The Topology of Fragile X

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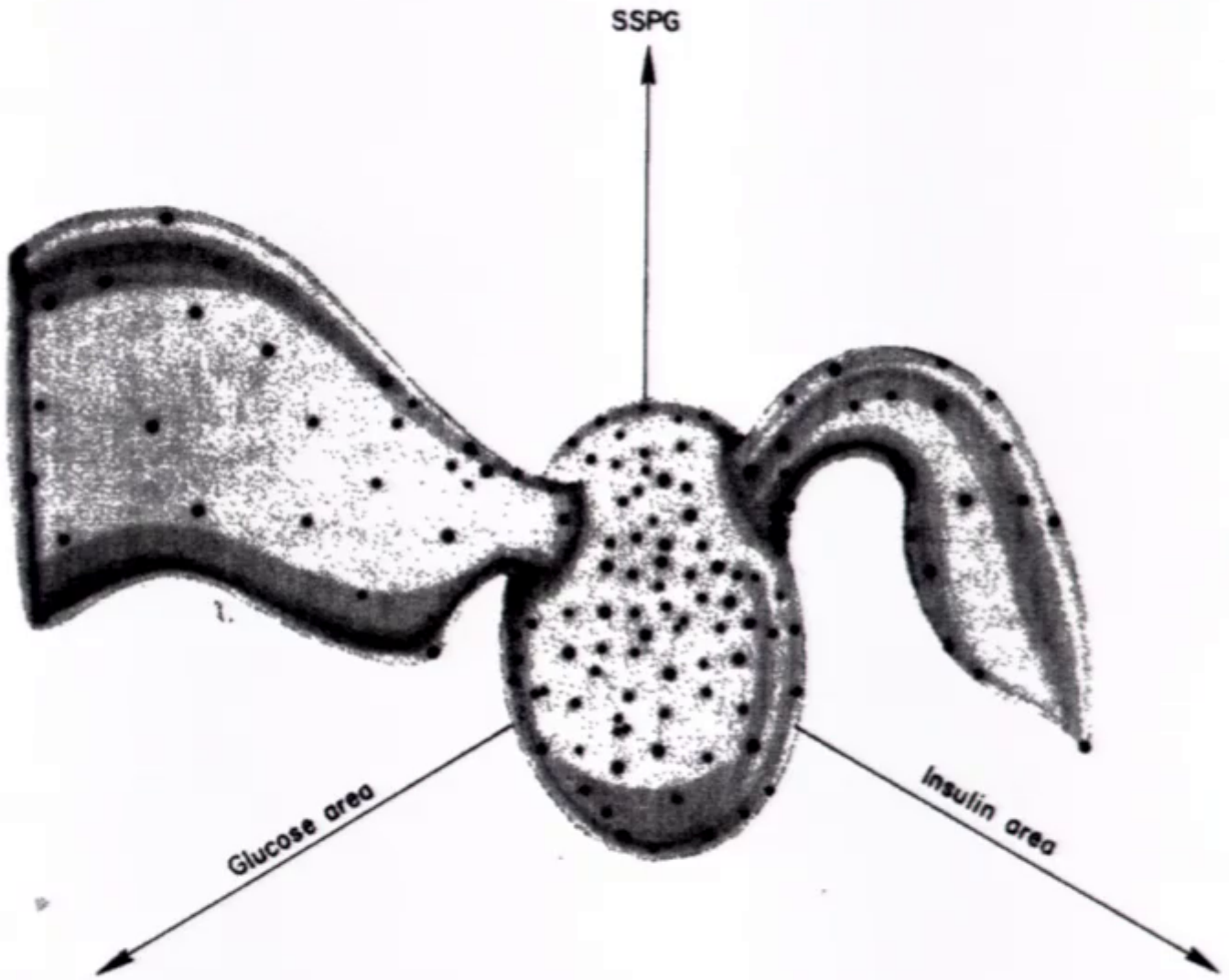
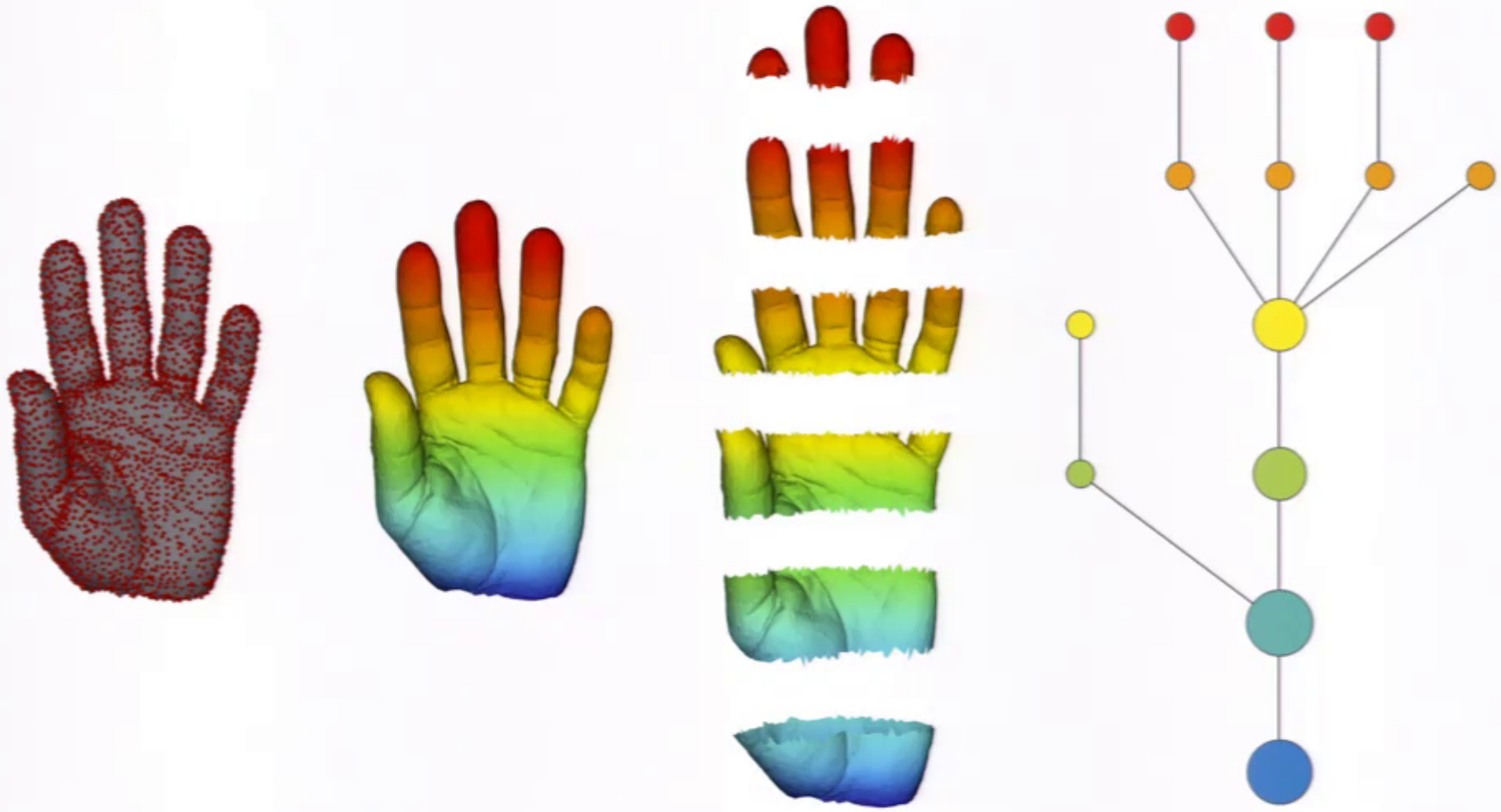


