Predicting the Size of Large RNA Molecules ARON YOFFE, PETER PRINSEN, AJAYKUMAR GOPAL, CHARLES KNOBLER, WILLIAM GELBART, University of California, Los Angeles, AVINOAM BEN-SHAUL, Hebrew University of Jerusalem — We present a qualitative theory of how the 3D sizes of large single-stranded (ss) RNA molecules depend on their sequences. The work is motivated by the fact that the genomes of many viruses are large ssRNA molecules and that these RNAs are spontaneously packaged into small rigid protein shells. We argue there has been evolutionary pressure for the genome to have large-scale spatial properties – including an appropriate radius of gyration, \( R_g \) – that facilitate and optimize this assembly process. We introduce the average maximum ladder distance (AMLD) as a measure of the ‘extendedness’ of the RNA secondary structure. We find that the AMLDs of viral ssRNAs are smaller than those of equal-length randomly permuted sequences. By mapping these secondary structures onto simple linear or star polymer models, and using AMLD as a measure of effective contour length, we predict that the \( R_g \)s of viral RNAs are smaller than those of random sequences. More generally, we derive results for how the AMLDs of large ssRNAs, and their \( R_g \)s, scale with the number of nucleotides.