Spatial clustering of binding motifs and charges reveals conserved functional features in disordered nucleoporin sequences DAVID ANDO, MICHAEL COLVIN, University of California, Merced, MICHAEL REXACH, University of California, Santa Cruz, AJAY GOPINATHAN, University of California, Merced — The Nuclear Pore Complex (NPC) gates the only channel through which cells exchange material between the nucleus and cytoplasm. Traffic is regulated by transport receptors bound to cargo which interact with numerous of disordered phenylalanine glycine (FG) repeat containing proteins (FG nups) that line this channel. The precise physical mechanism of transport regulation has remained elusive primarily due to the difficulty in understanding the structure and dynamics of such a large assembly of interacting disordered proteins. Here we have performed a comprehensive bioinformatic analysis, specifically tailored towards disordered proteins, on thousands of nuclear pore proteins from a variety of species revealing a set of highly conserved features in the sequence structure among FG nups. Contrary to the general perception that these proteins are functionally equivalent to homogeneous polymers, we show that biophysically important features within individual nups like the separation, spatial localization and ordering along the chain of FG and charge domains are highly conserved. Our current understanding of NPC structure and function should therefore be revised to account for these common features that are functionally relevant for the underlying physical mechanism of NPC gating.

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