Image from Reaven and Miller, Diabetologia, 1979

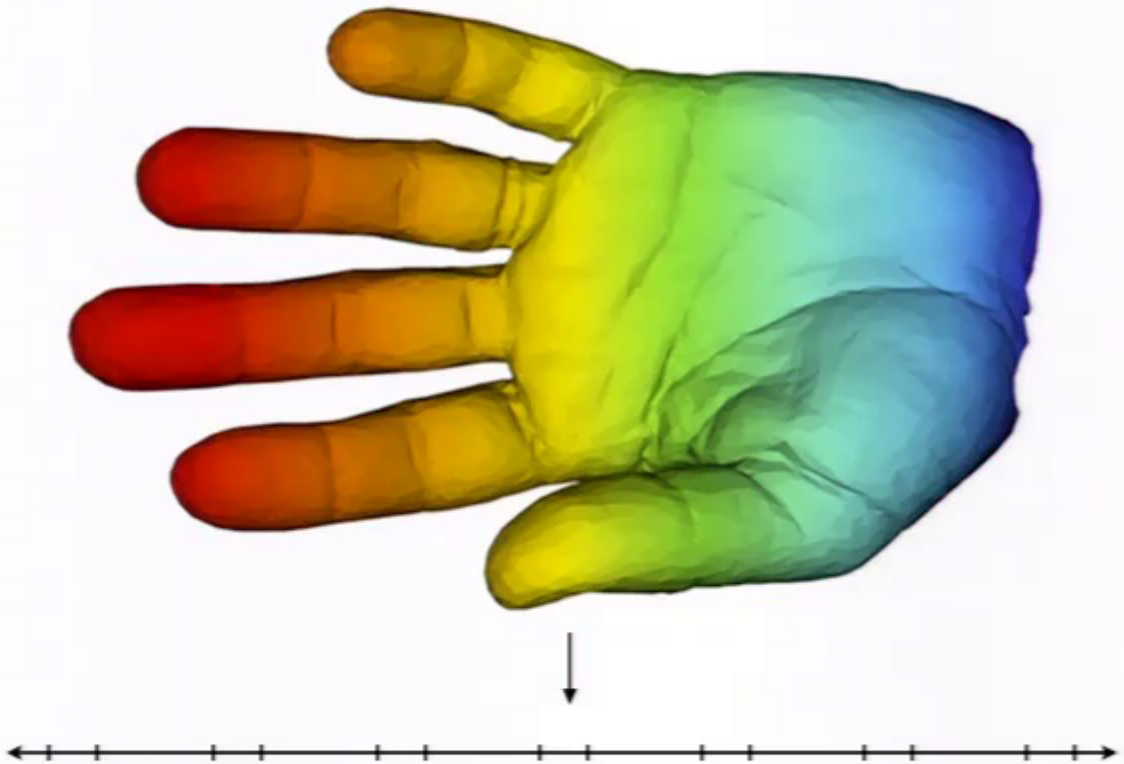
Overview of TDA (Mapper algorithm)



