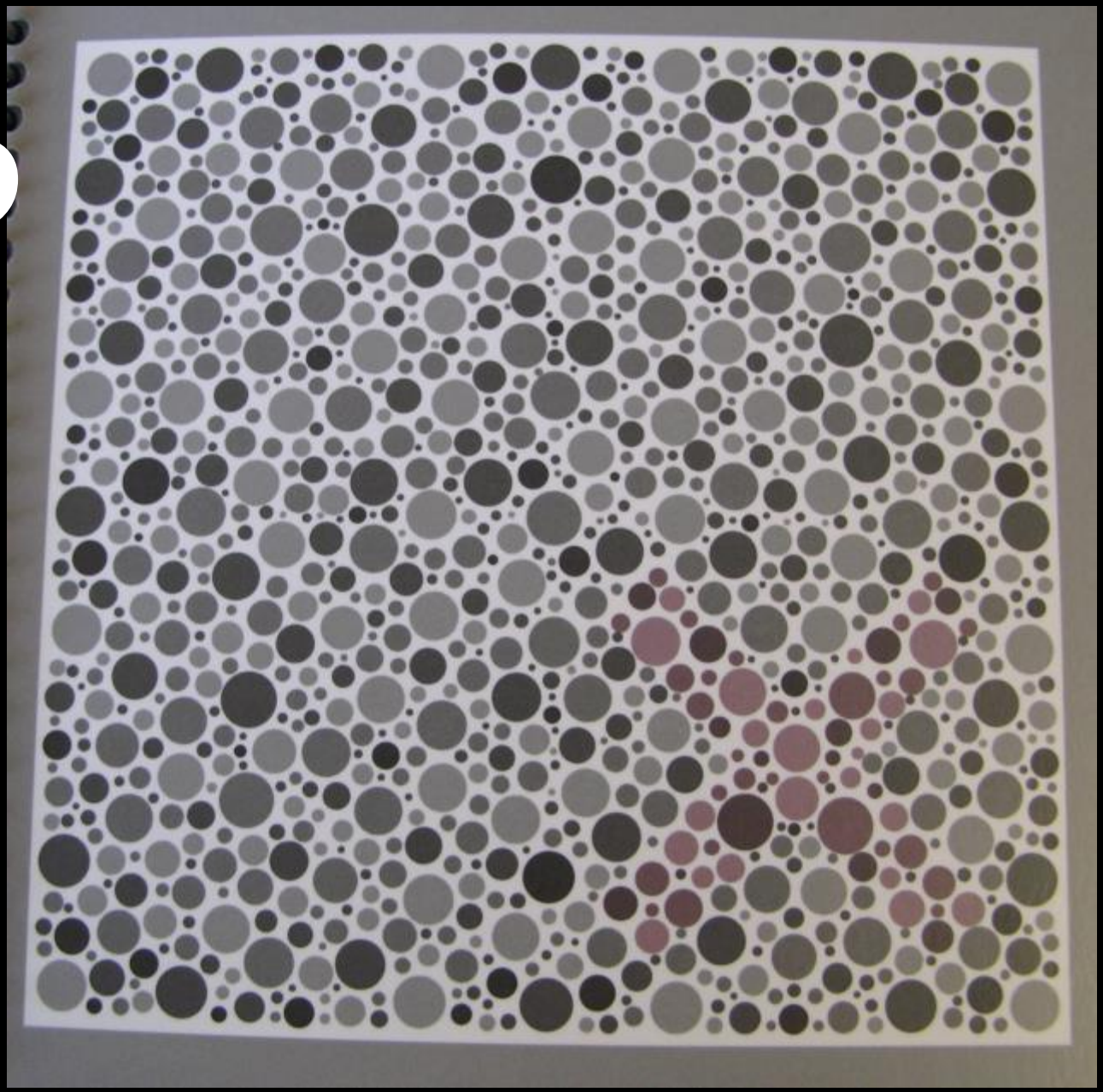

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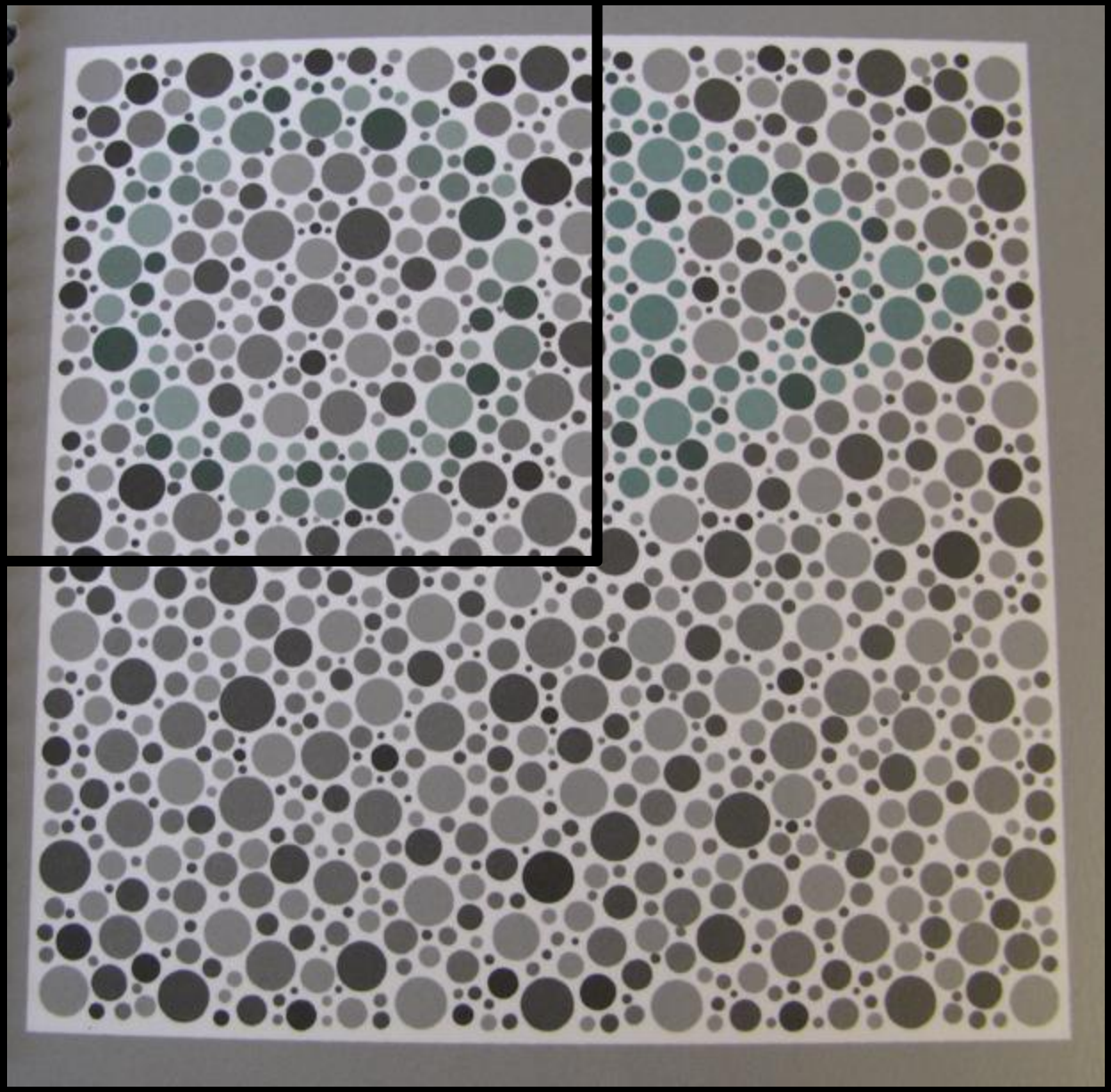
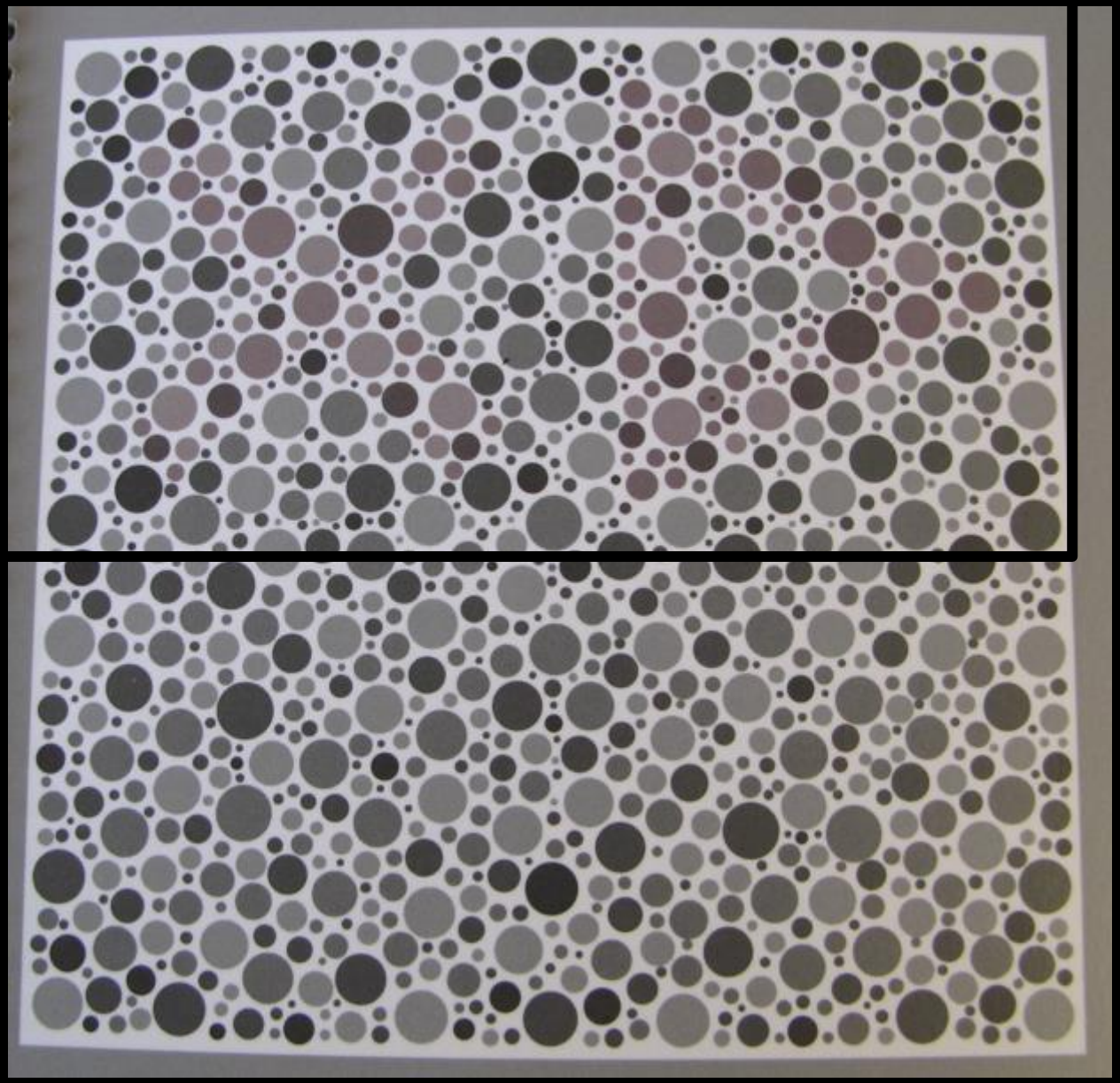


