Figure 3. (A) Community structure of the PSP network using the Spectral modularity method. Communities are coloured using the average gene-community probability values: bluer coloured a community is, the more probable the genes are of belonging to that community on average. ~~Respectively, all the singlet clusters are white, meaning the gene is not likely to belong to a single cluster~~. Nodes coloured magenta highlight the core PSD95 interactors, which is also highlighted magenta in the Bridgeness plot in ( C)~~. – condensed in left bottom cluster with “most probable” structure.~~ (B) We use graph entropy to compare the structure of the PSP network (0.668) against 1000 randomised Erdos-Renyi (E-R=0.989+-0.0005) and Power-Law (P-L=0.9127+-0.0032, αPSP=2.41(6)) models of similar size. Graph entropy was also used to quantify each proteins ability to inhibit or enhance propagation of signals through the PSP network when the protein was either over- or under-expressed (Teschendorff et al., 2014). ( C) Bridging proteins, estimated using the Spectral modularity algorithm, plotted against semi-local centrality (Methods) to categorise proteins in the PSP network to three important groups: Region 1, proteins that are likely to have a 'global' rather than 'local' influence in the network (also been called bottle-neck bridges (Najafi et al., 2016)[55], connector or kinless hubs (Guimera & Amaral, 2004)) lie in the range (DLG4, GRIN2B, CAMK2A, etc). Region 2, proteins likely to have an influential 'globally' and 'locally' in the network (EGFR, HRAS, NRAS, etc). Region 3, more likely to be centred within the community they're found in, but also focused on communicating with a few other specific communities (GRIN1, GRIA2-4). Region 4, proteins whose impact is mostly 'locally', primarily within one or two communities (local or party hubs [64]. (D) Correlation plot for different node centrality measures estimated for PSP network. The anti-correlation between SR\_UP and Bridgeness (-0.38) indicates protiens with higher Bridgeness values also have lower graphs entropy values when active~~, which allows the signal to pass more freely~~. (E) left: Disease-disease relationship for presynaptic (red circles), PSP (blue triangles) and PSP consensus (green squares) interactome. Where significance q-values < 0.05 is delineated by the dashed line. Schizophrenia (SCH), Autistic Spectrum Disorder (ASD), Autistic Disorder (AUT), Bipolar Disorder (BD), Intellectual Disability (ID), Alzheimer disease (AD), Epilepsy Syndrome (Epi), Parkinson's Disease (PD), Frontotemporal Dementia (FTD), Huntington's Disease (HD) and Multiple Sclerosis (MS) are considered; (E) right: randomisation studies for disease-disease pair overlap, with orange arrows showing the measured Z-score compared to 10,000 AD-HTN, PD-HTN and AD-PD randomised models. (F) We investigate the colocalization of AD and HTN on the PSP network by propagating these gene-disease associations (GDA) through the network using the ~~zeroth-order~~ Belief Propagation DC-SBM algorithm (M.E.J. Newman & A. Clauset., 2016). The colocalization of AD and HTN shared common molecular pathways in communities 31 and 43, which were also found enriched for axon guidance, stress-activated MAPK cascade and response to oxidative stress GO BP terms.