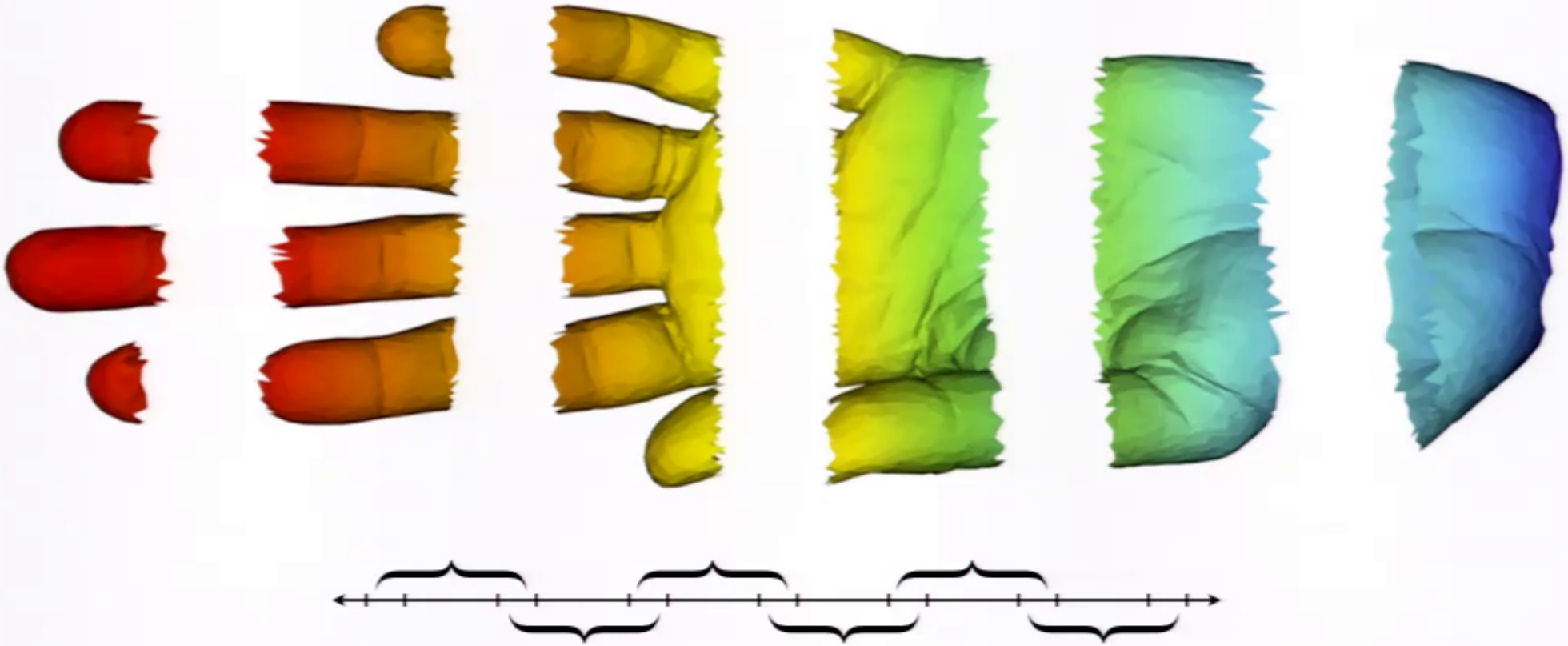
A Original Point Cloud

Images A-D from Lum et al., nature: Scientific Reports, 2012

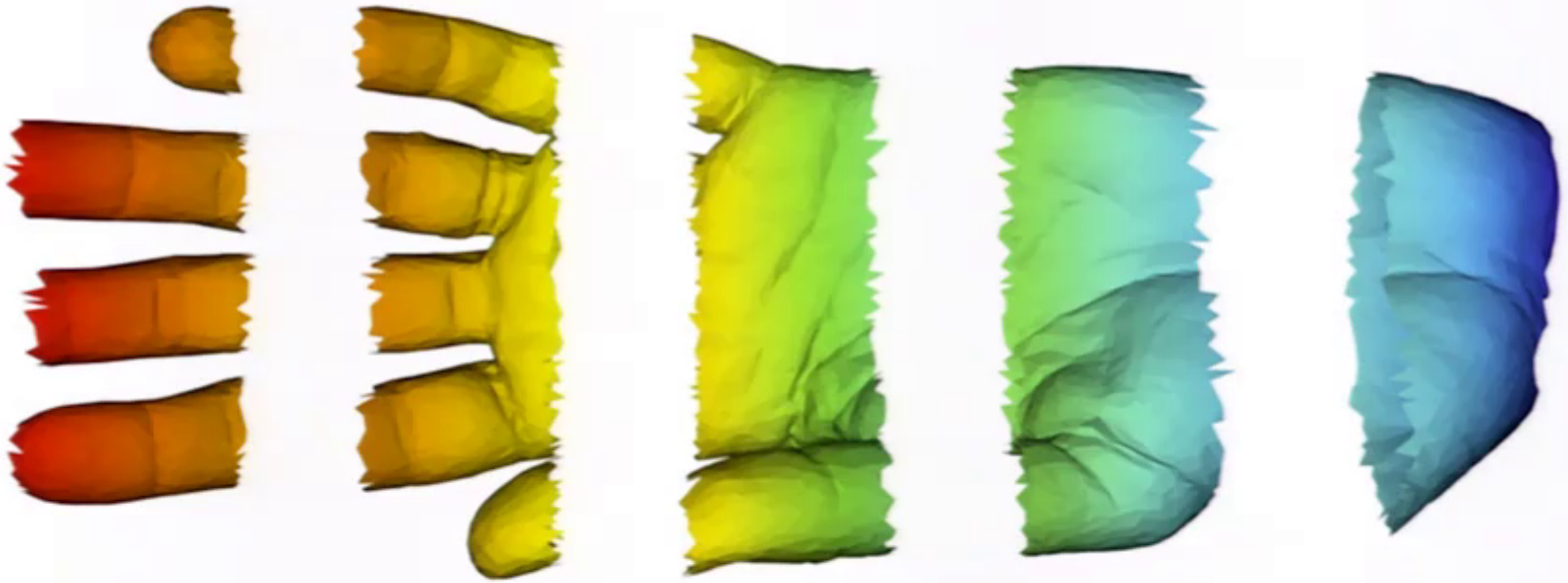
B Coloring by filter value



C Binning by filter value



D Clustering and network construction



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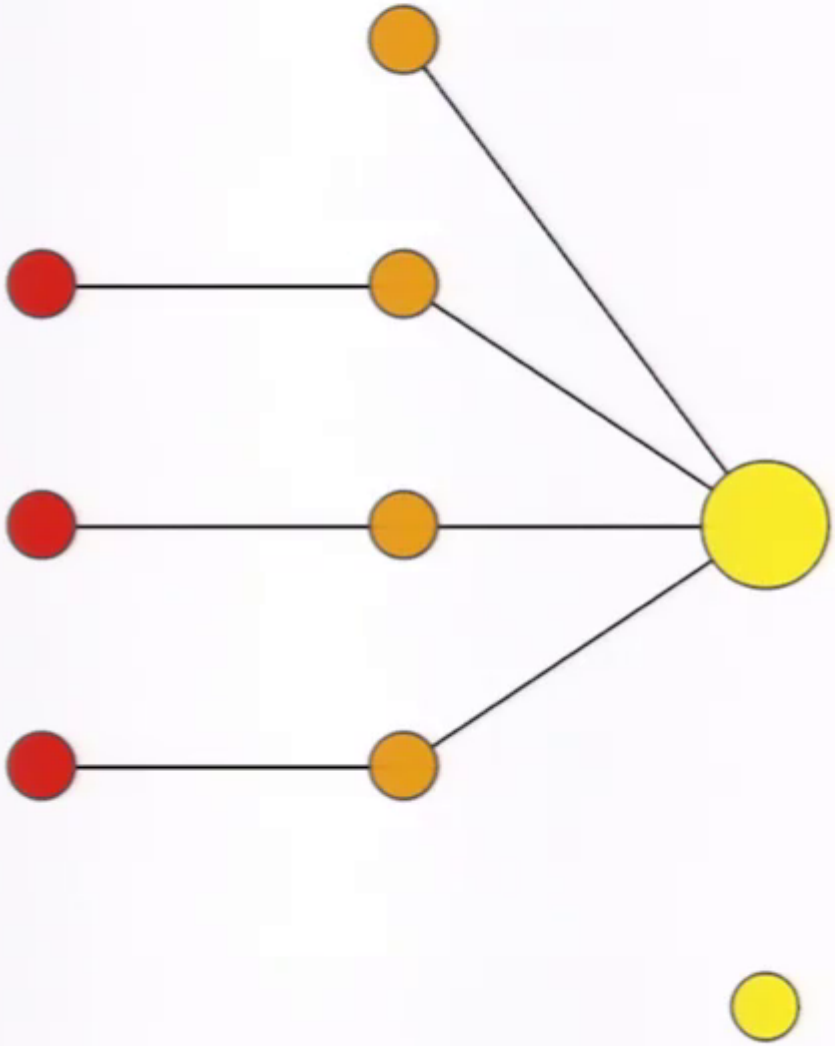

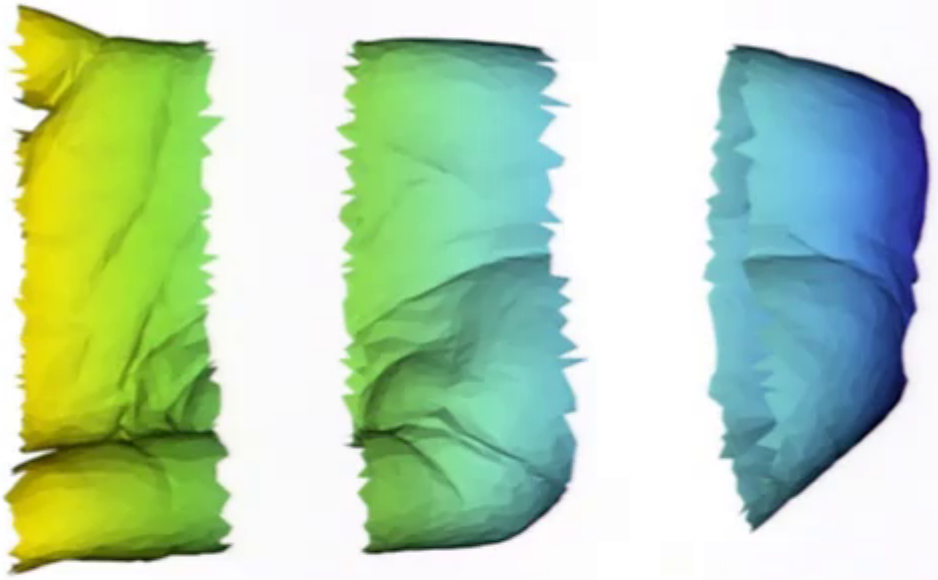

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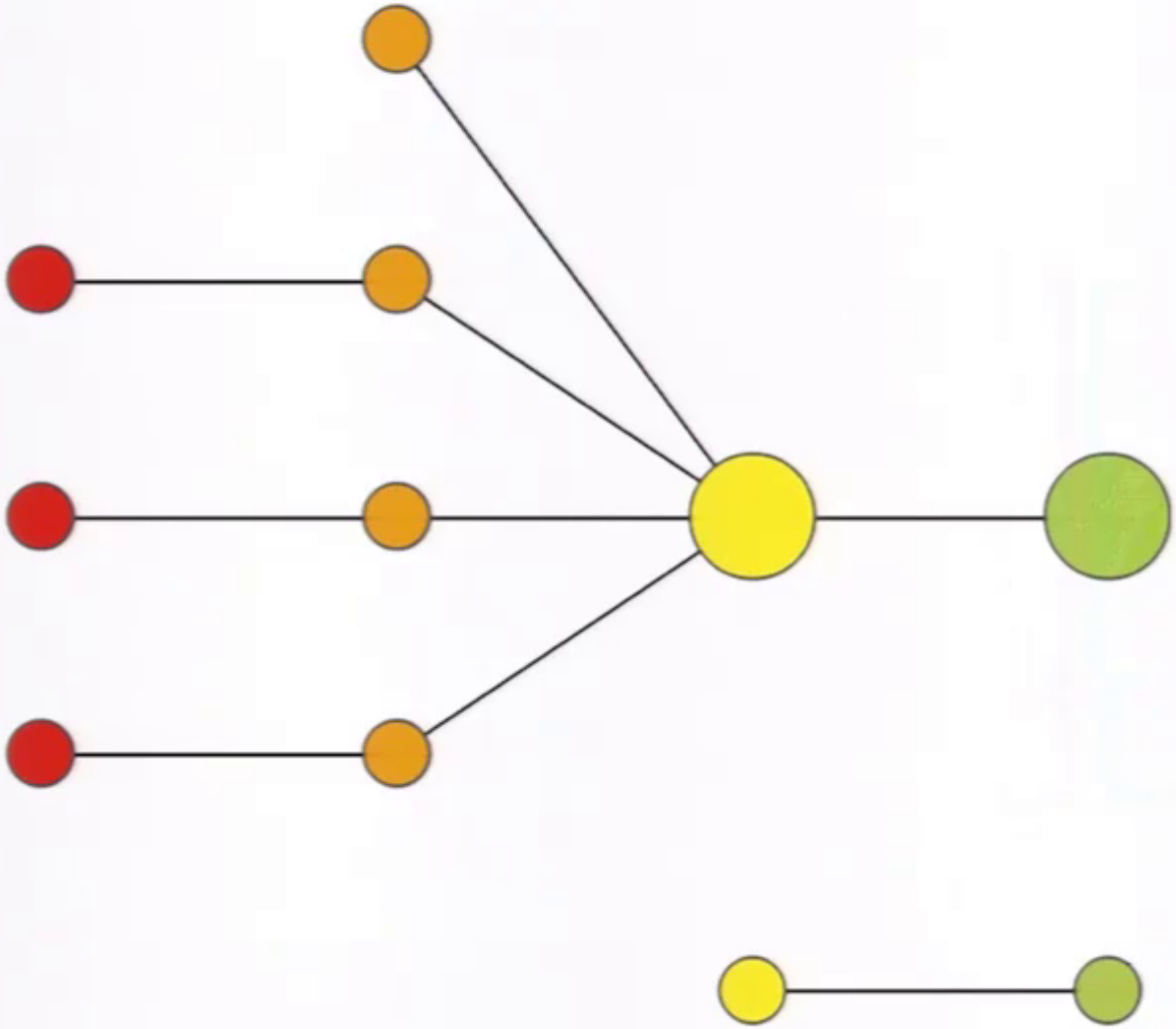