OS



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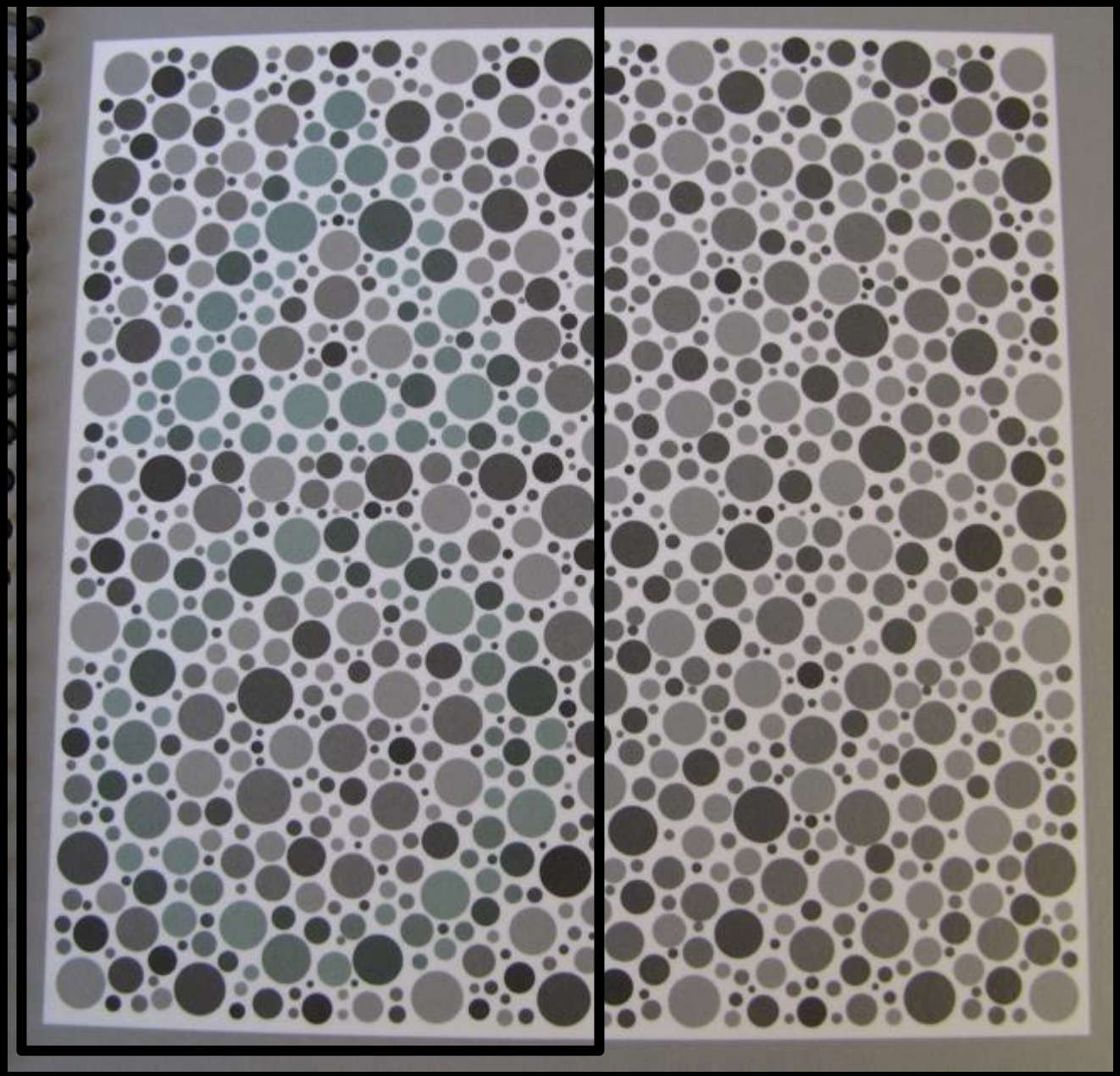

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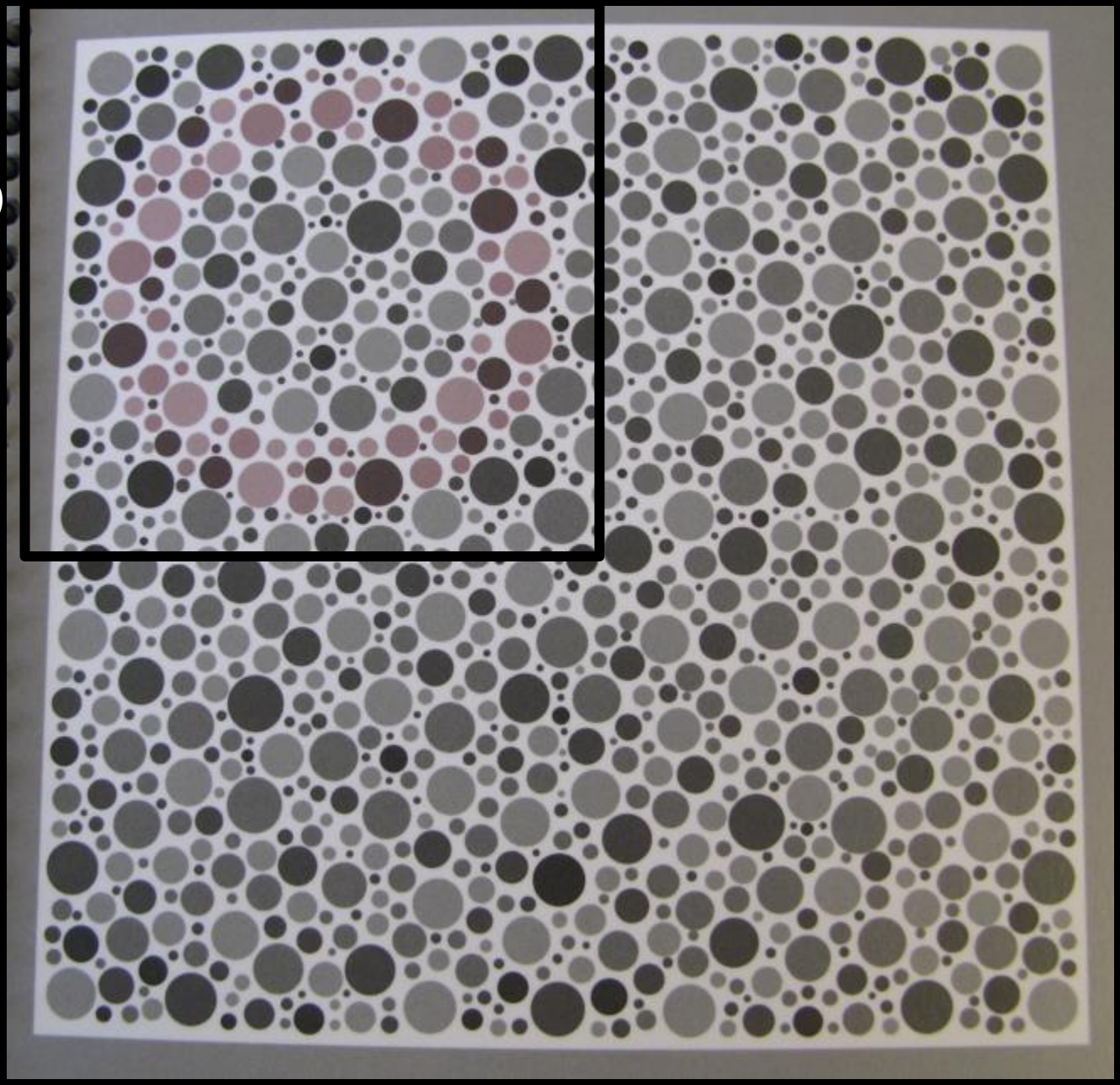

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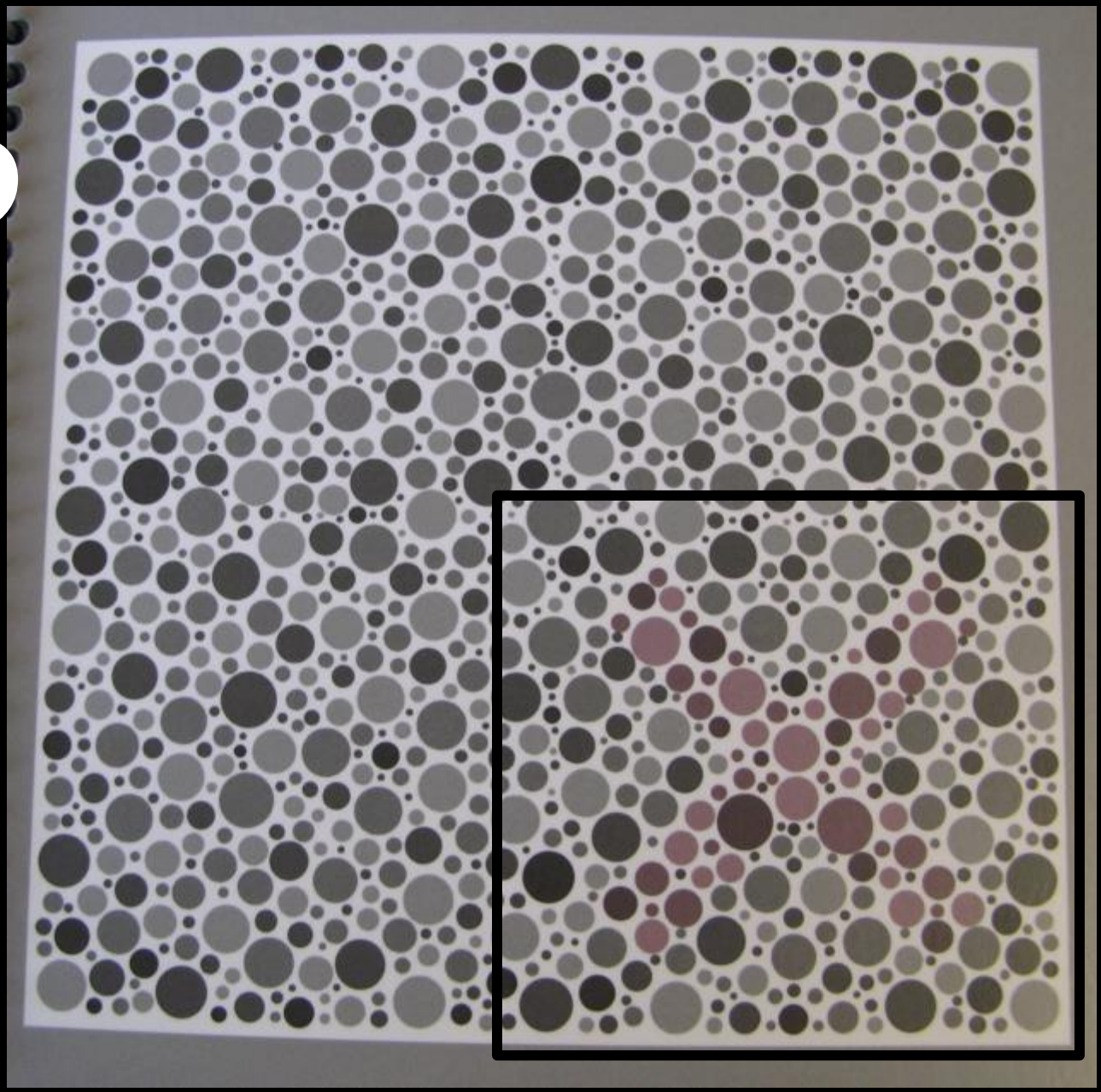

