NMF initialization W (gene x topic) H (topic x cell) V (gene x cell) 0 0 0 0 1 0 0 0 0 0 0 Χ 1 0 0 0 \approx 0 0 1 0 0 0 0 Gene E 0 0 0 0 0 0 1 0 Factorization W (gene x topic) H (topic x cell) $V' \; (\mathsf{gene} \; \mathsf{x} \; \mathsf{spot})$ Gene E **NNLS** Spot topic profiles Cell type topic profiles Spot 1 Spot 2 Spot 3 Spot n **NNLS** Spot Deconvolution

17% 17%

33%

33%