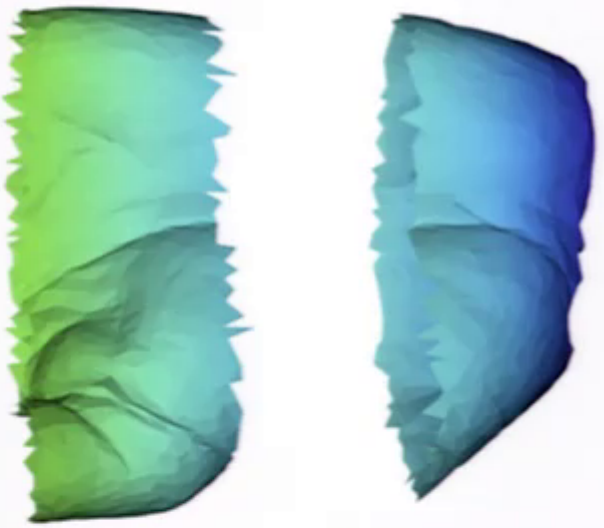

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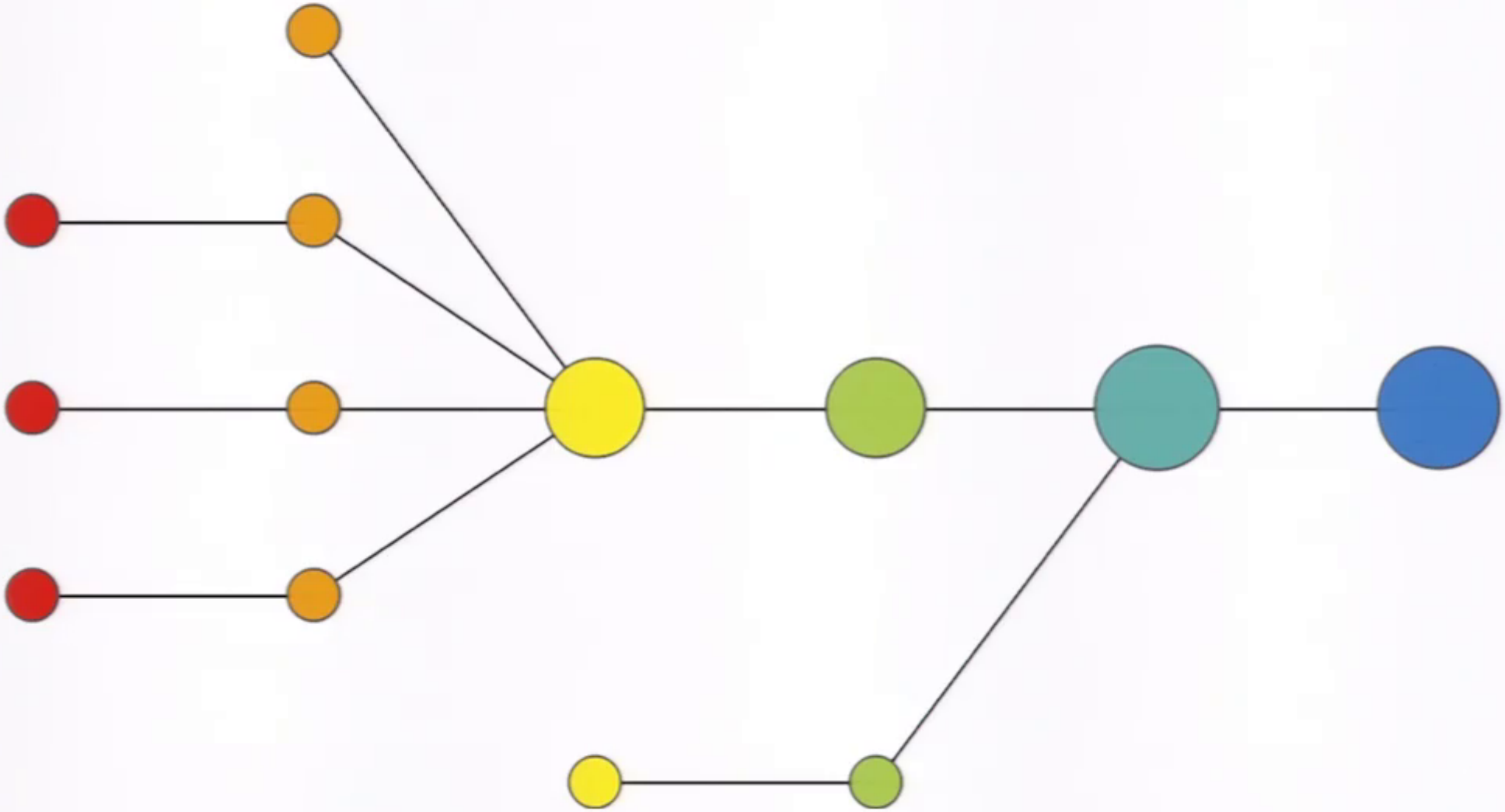
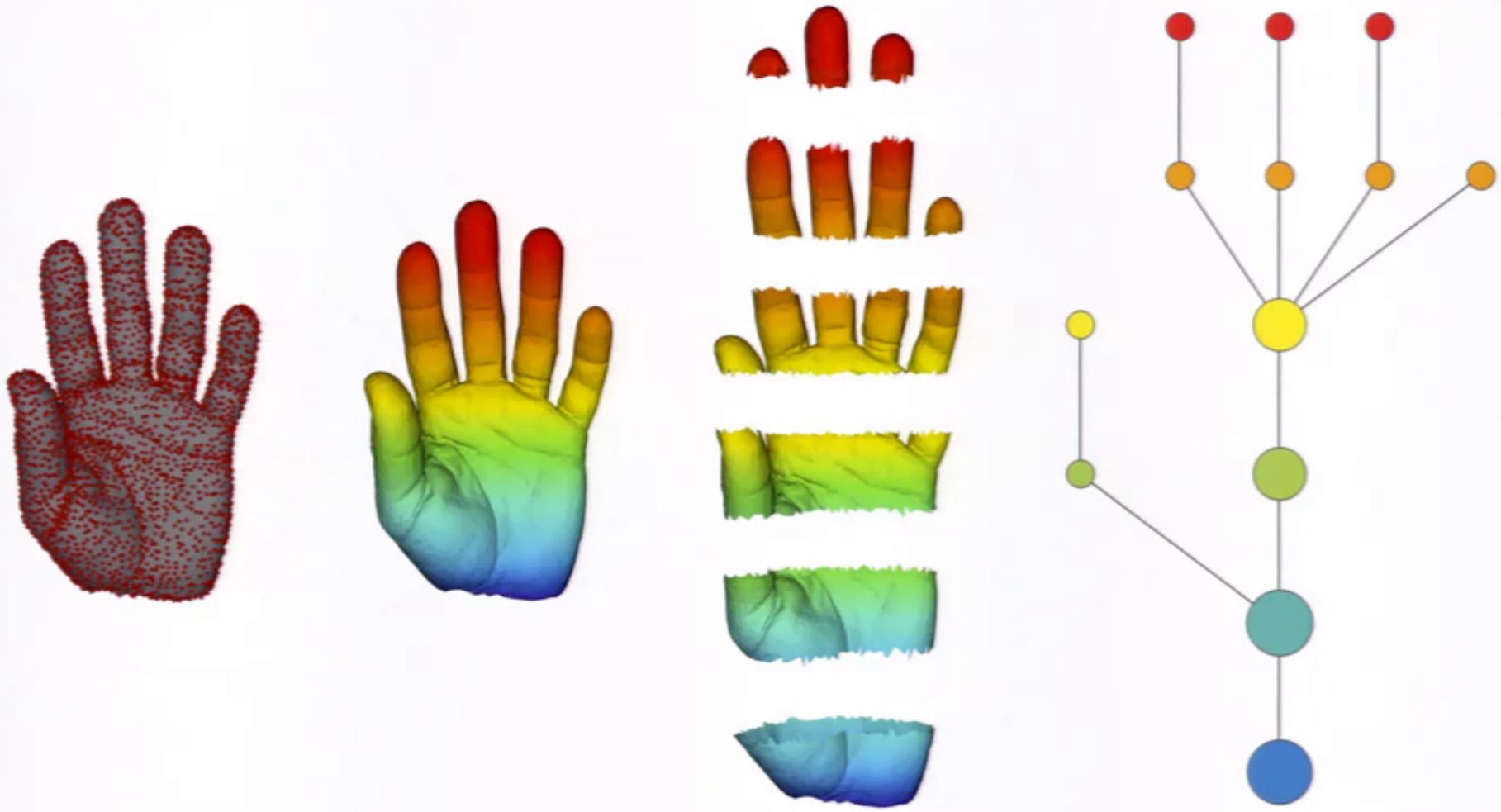