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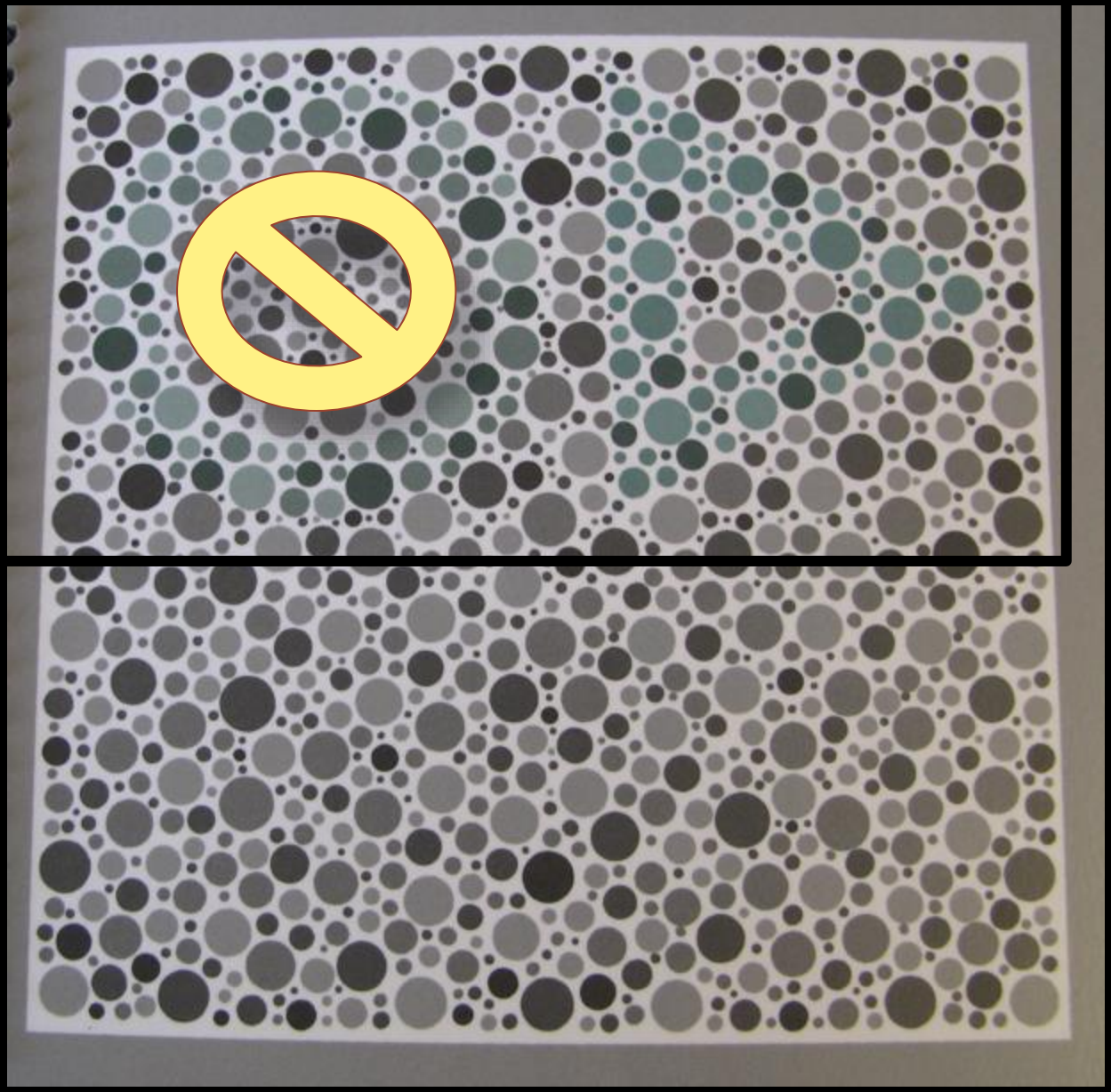
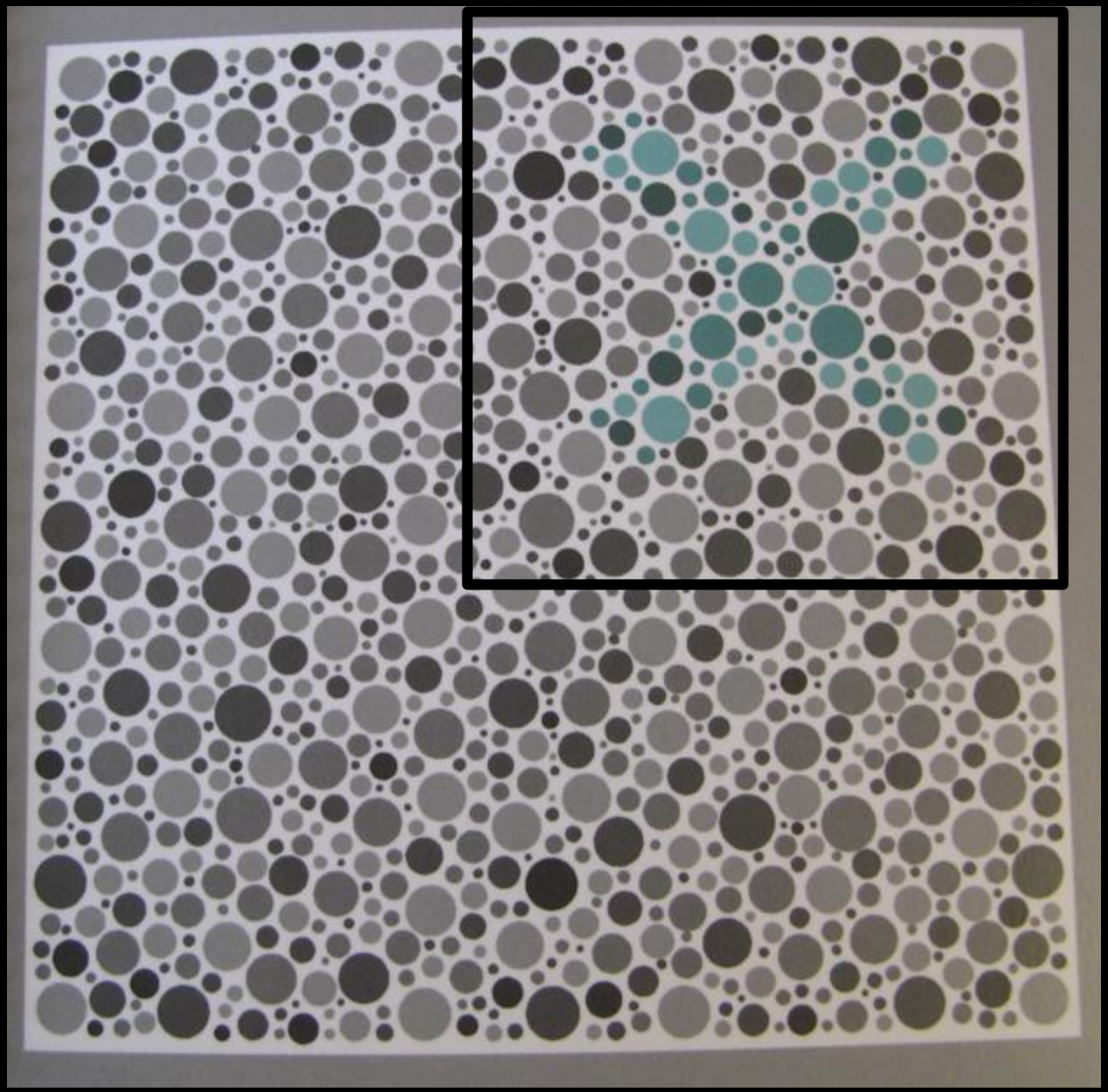


Last error With OD

OS



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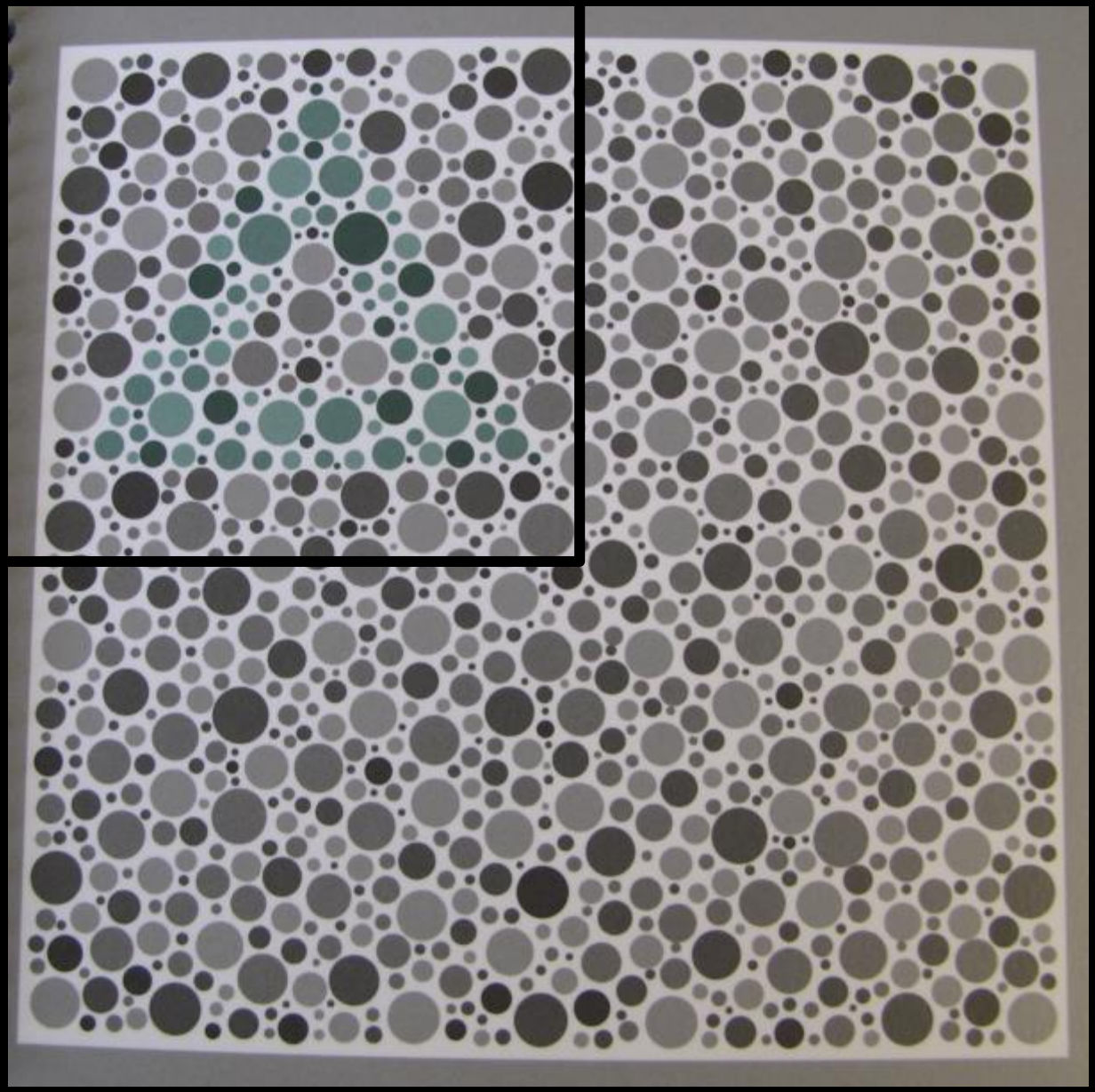

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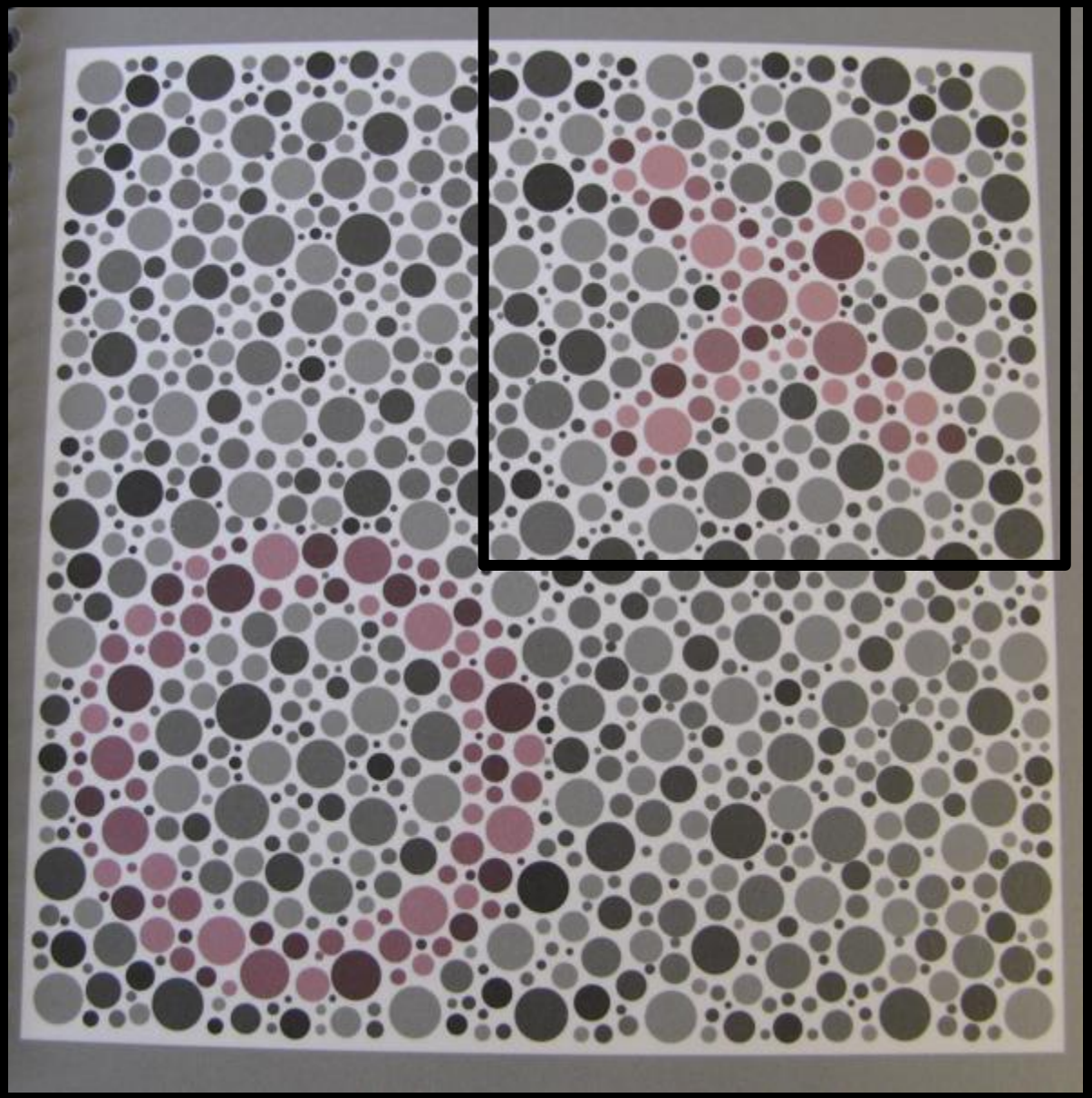

