Electronic Supplementary Information

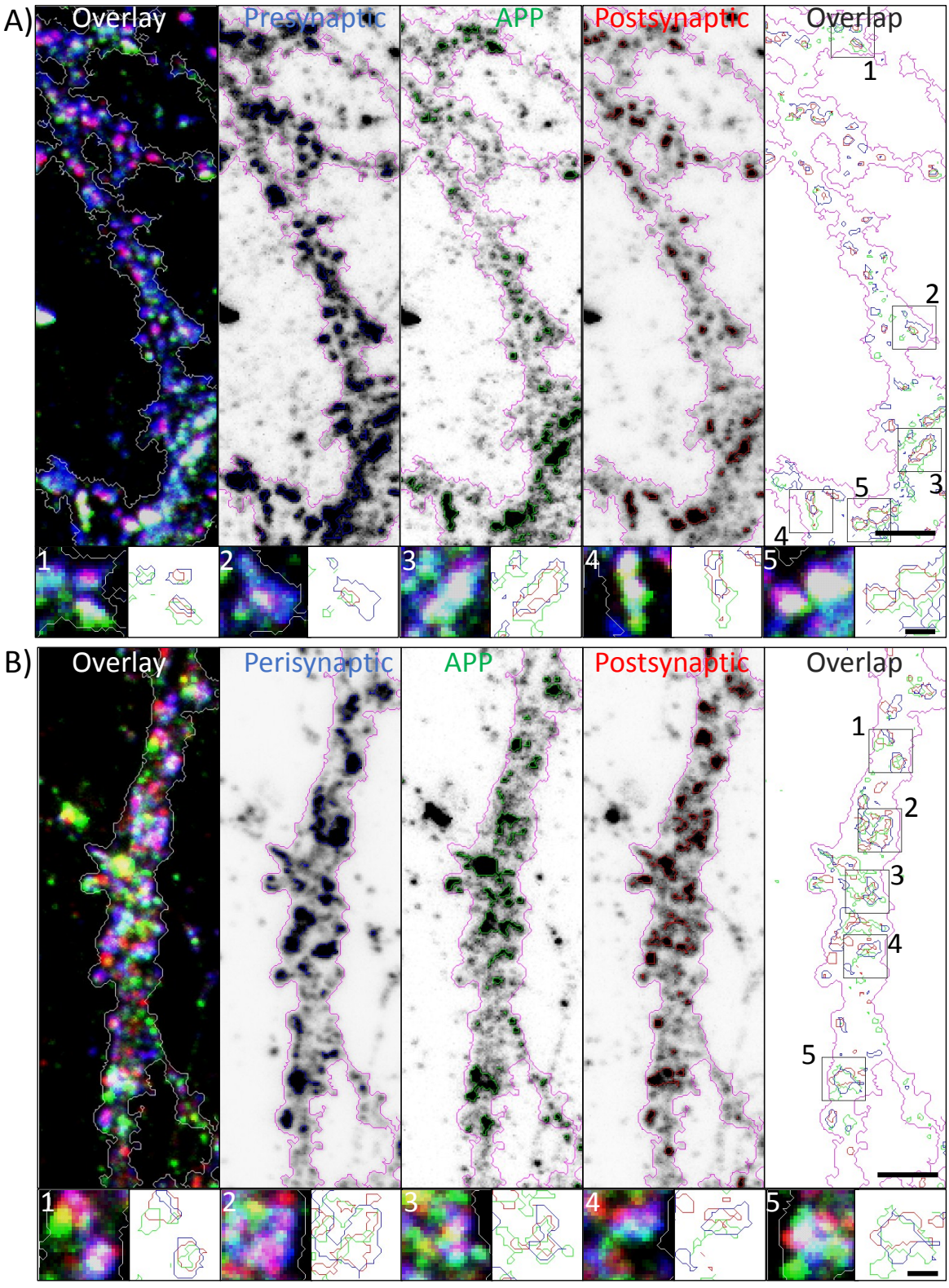


Figure S1