Application to Breast Cancer

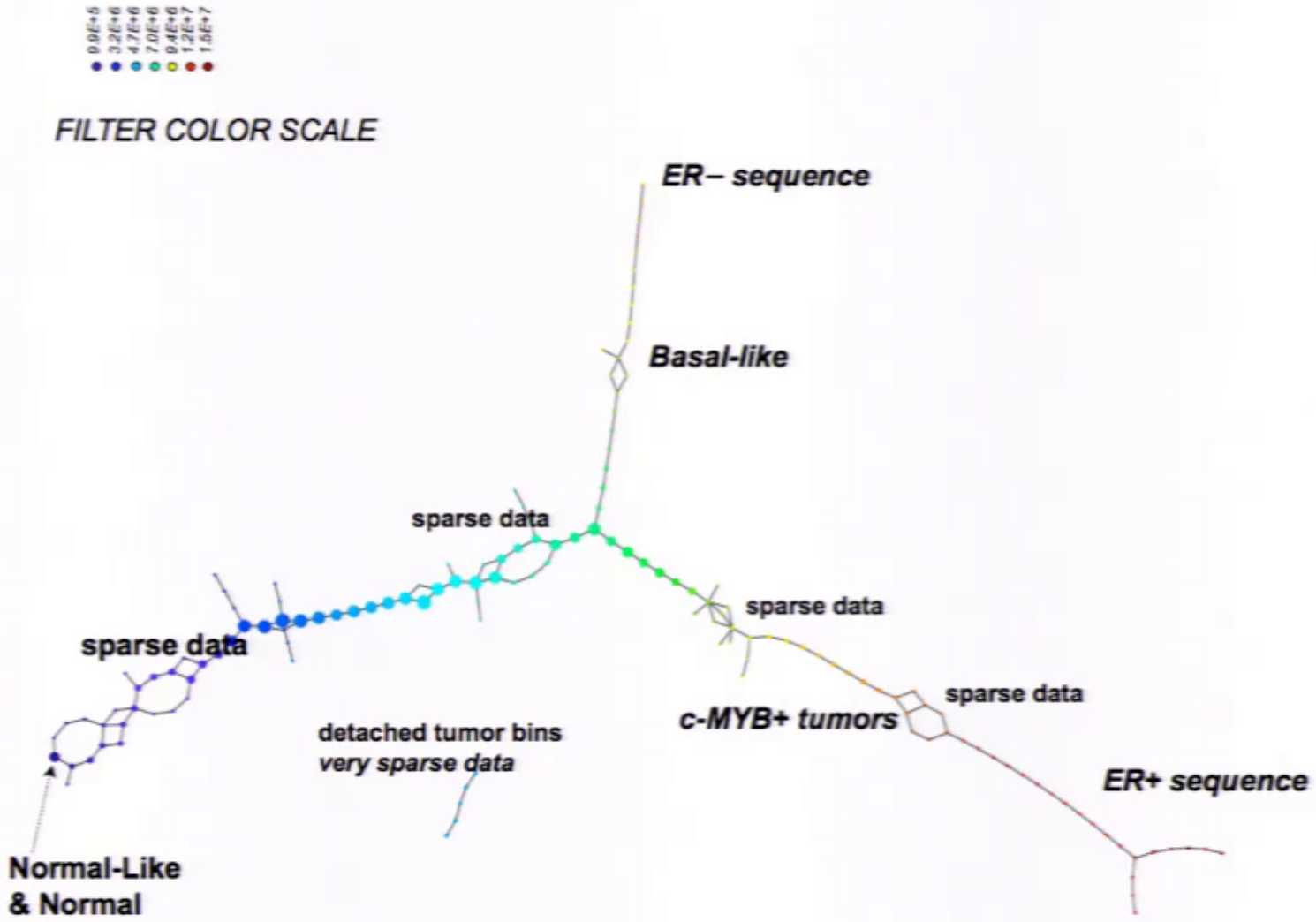
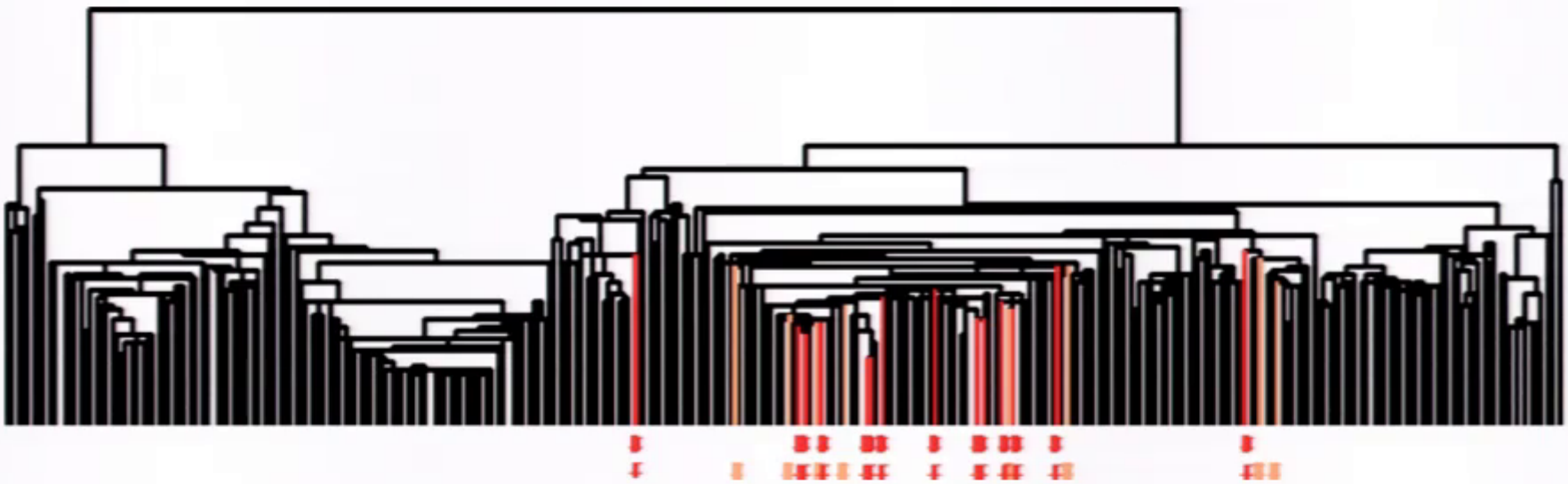
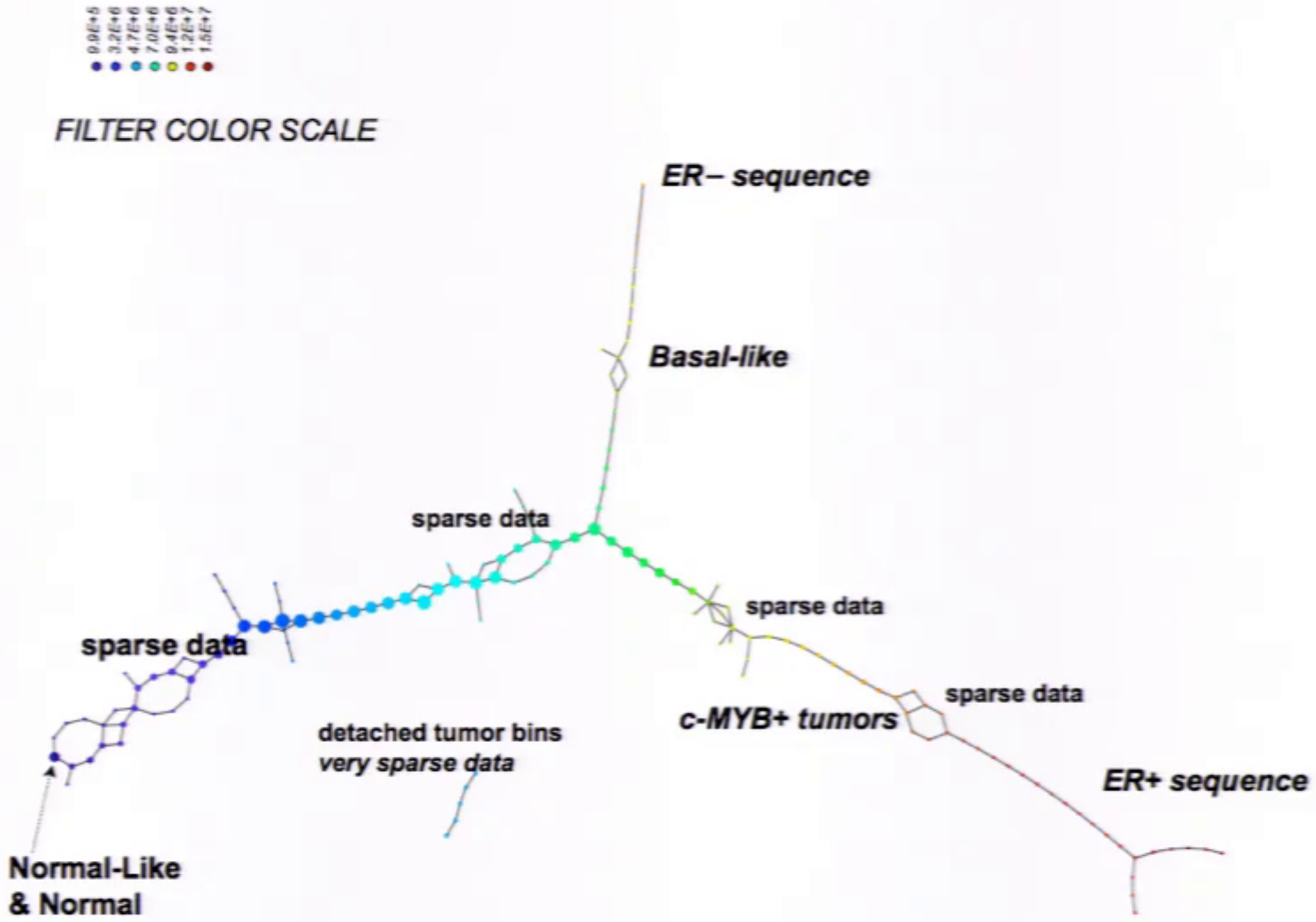