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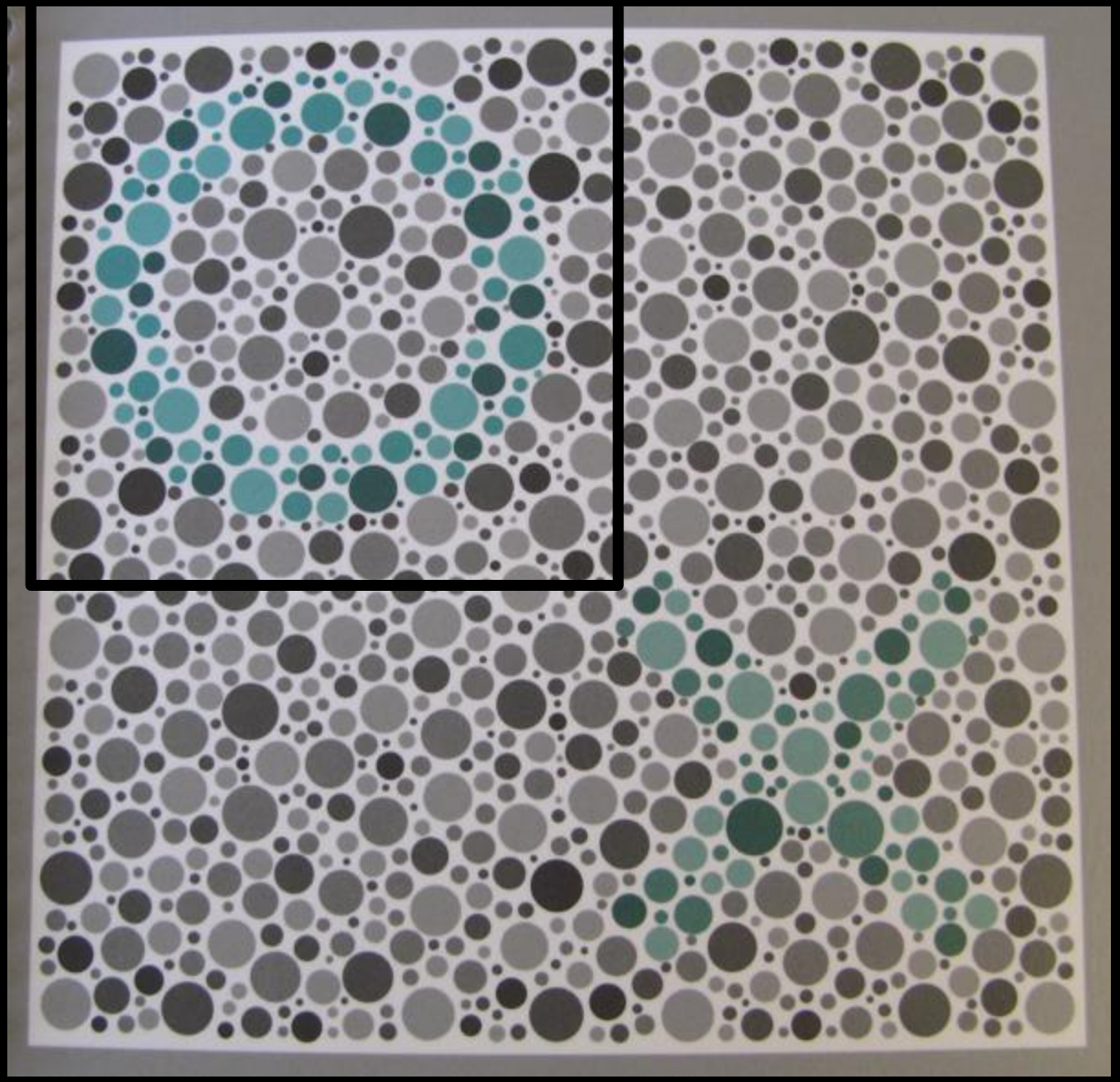

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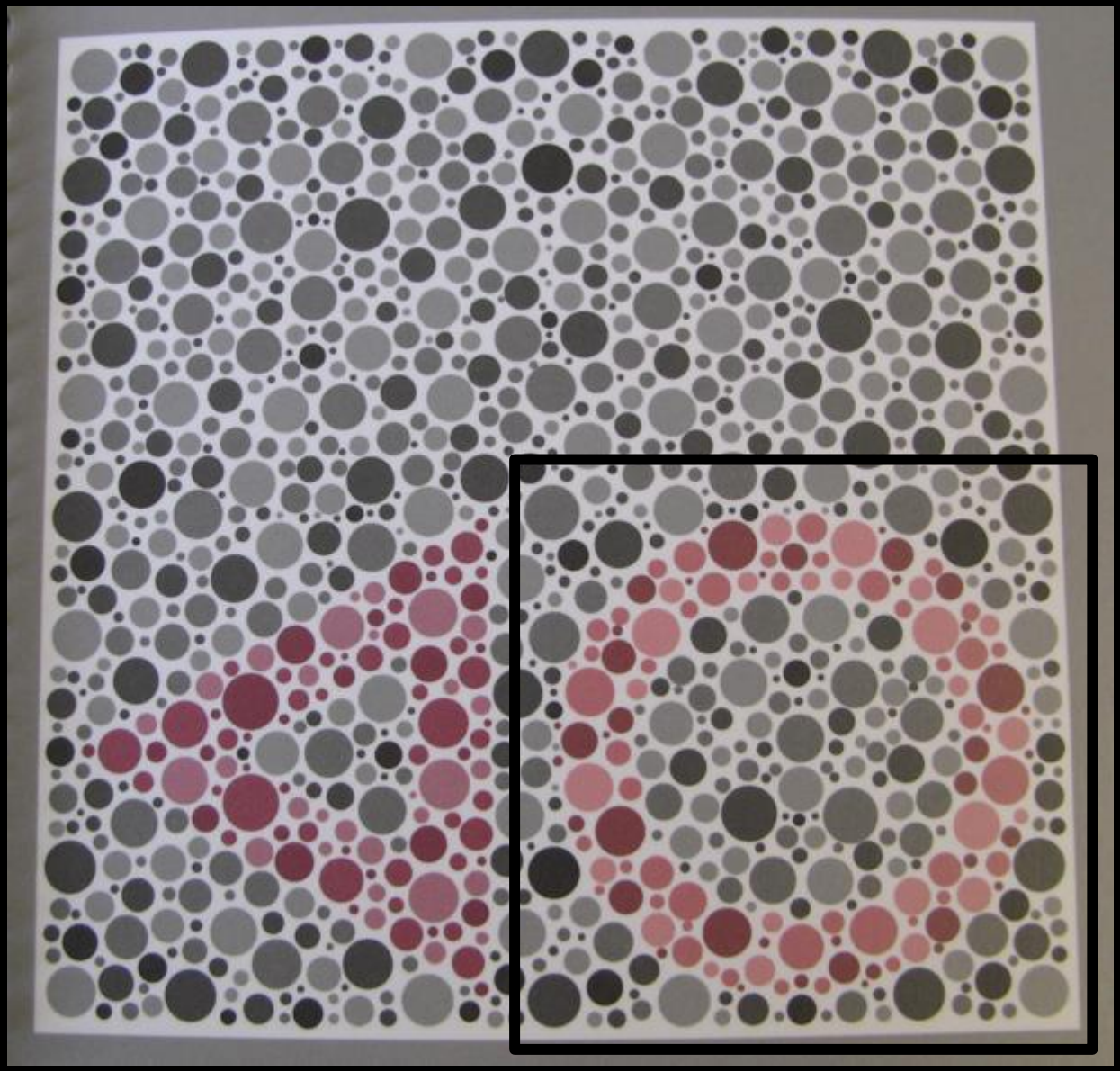

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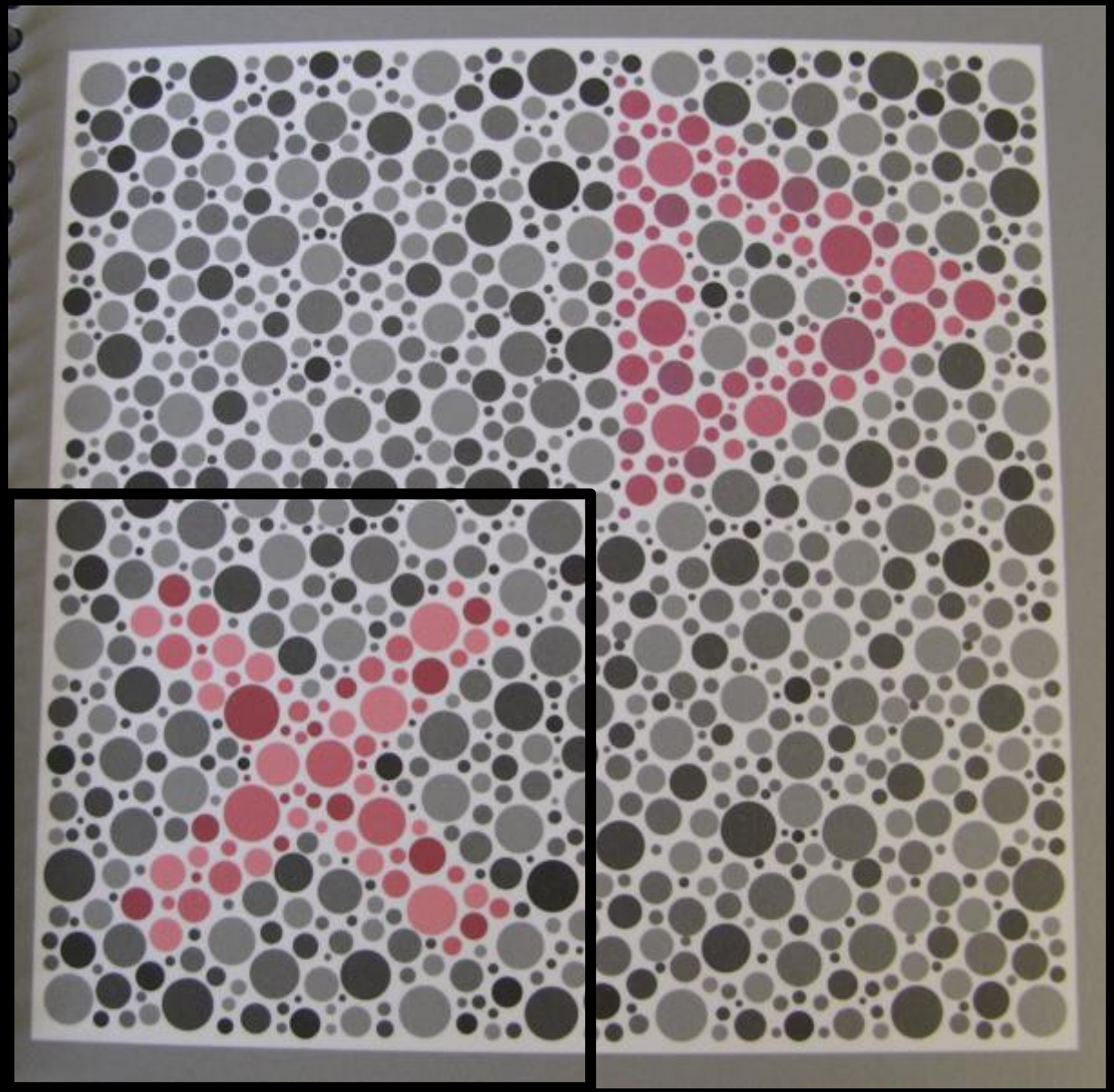
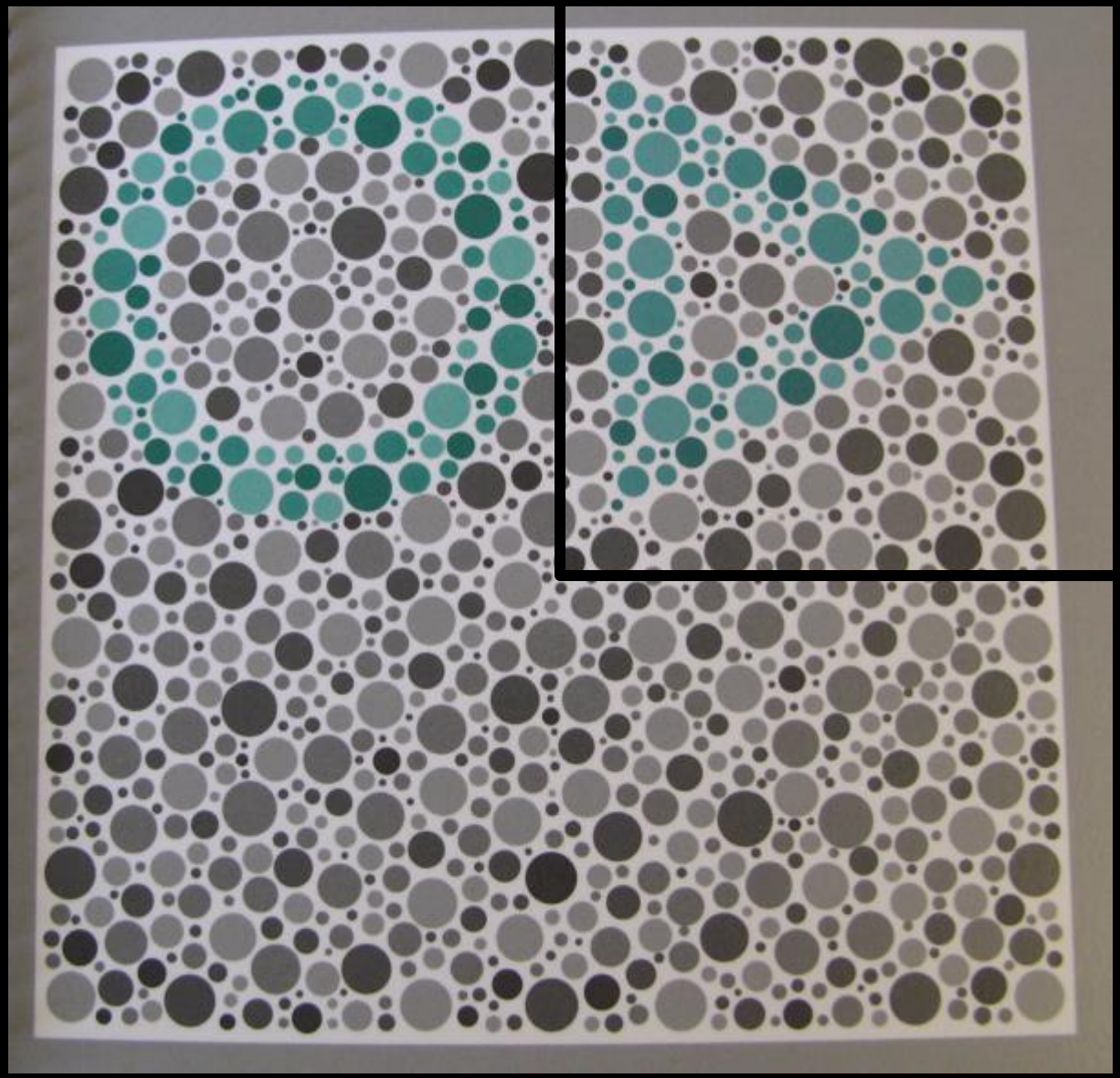