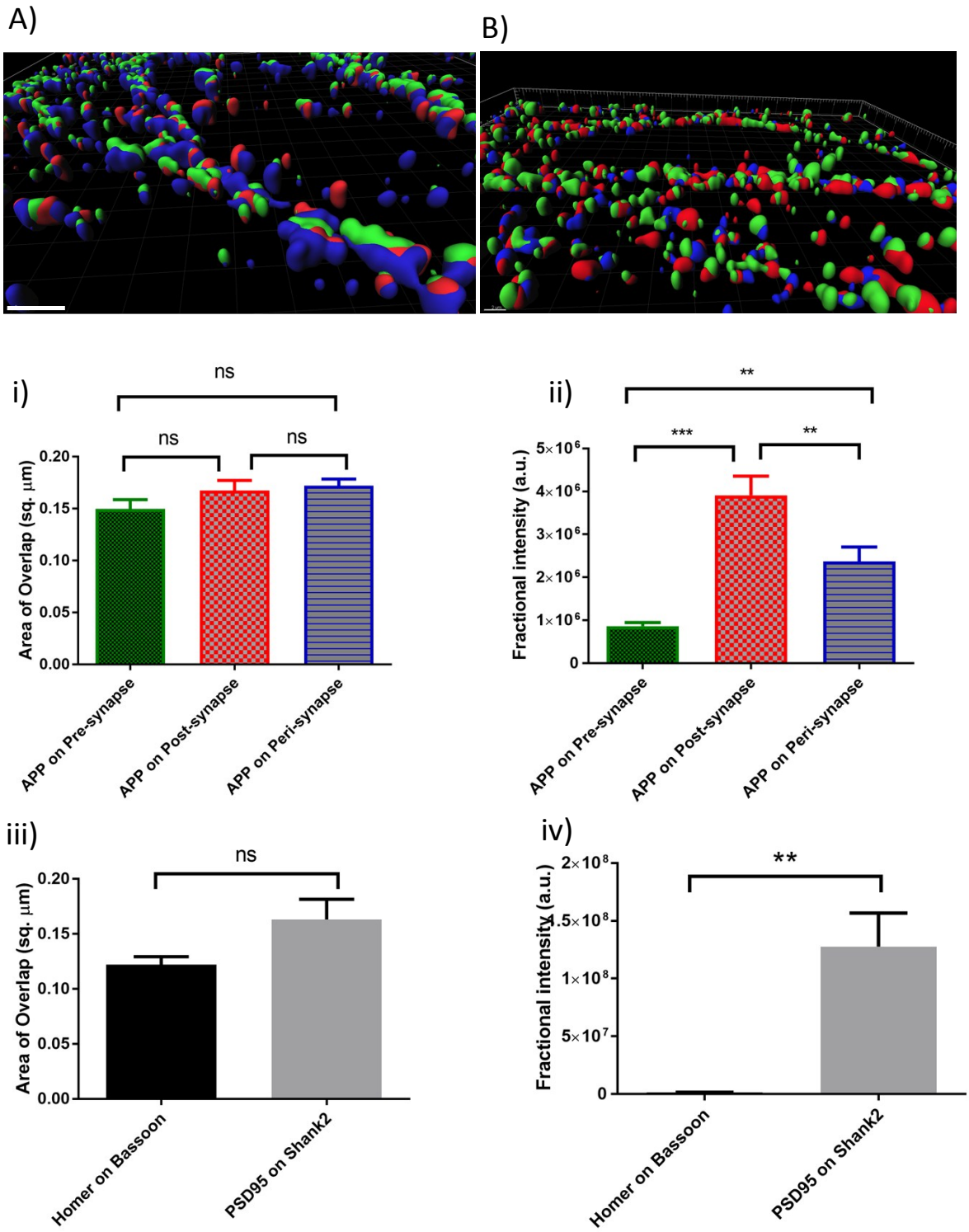


Figure S2

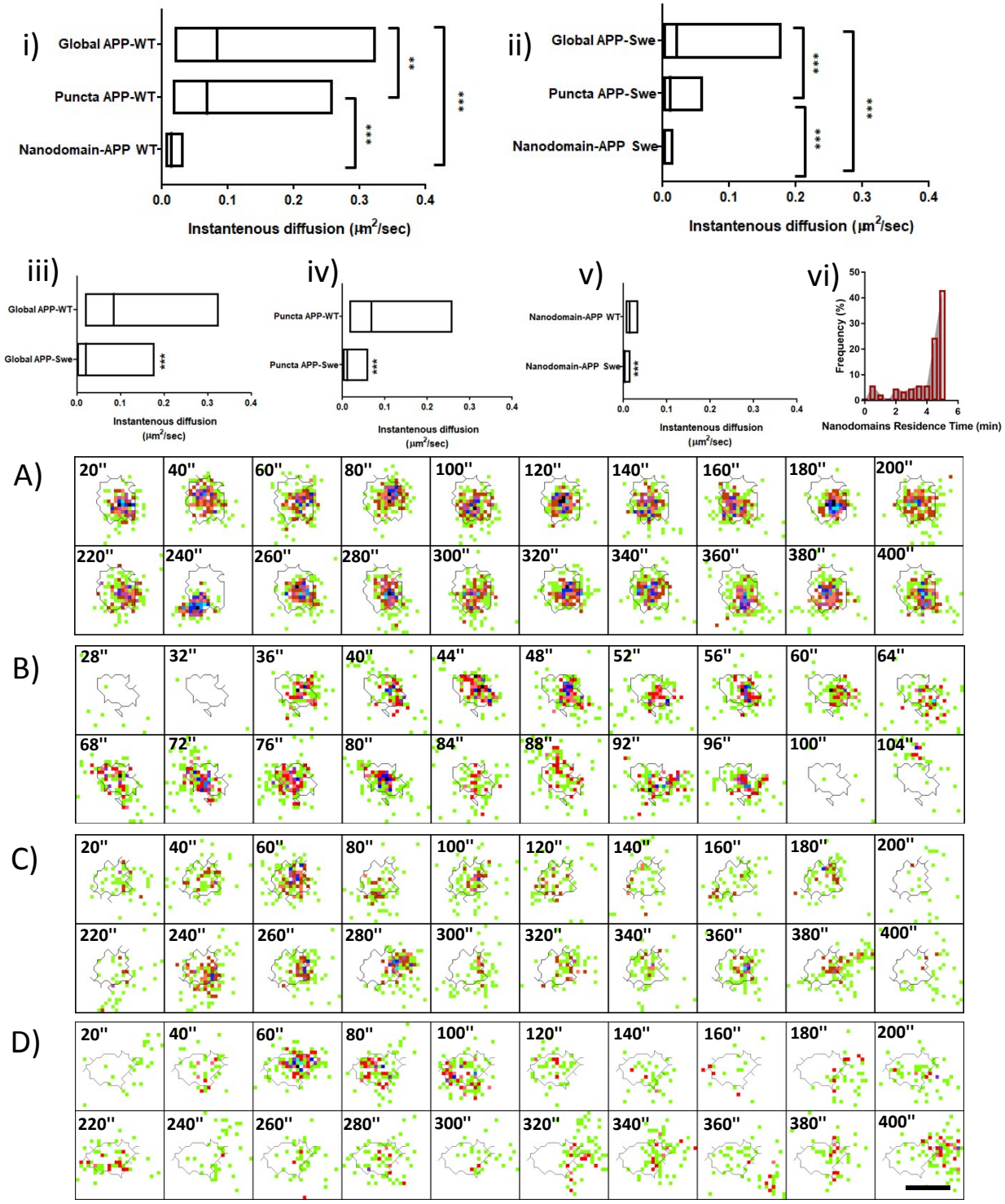


Figure S3