Image from Nicolau et al., PNAS, 2011





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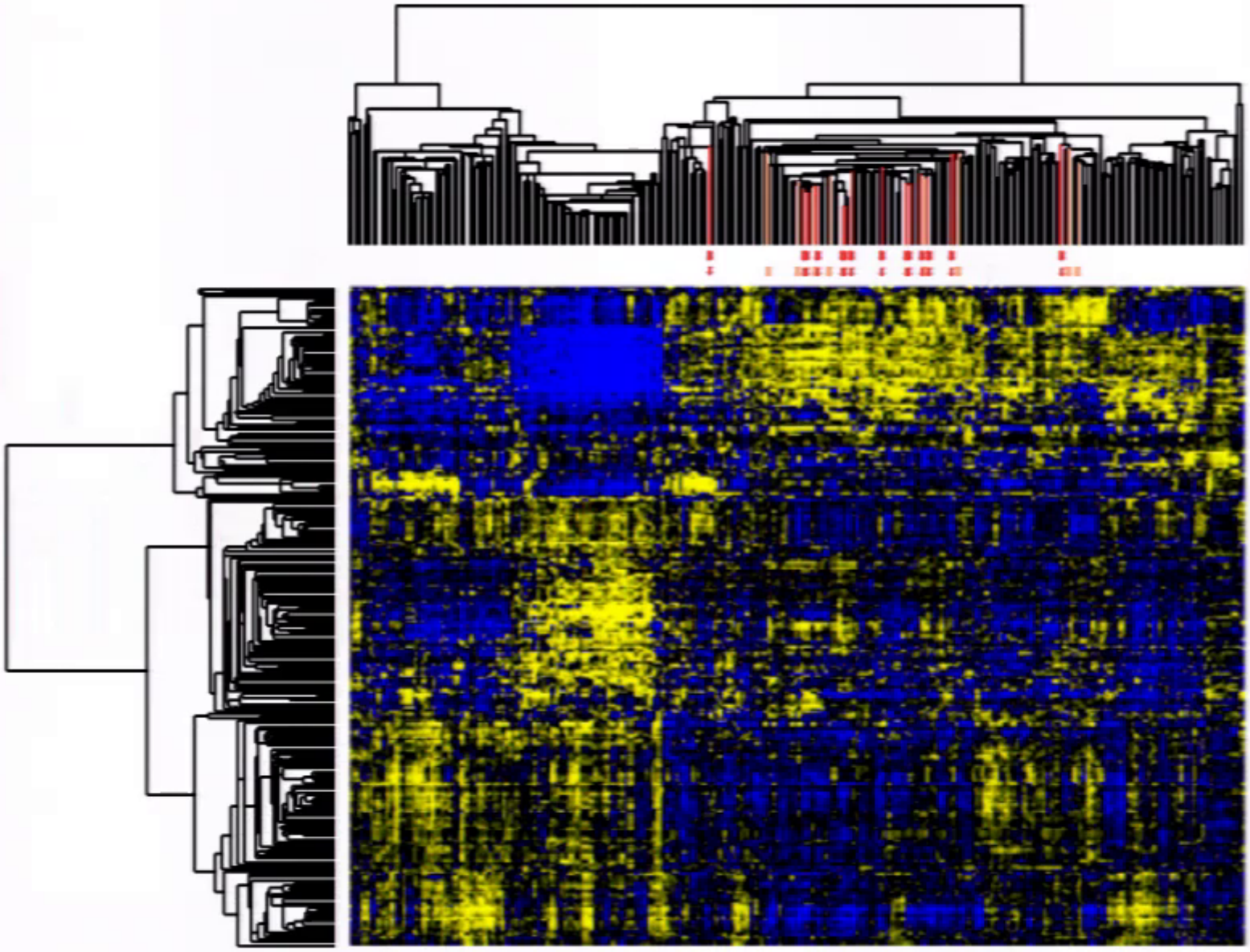


Application to neuropsychiatric disorders

www.autismspeaks.org:

DSM-5 Diagnostic Criteria

Autism Spectrum Disorder 299.00 (F84.0)

Diagnostic Criteria

A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history (examples are illustrative, not exhaustive, see text):

1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.

2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.

3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative paly or in making friends; to absence of interest in peers.

Specify current severity:

Severity is based on social communication impairments and restricted repetitive patterns of behavior (see Table 2).

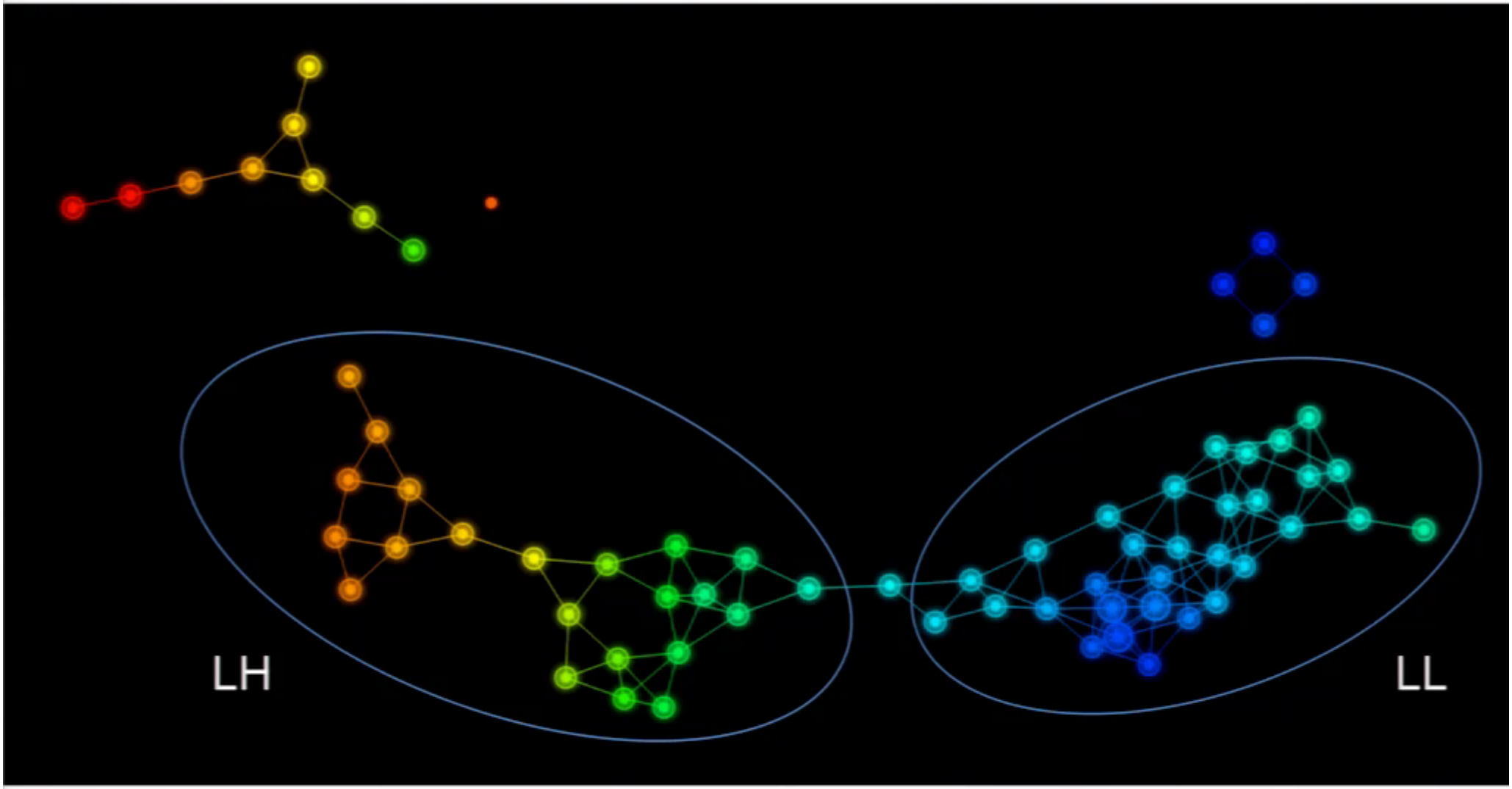
B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive; see text):

1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia,

Fragile X Syndrome

Characterized by a mutation of the FMRI gene on the X chromosome. This reduces production of FMRP, a protein thought to be involved in synaptic pruning.