OS



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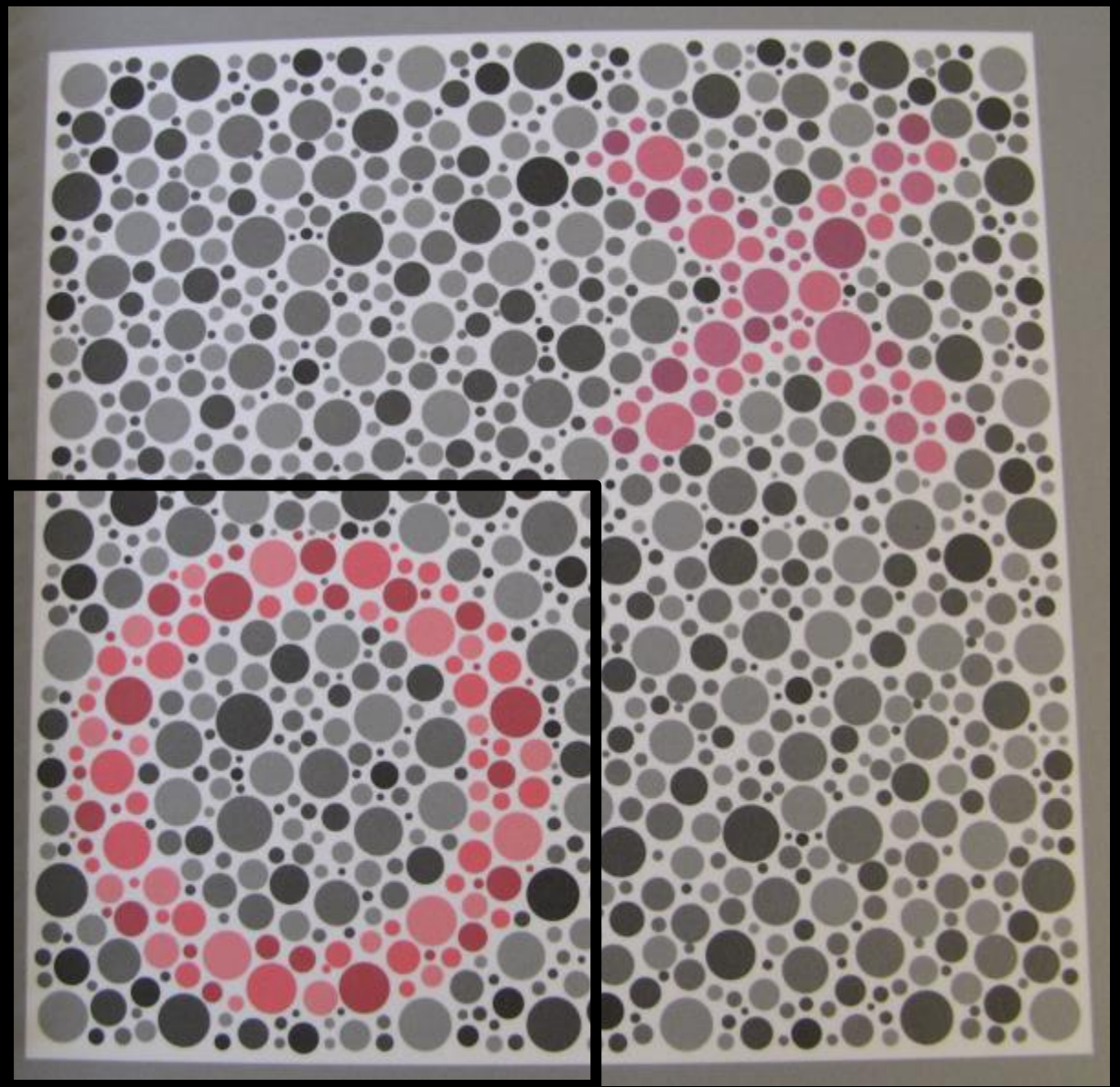

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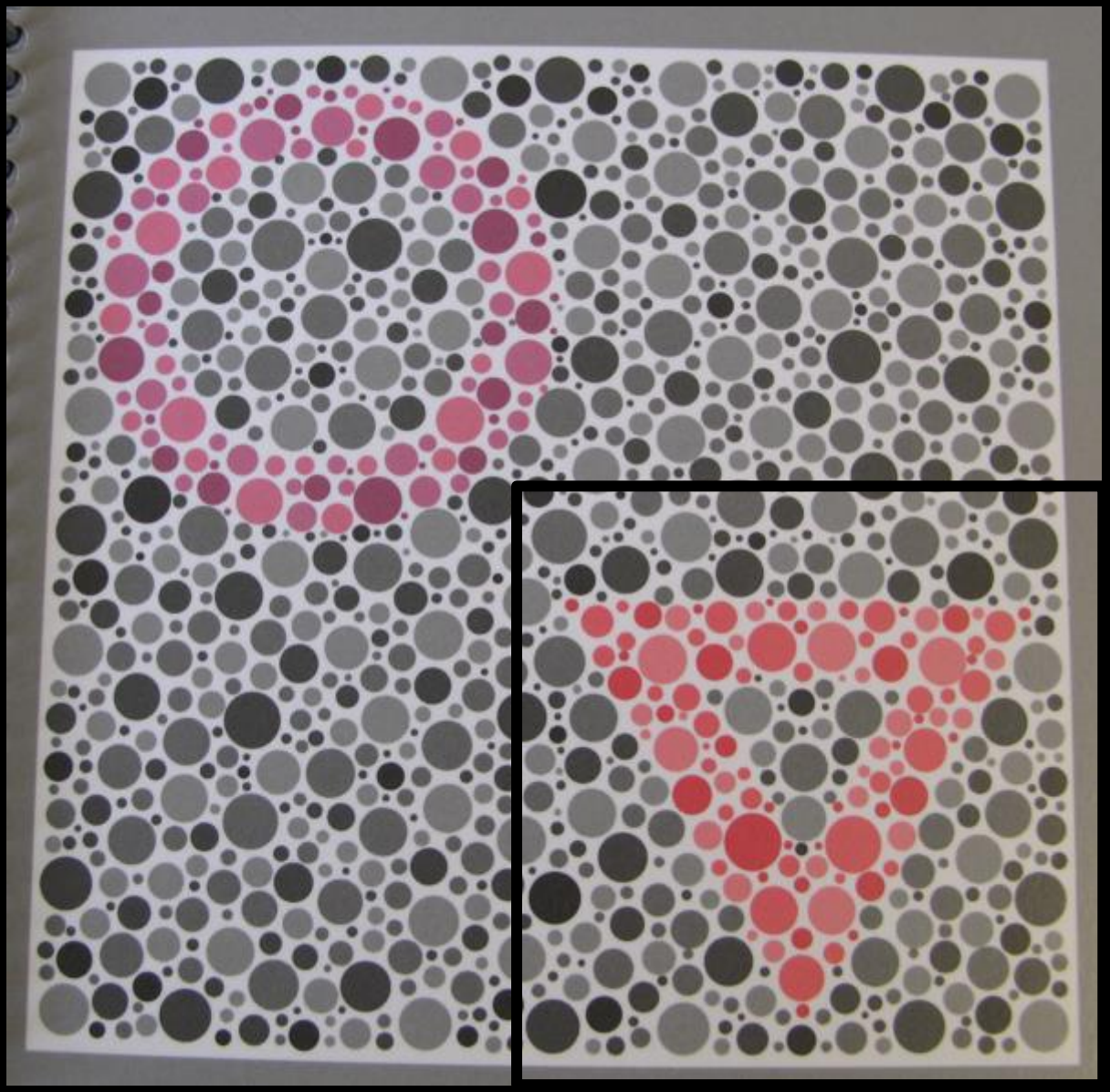


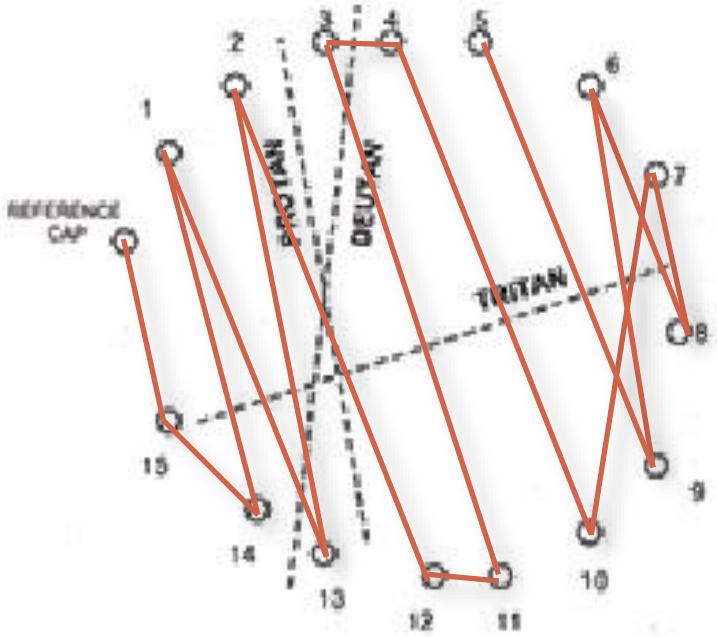
	OD Normal Sees	OS Protan Sees	Deutan Sees	
—	X -	- -	X -	Mild R – G
—	Δ -	Δ -	- -	
O —	O X	O -	- X	
X —	O X	- X	O -	
Δ —	Δ O	Δ -	- O	Medium R – G
O —	O Δ	O -	- Δ	
Δ —	X Δ	- Δ	X -	
X —	O X	- X	O -	Strong R - G
O —	O Δ	O -	- Δ	