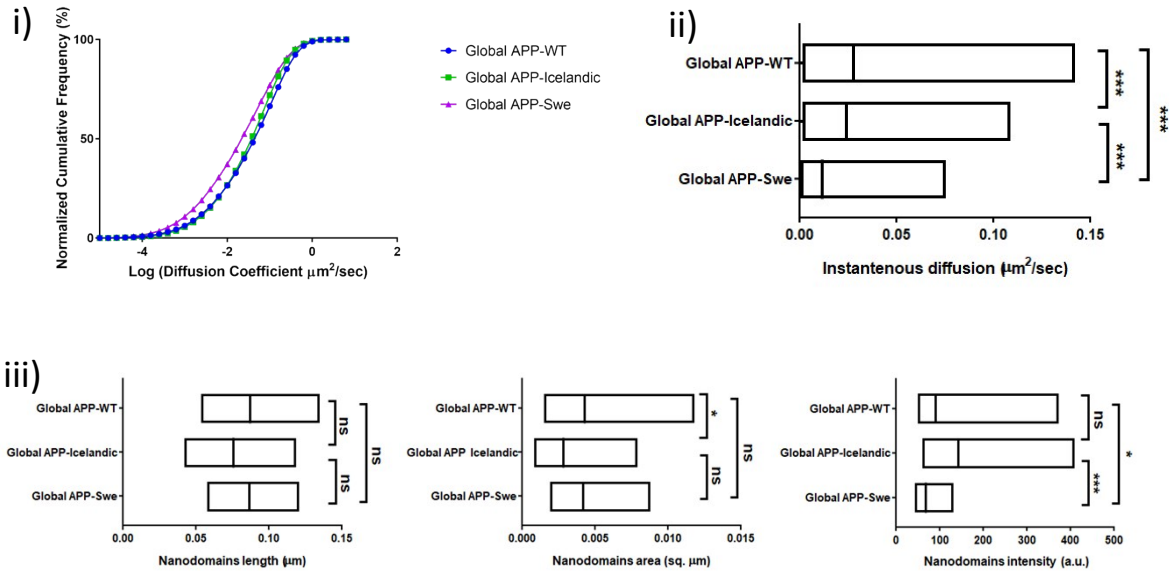
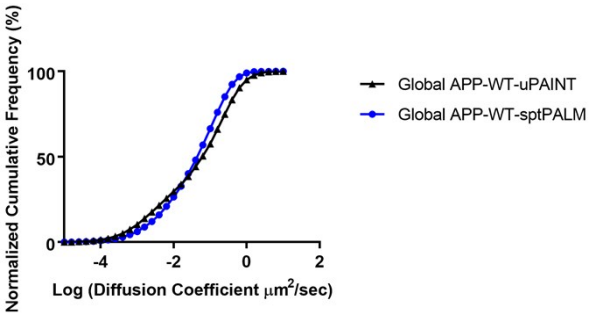


Figure S4

i)



ii)