Without genetic testing, likely diagnosis is autism.



Generalized Reeb graph of fragile X MRI data

Table 2: Mullen Scales of Early Learning

standardized subscale	LL mean(SD)	LH mean(SD)	difference	p-value	Cohen's d
Composite	58.68(11.29)	50.67(3.43)	8.02	0.004	0.95
Receptive Language	27.89(10.65)	20.94(2.04)	6.95	0.006	0.89
Visual Reception	28.89(10.32)	22.11(5.18)	6.78	0.008	0.82
Expressive Language	26.21(8.84)	21.72(3.61)	4.49	0.026	0.65
Fine Motor	23.37(4.34)	20.50(2.12)	2.87	0.043	0.58

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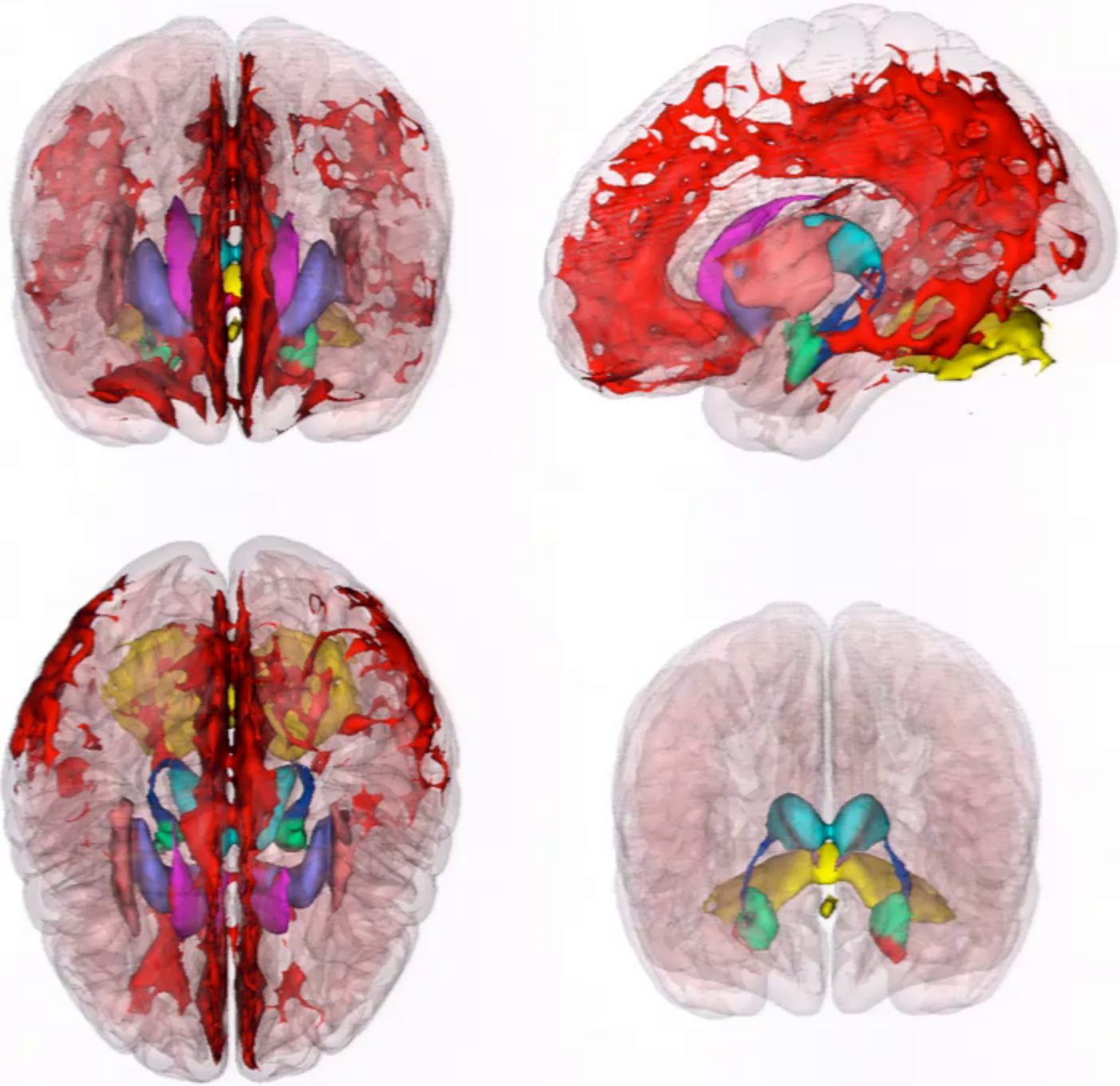
Table 3: Autism Diagnostic Observation Schedule - Generic