OS

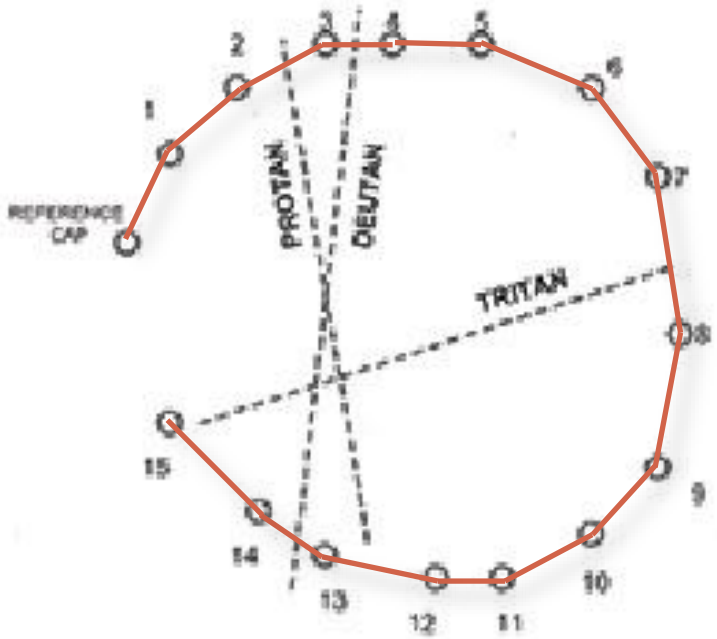
OD

Score Sheet Template for 15 Disc Color Vision Test

OS

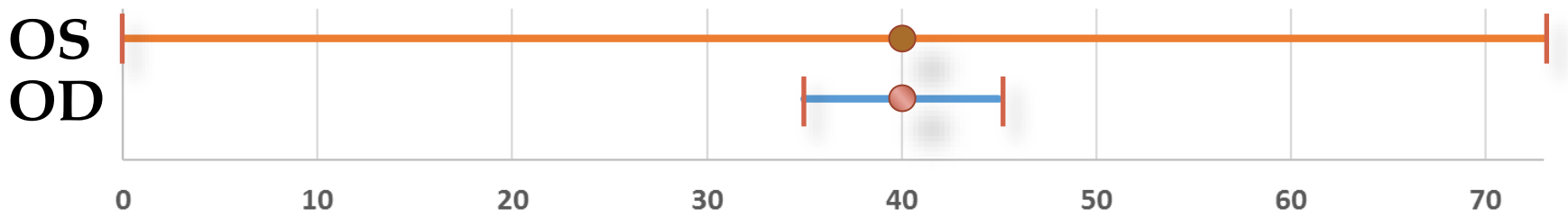


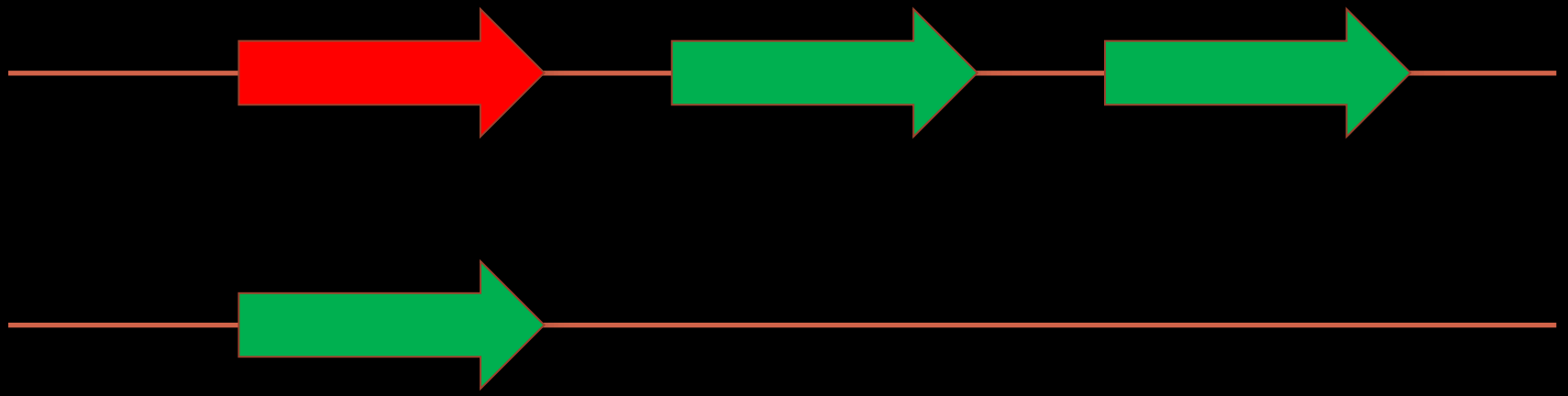
OD

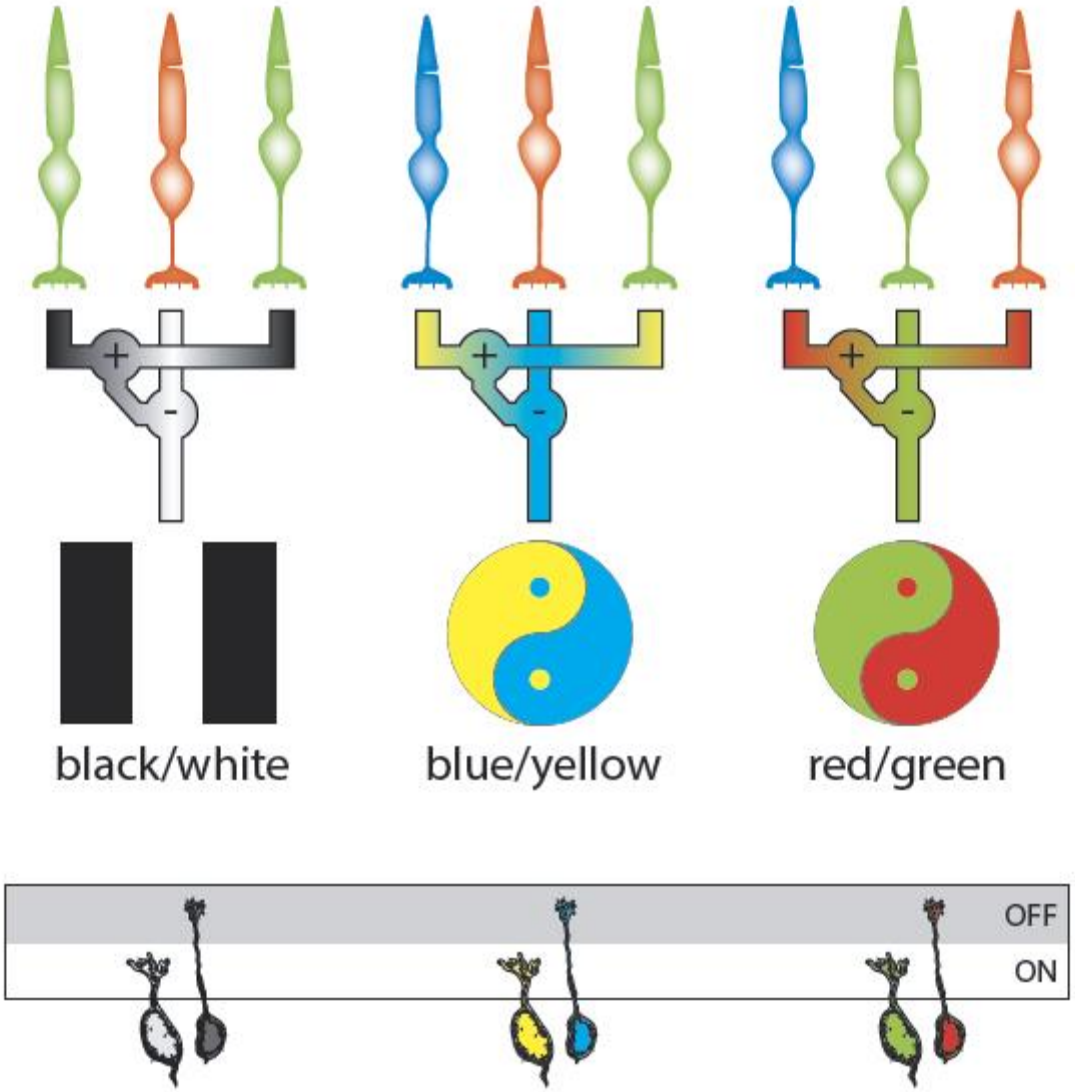


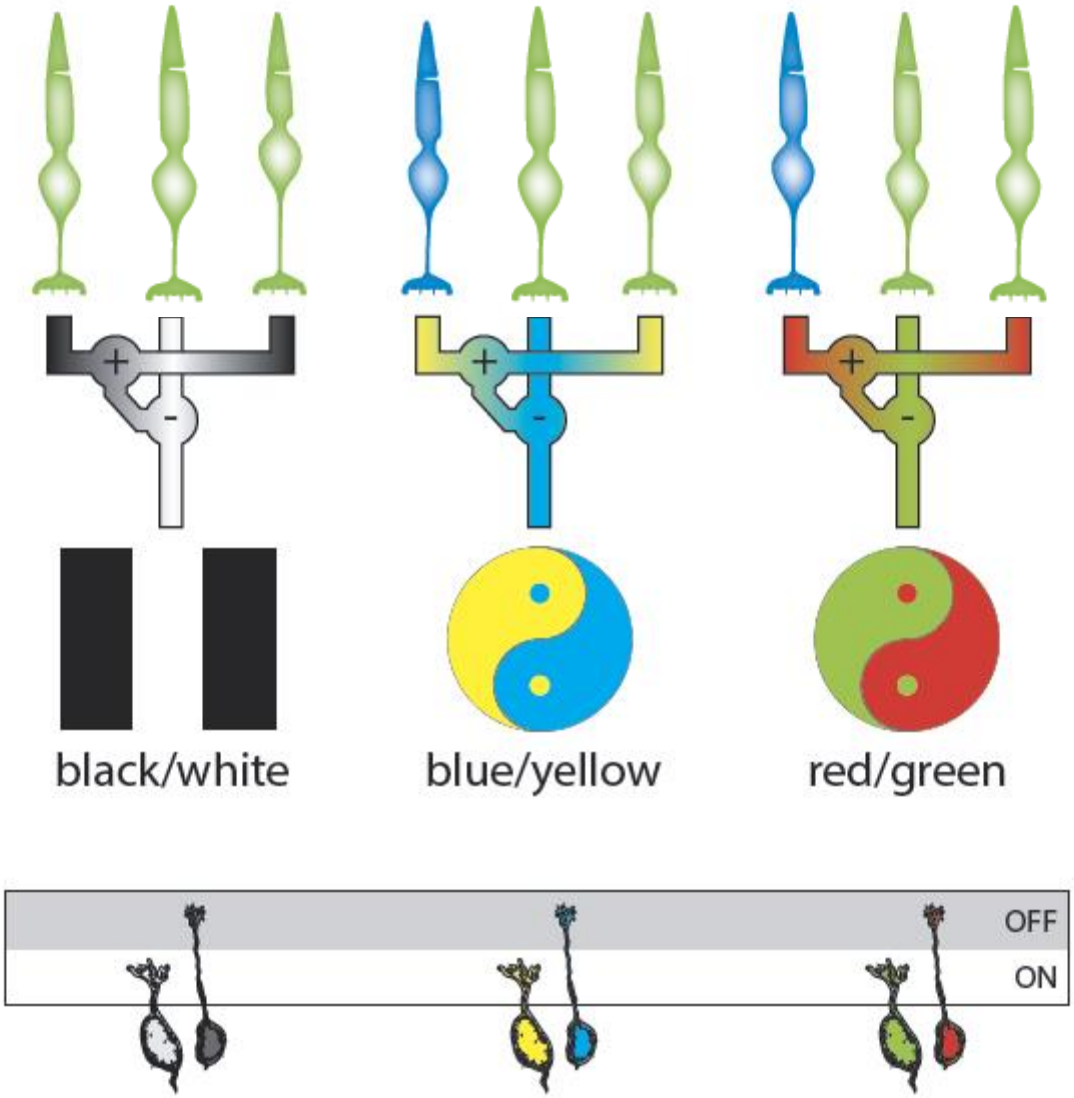
Richmond Products
4400 Silver Ave. SE Albuquerque NM 87108