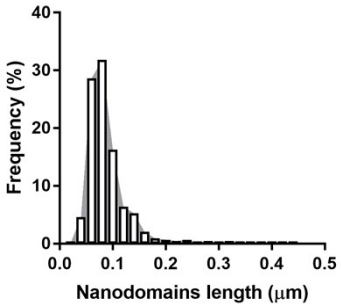


Figure S5

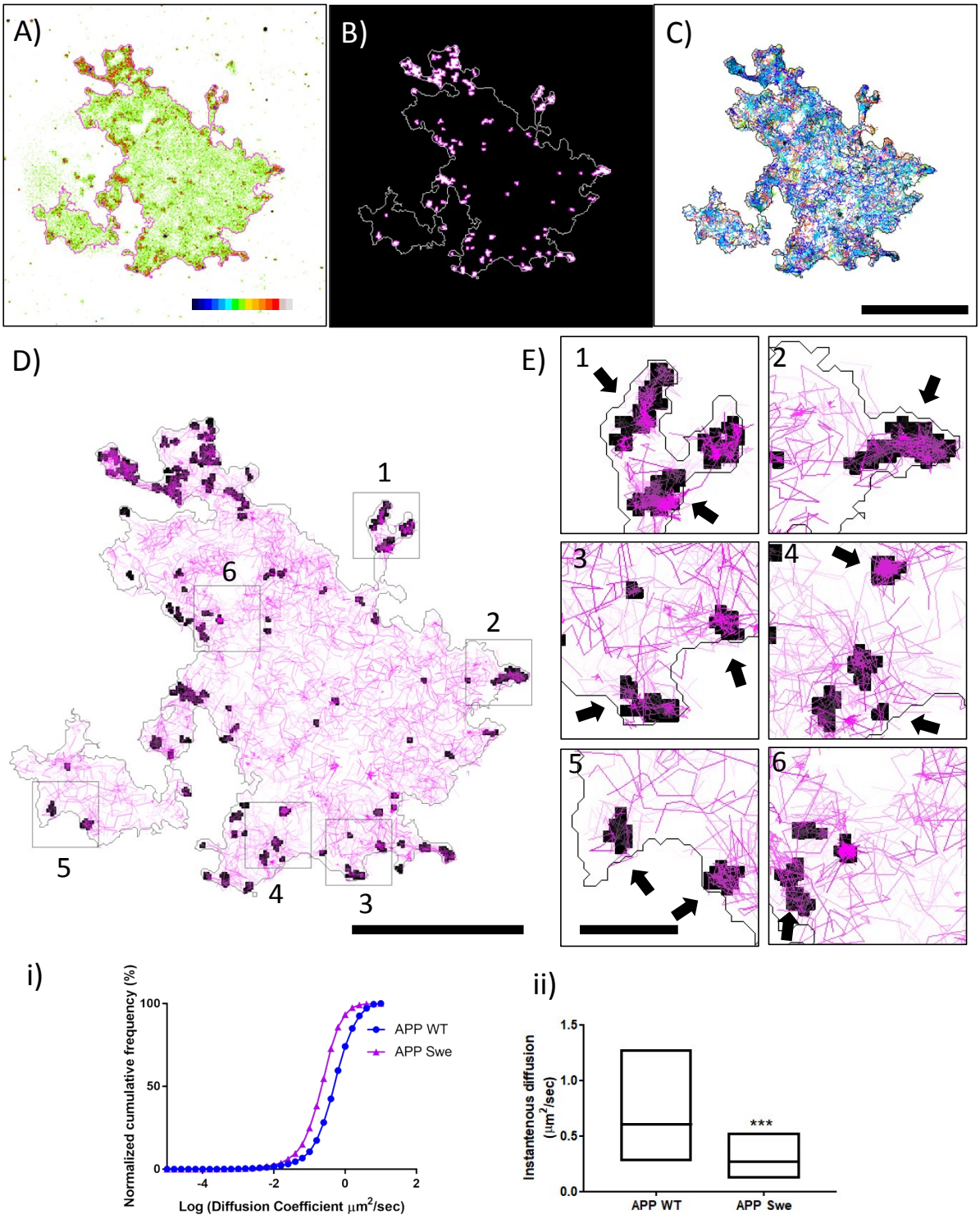