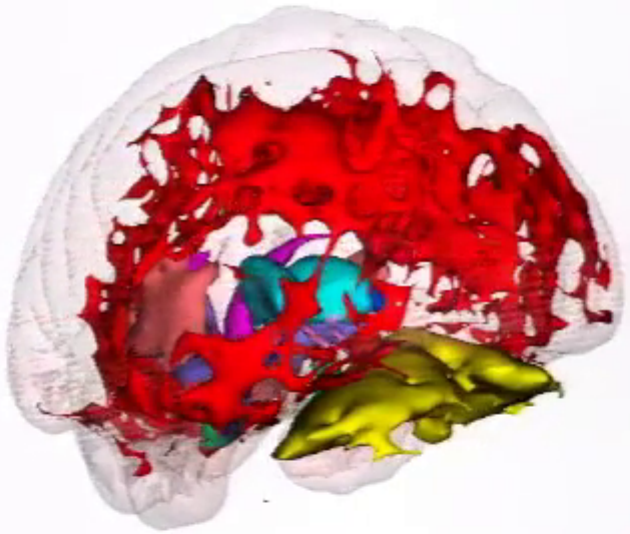
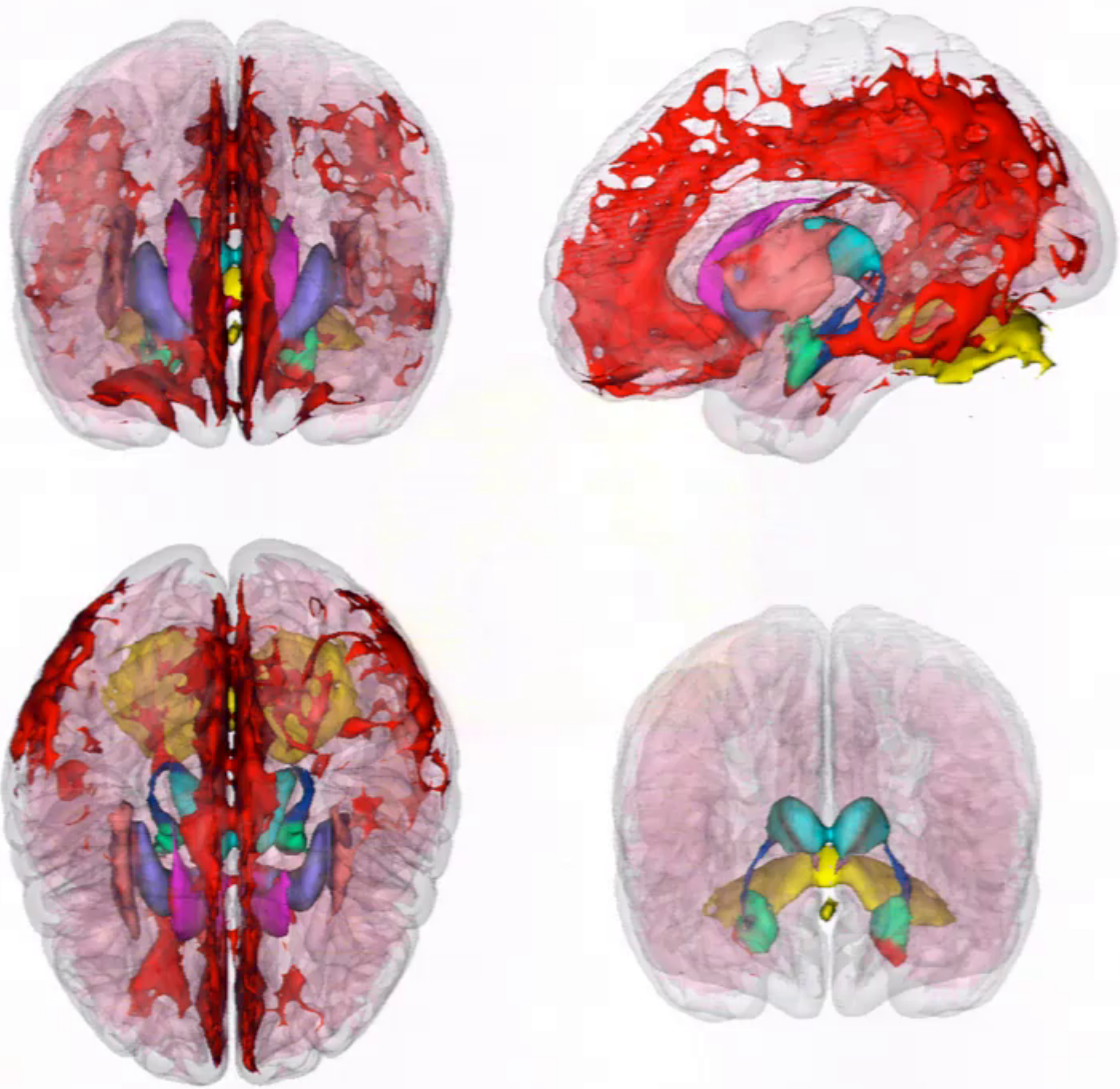
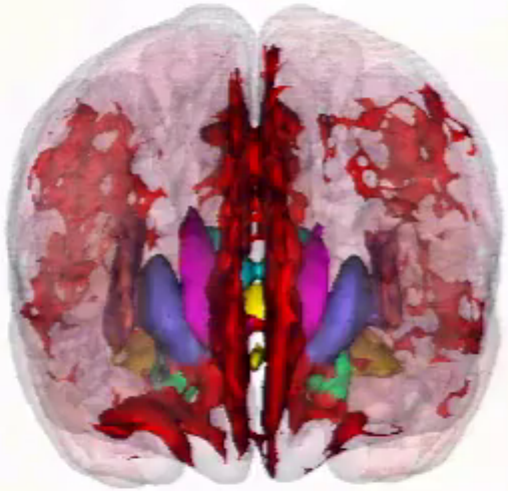
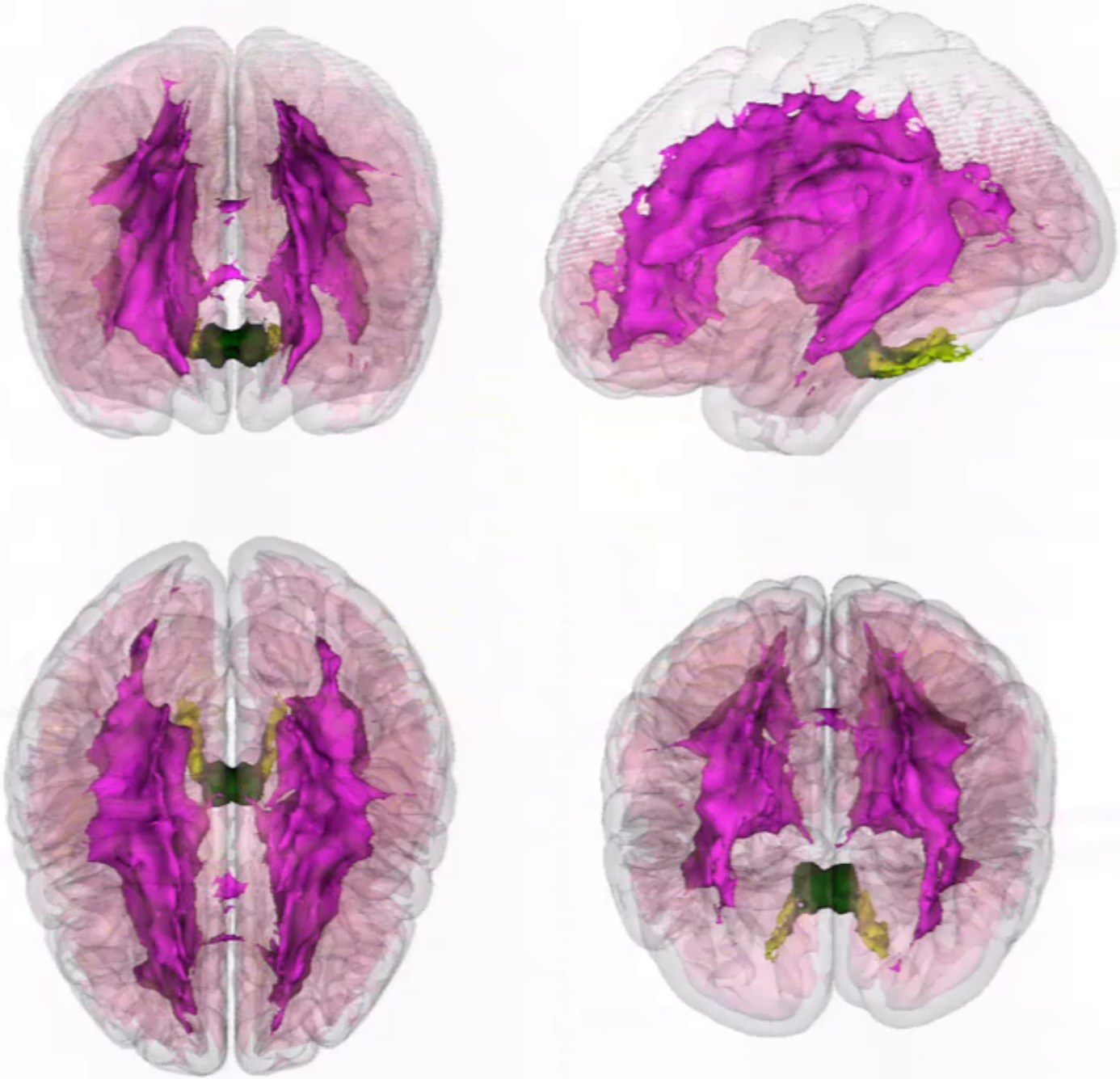
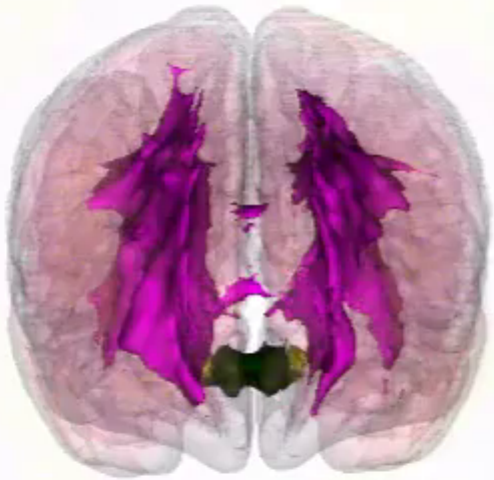
subscale	LL mean(SD)	LH mean(SD)	difference	p-value	Cohen's d
Social	5.00(3.99)	7.83(3.71)	-2.83	0.016	-0.73
Communication/Social	8.47(6.02)	12.39(4.96)	-3.92	0.019	-0.71
Communication	3.47(2.20)	4.56(1.65)	-1.08	0.049	-0.55
Stereotyped Behavior	1.53(1.80)	2.28(1.41)	-0.75	0.083	-0.46
Play	2.63(1.34)	3.22(1.26)	-0.59	0.088	-0.45

Table 4: Autism Diagnostic Interview - Revised

subscale	LL mean(SD)	LH mean(SD)	difference	p-value	Cohen's d
Social	7.56(4.88)	10.71(5.46)	-3.15	0.041	-0.61
Communication (non-verbal)	7.81(4.39)	10.19(3.17)	-2.38	0.045	-0.62
Abnormal Development	3.89(1.02)	4.41(0.80)	-0.52	0.050	-0.57
Communication (verbal)	3.67(3.79)	10.00(2.83)	-6.33	0.064	-1.88
Repetitive and Stereotyped Behavior	3.06(1.80)	3.24(1.30)	-0.18	0.368	-0.11

grey matter differences
between LH and LL





white matter differences
between LH and LL