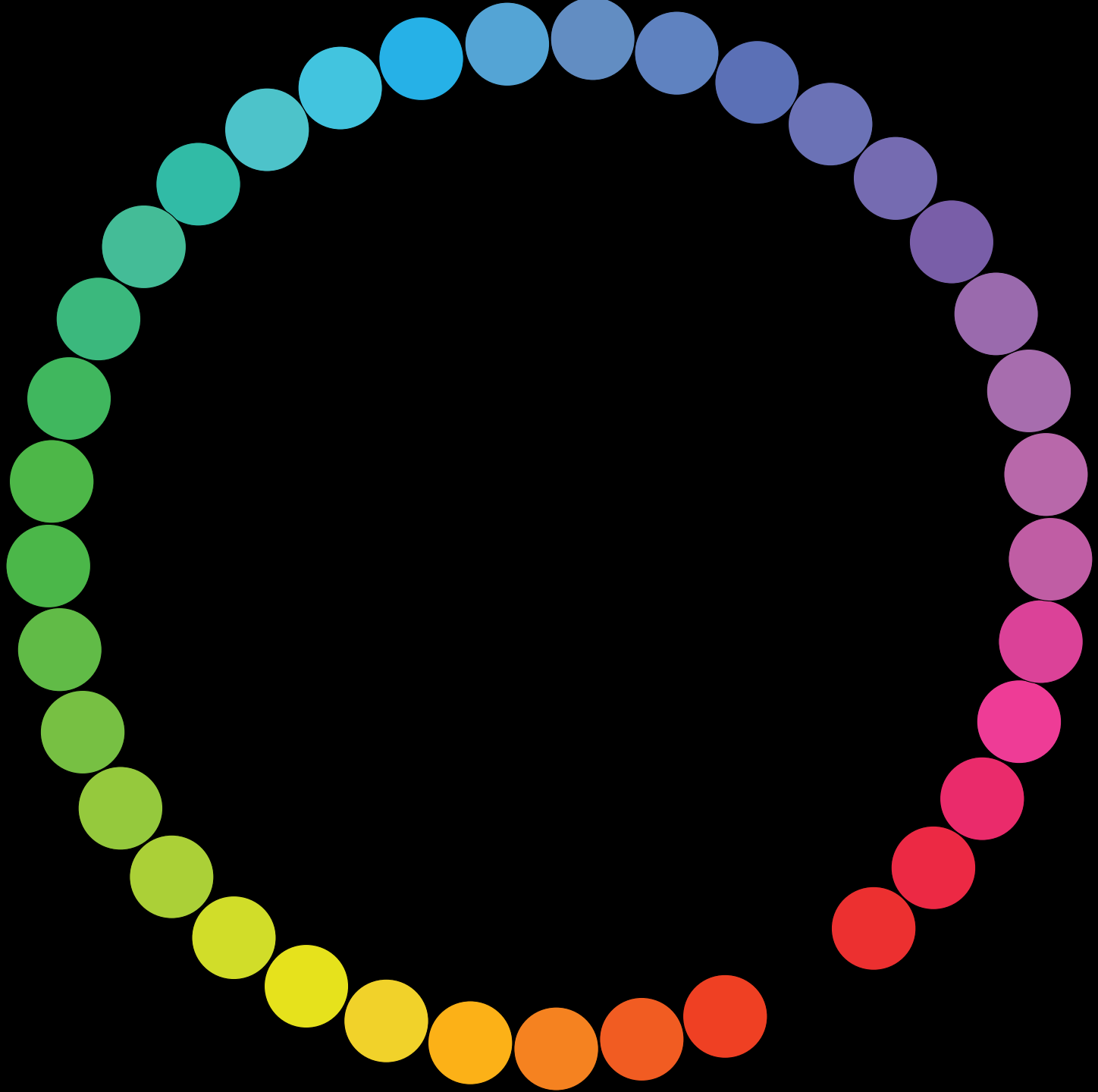
Richmond Part Number 4426


OS
OD
0
10
20
30
40
50
60
70




+
-
black/white
blue/yellow
red/green
OFF
ON


+
-
black/white
blue/yellow
red/green
OFF
ON



Grey

Blue

Yellow

Blue

Yellow

Blue

Yellow

Blue

Off-white

Blue

Light-blue

Yellow

Blue

Yellow

Blue

Yellow

Grey

White

Yellow

Blue

Yellow

Yellow

Blue

White

Colorless --light

Yellow

Blue

No color

Yellow

Yellow

Blue

Yellow

Blue-grey

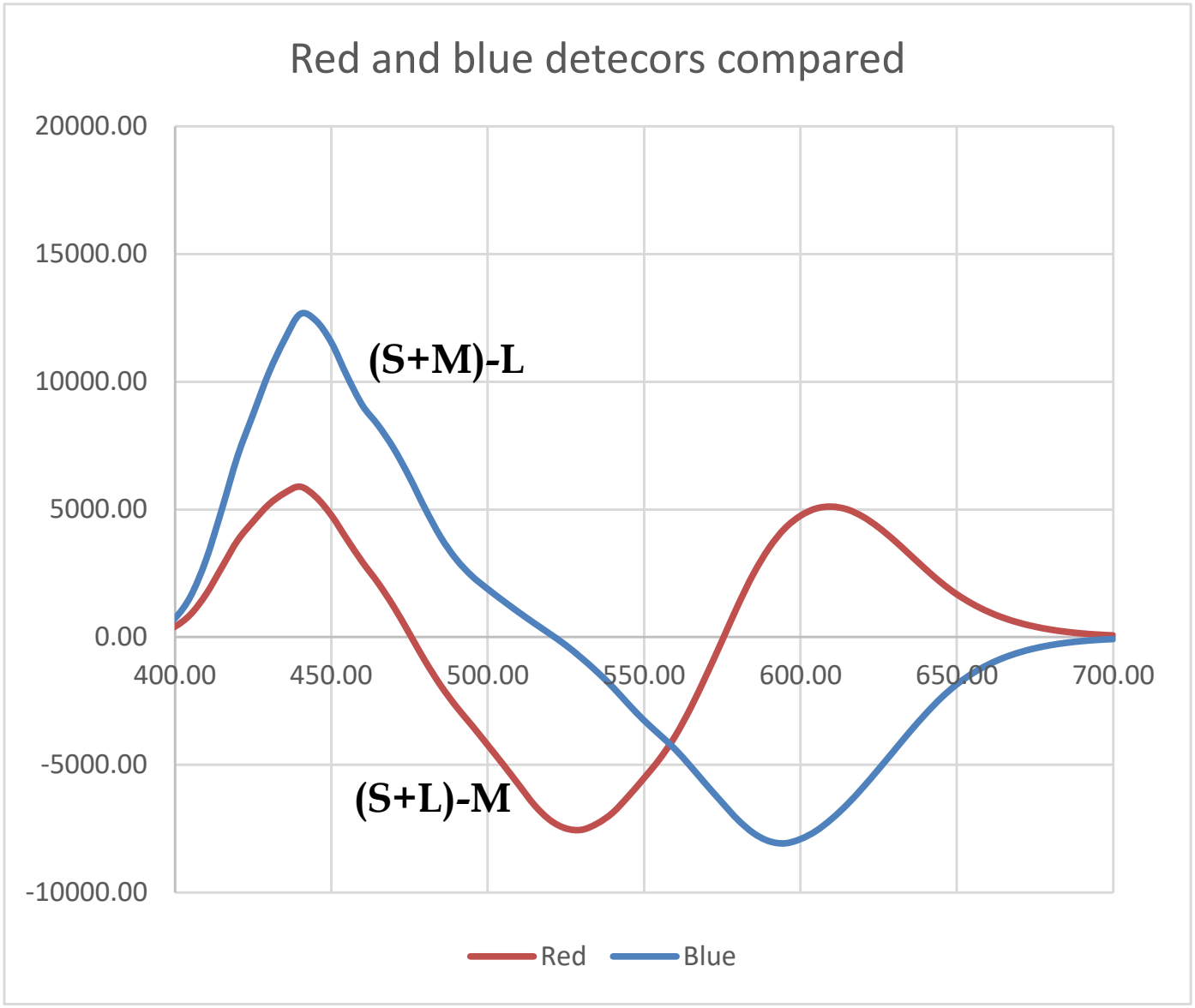
Yellow

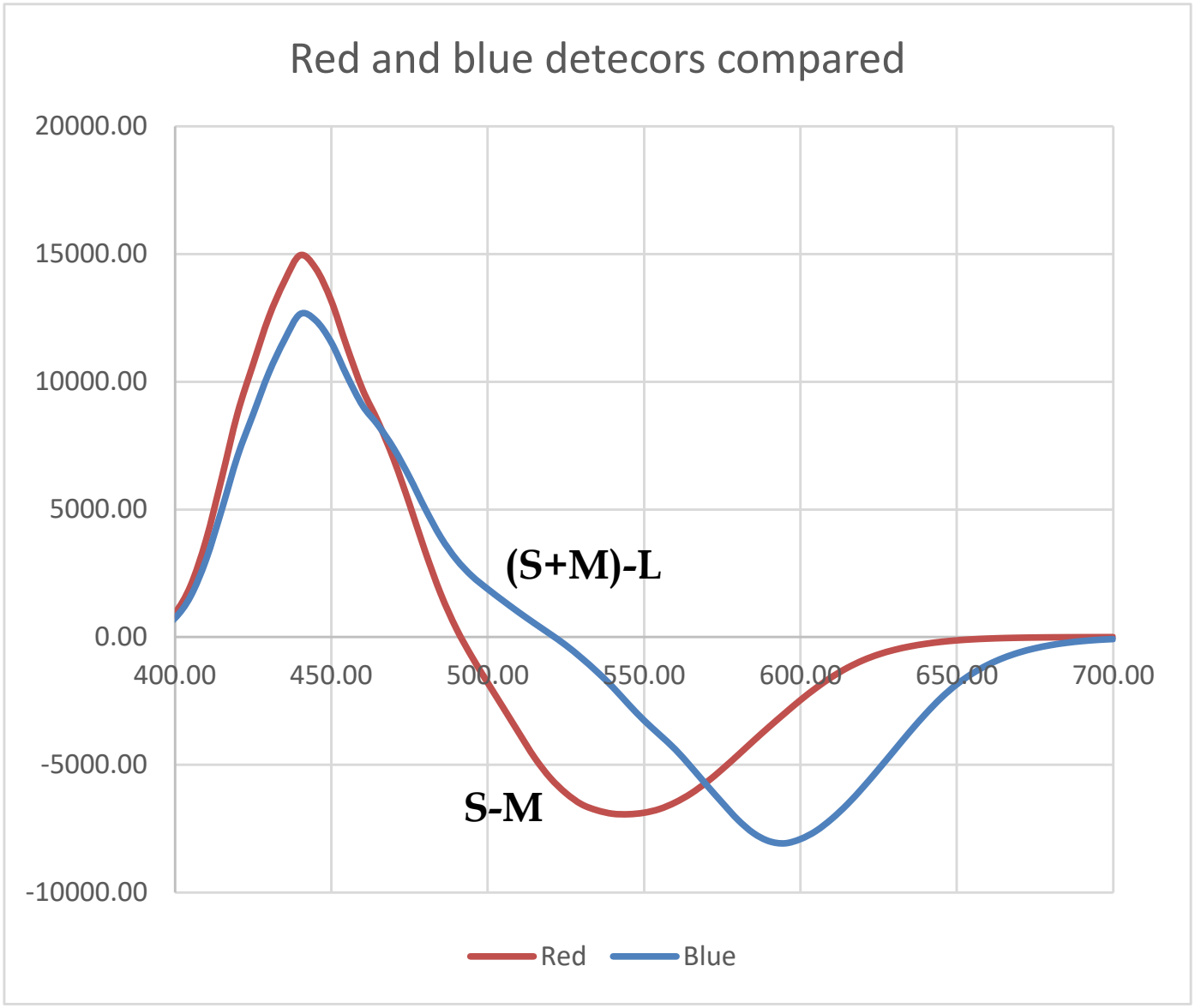
Bright, no-color

White

This is the first case ever, of a person who has been confirmed to have the opsin genes required for both normal color vision and dichromacy who is legitimately color blind in one eye