Figure S6

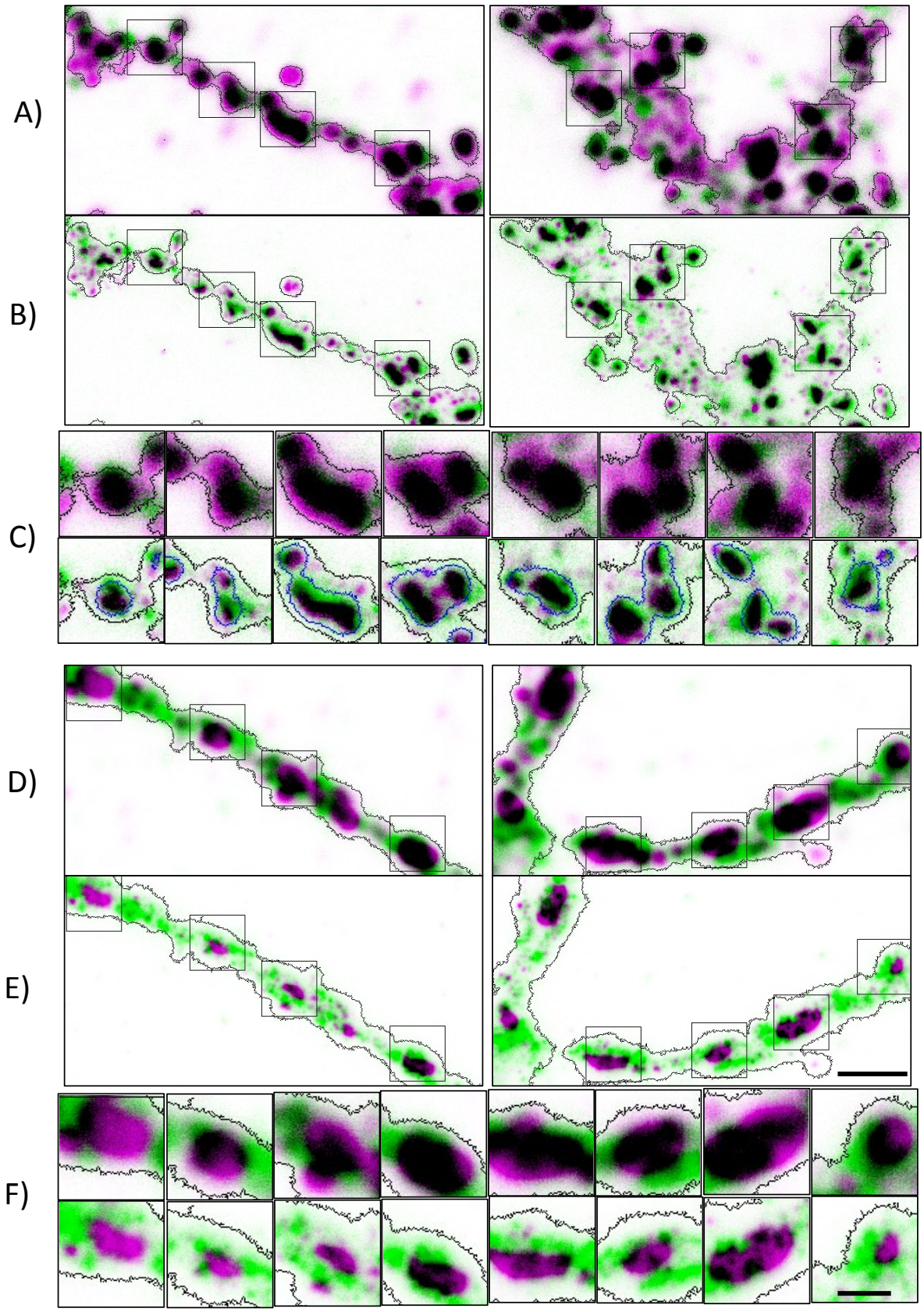


Figure S7

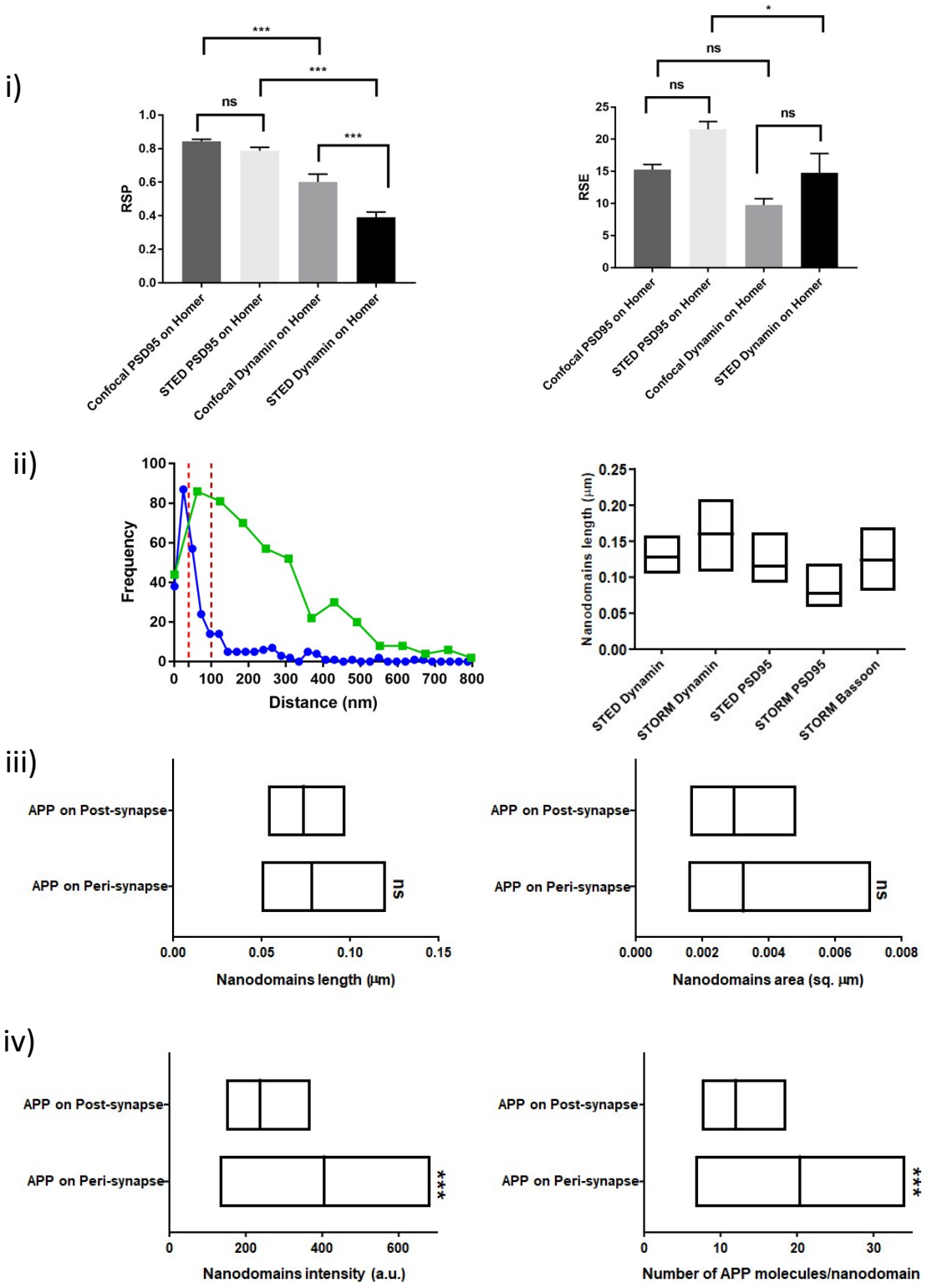


Figure S8

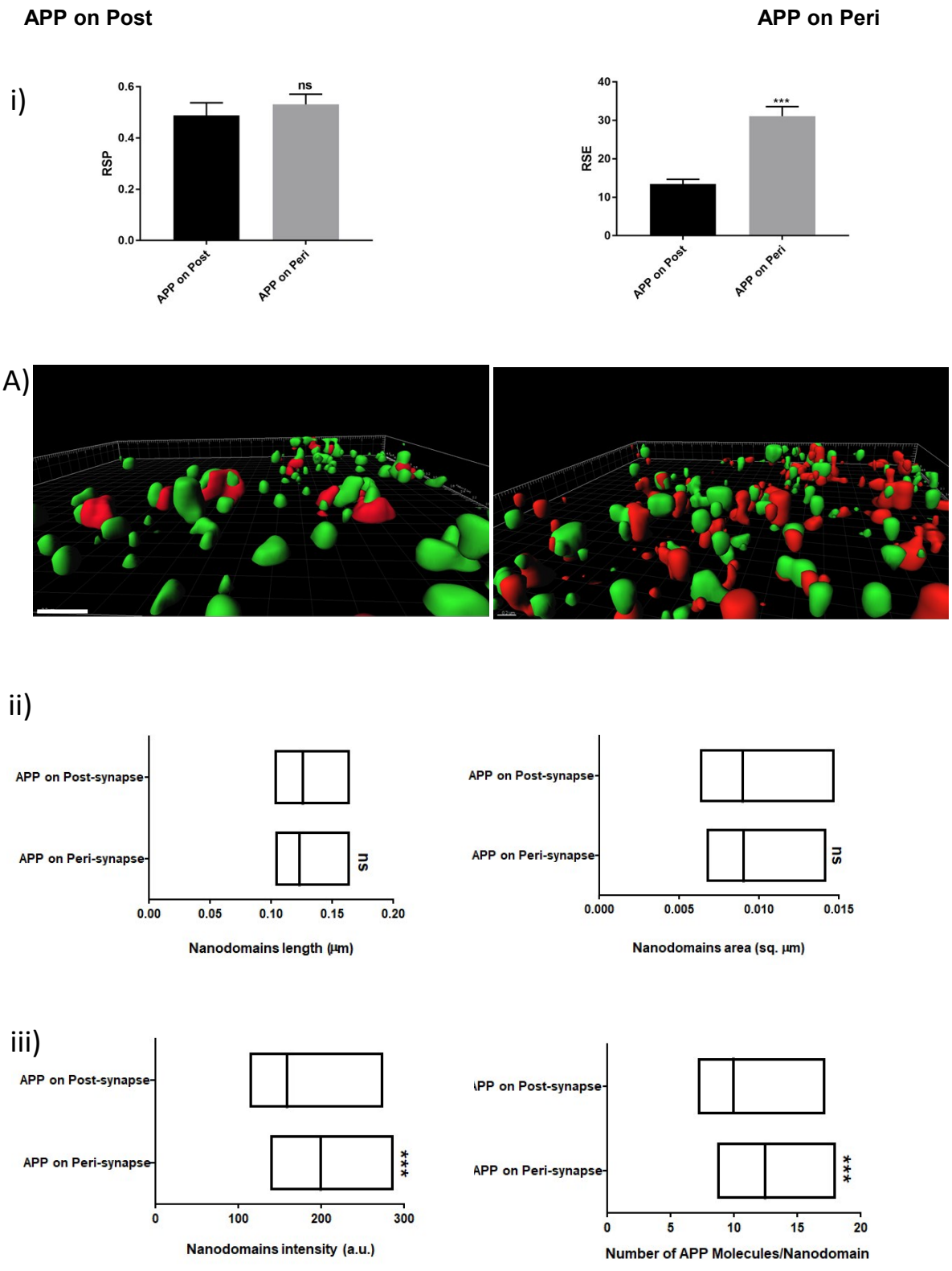


Figure S9

i)