Crayola®
™


Red and blue detecors compared
20000.00
15000.00
10000.00
5000.00
0.00
-5000.00
-10000.00
400.00
450.00
500.00
550.00
600.00
650.00
700.00
(S+M)-L
(S+L)-M
Red
Blue

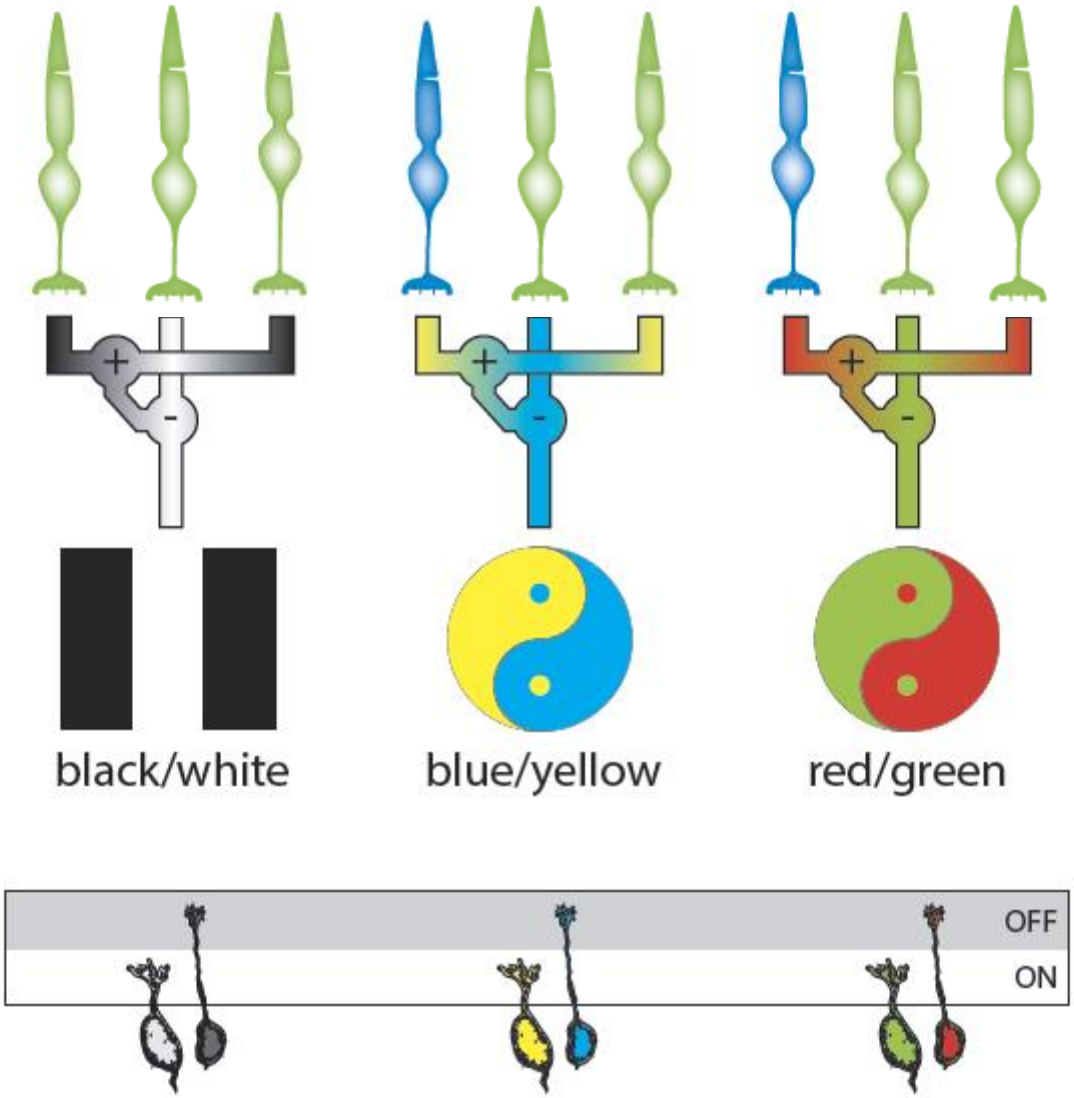

Red and blue detecors compared
20000.00
15000.00
10000.00
5000.00
0.00
-5000.00
-10000.00
400.00
450.00
500.00
550.00
600.00
650.00
700.00
(S+M)-L
S-M
Red
Blue

So how is it that gene therapy can cure color blindness?

We postulate the following hypothesis

Depending on what types of cone submosaics are in the retina, the circuitry automatically sets of a variety cone opponent detectors at the very first synapse.

Over time, with visual experience, the cortex uses correlations among midget ganglion cell inputs to sort them into subclasses with each subclass being responsible for a distinct color percept


+
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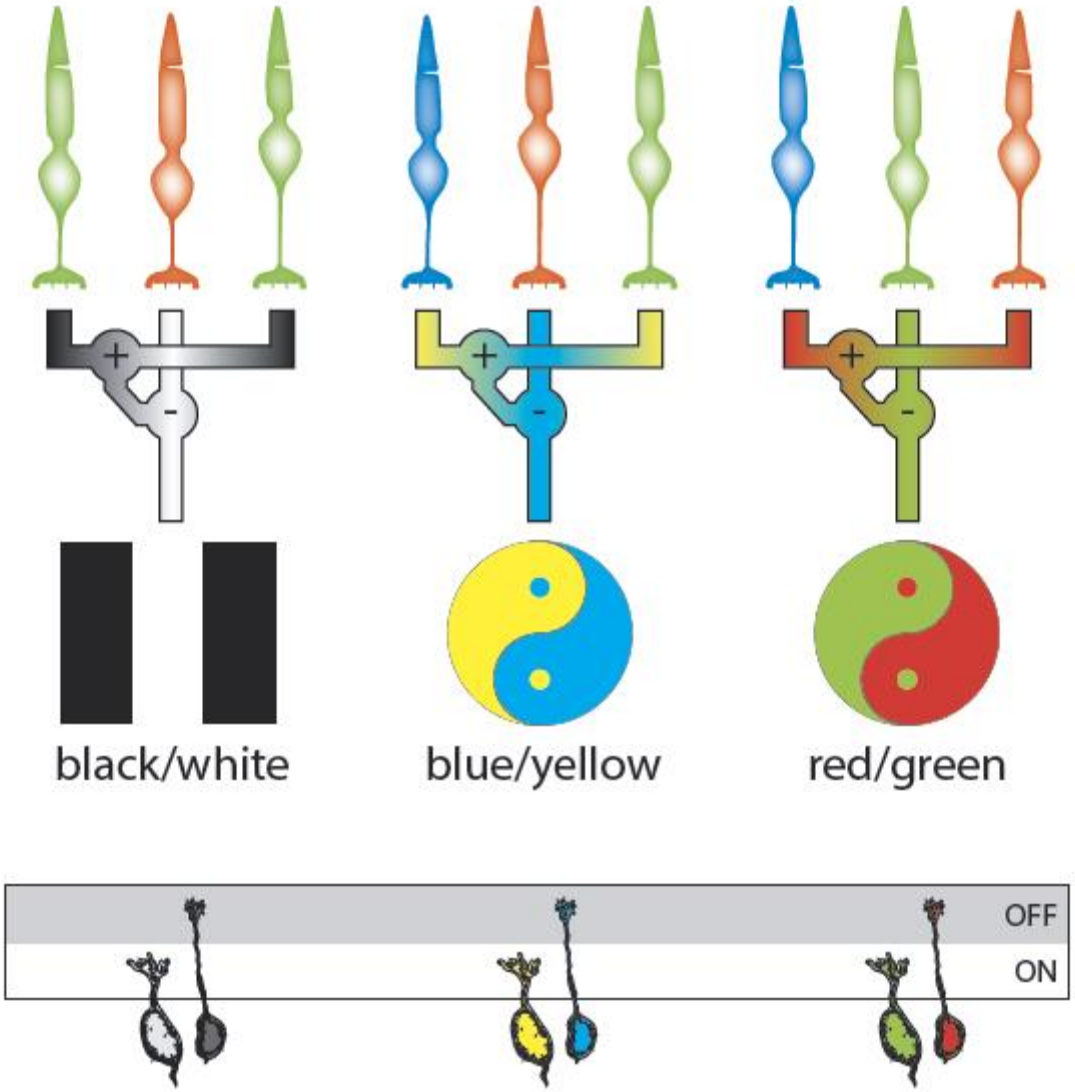
black/white
blue/yellow
red/green
OFF
ON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black/white
blue/yellow
red/green
OFF
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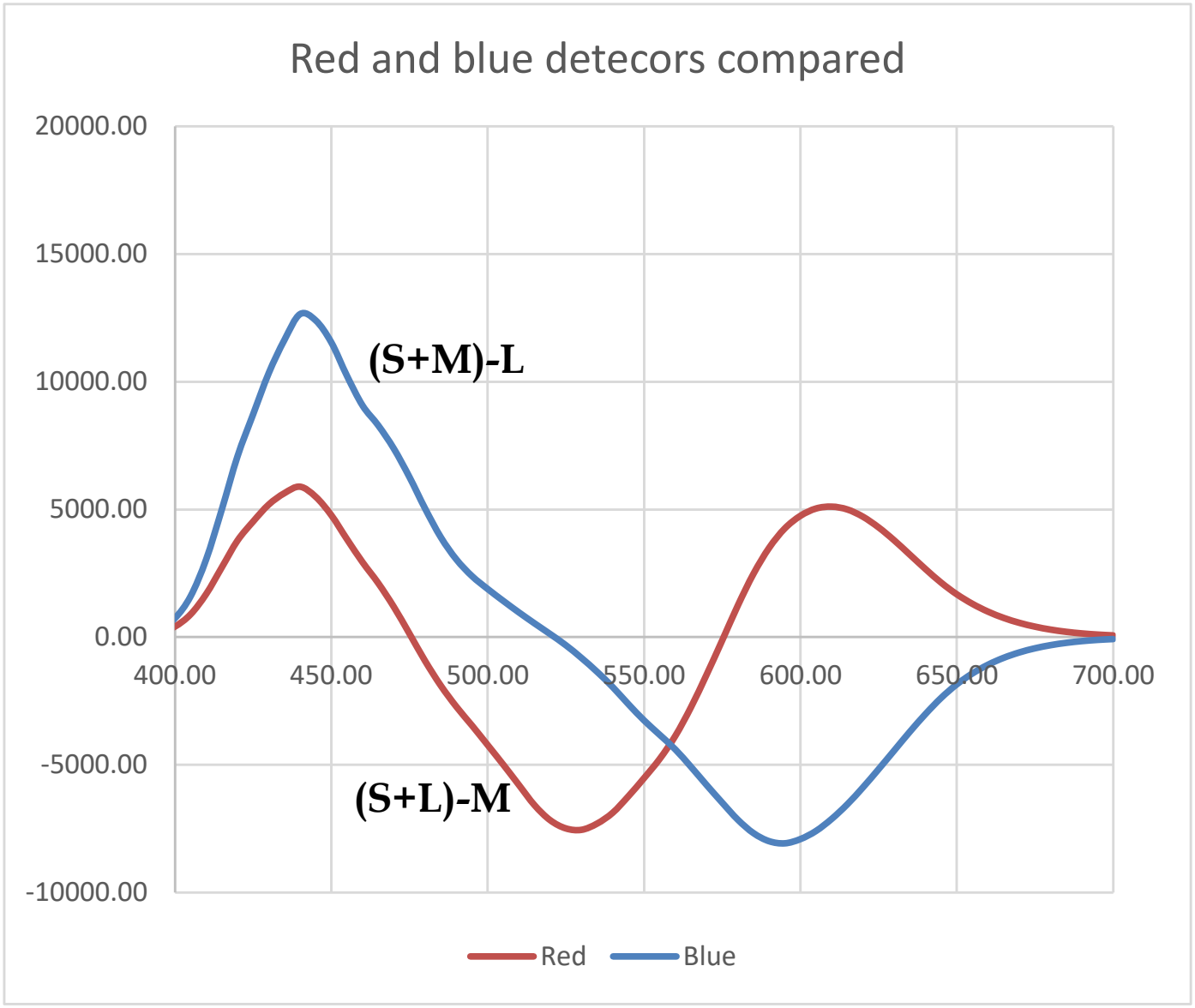
Red and blue detecors compared
20000.00
15000.00
10000.00
5000.00
0.00
-5000.00
-10000.00
400.00
450.00
500.00
550.00
600.00
650.00
700.00
(S+M)-L
(S+L)-M
Red
Blue

Thank You for Your Attention