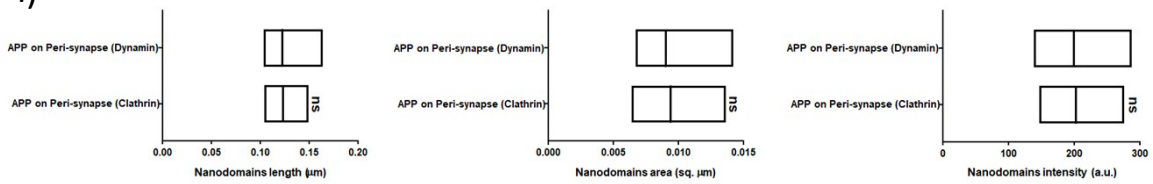


Figure S10

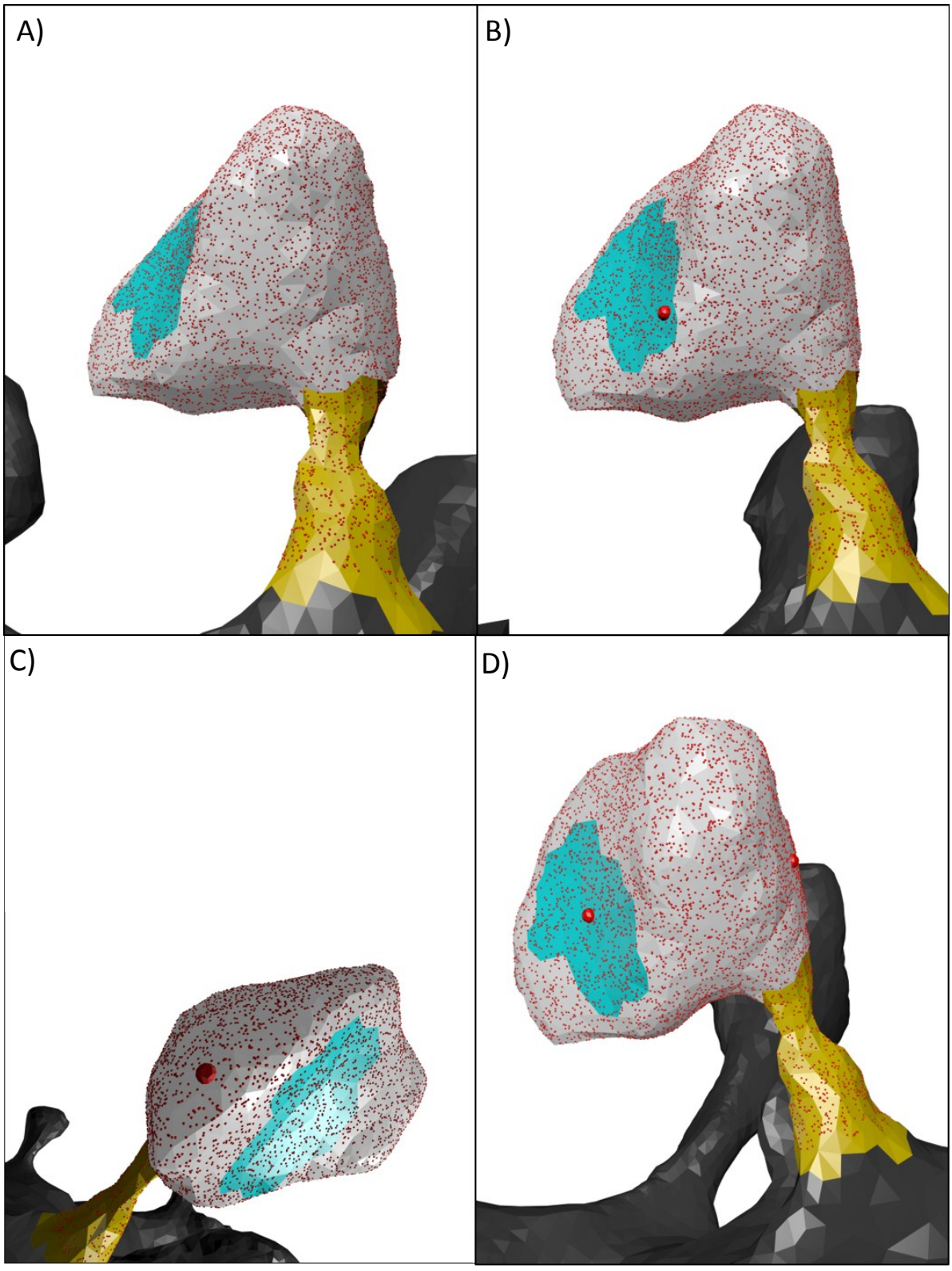


Figure S11

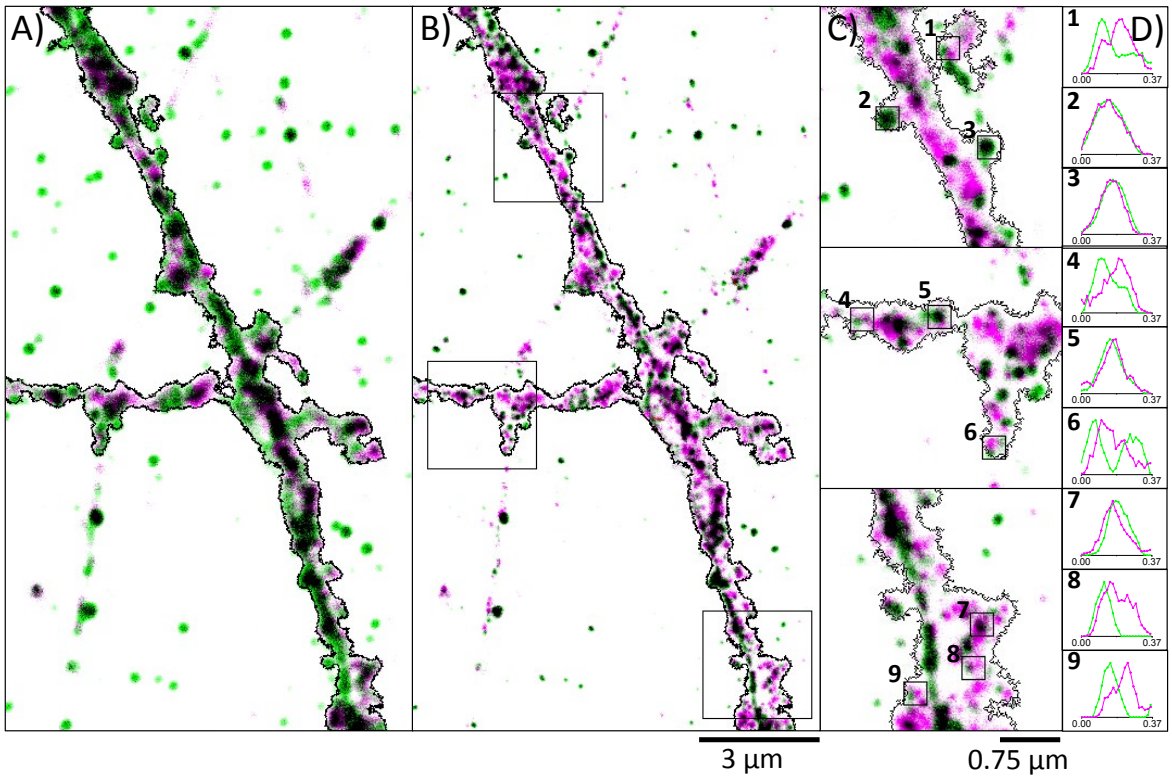


Figure S12

Table S1: Summary of quantitative estimation of nanodomain size for different markers obtained through STORM and STED microscopy

Category/Method/Parameter	Microscopy	Length (µm)
$nanodomain_{Bassoon}$	**STORM**	0.133+/-0.003 (0.124, 0.081-0.169)
$nanodomain_{PSD95}$	**STORM**	0.102+/-0.001 (0.077, 0.059-0.119)
	STED	0.140+/-0.002 (0.115, 0.092-0.163)
$nanodomain_{Dynamin}$	**STORM**	0.159+/-0.002 (0.160, 0.108-0.208)
	STED	0.140+/-0.002 (0.127, 0.105-0.158)

values indicated are Mean+/-SEM while values in brackets represent median, IQR from 25% percentile to 75% percentile

Table S2: Summary of parameters that was used to reconstruct CA1-CA3 dendrite

Parameter	Value
Density of APP	5000 molecules/µm²
Density of APP clusters	1 nanodomain/µm²

Table S3: Summary of parameters that was used to reconstruct an excitatory synapse from CA1-CA3 dendrite

Parameter	Value
Area of PSD[1]	0.26 μm^2
Area of Perisynapse[1]	1.48 μm^2
APP nanodomain density in PSD	2 nanodomain/µm²
APP nanodomain density in EZ	1 nanodomain/µm²
Probability of finding 0 APP nanodomain on a given large PSD (area 0.26 μm^2)	~0.5 (approx.)
Probability of finding 1 APP nanodomain on a given large PSD (area 0.26 μm^2)	~0.2(approx.)
Probability of finding >1 APP nanodomain on a given large PSD (area 0.26 μm^2)	~0.3(approx.)
Density of APP in PSD	7600 molecules/µm²
Density of APP in EZ	6200 molecules/µm²

Table S4: Database of primary and secondary antibodies used for immunocytochemistry

Antibody	Epitope/Isotype Specificity	Dilution	Catalogue Number	Company
Anti-PSD95	Mouse	1:500	MA1-046	Thermo Scientific
Anti-Homer1	Rabbit	1:1000	160002	Synaptic Systems
Anti-Shank2	Guinea Pig	1:500	162204	Synaptic Systems
Anti-Bassoon	Guinea Pig	1:1000	141004	Synaptic Systems
Anti-Bassoon	Mouse	1:1000	141021	Synaptic Systems
Anti-Dynamin	Mouse	1:1000	05-319	Upstate/Millipore
Anti-APP-CT	Rabbit	1:500	171610	Calbiochem/Millipore
Anti-Clathrin	Mouse	1:300	Ab2731	Abcam
Anti-BACE1	Rabbit	1:500	840101	Biolegend/Covance
Anti-APP-CT	Mouse	1:500	MAB343-C	Merck Millipore
Alexa Fluor 488	Rabbit	1:500	A11034	Life Technologies
Alexa Fluor 647	Rabbit	1:500	A21245	Life Technologies
Alexa Fluor 647	Mouse	1:500	A21236	Life Technologies
Alexa Fluor 647	Guinea Pig	1:500	A21450	Life Technologies
Alexa Fluor 568	Guinea Pig	1:500	A11075	Life Technologies
Alexa Fluor 568	Mouse	1:500	A11031	Life Technologies
Alexa Fluor 532	Mouse	1:500	A11002	Life Technologies
Alexa Fluor 594	Rabbit	1:300	A11037	Life Technologies
ATTO647N	Anti-GFP Nanobody	1:50000	gba647n-100	ChromoTek
Abberior Star Red	Mouse	1:300	2-0002-011-2	Abberior

References

1 Harris, K. M. *et al.* A resource from 3D electron microscopy of hippocampal neuropil for user training and tool development. *Sci Data* **2**, 150046, doi:10.1038/sdata.2015.46 (2015)

