

Fig. 1. Complex network representation of the human cell differentiation process. The first steps of the NHCD construction are shown in the inset of this figure. These steps, known to also be present in the formation of the majority of multicellular organisms, include the first cleavage of a fertilized egg, which is subsequently followed by the ball stage and the formation of primary germ cell layers, namely, the ectoderm, mesoderm, and endoderm. The fertilized egg is a totipotent stem cell. The blastocyst, in turn, gives rise to both trophoblast and inner cell mass. These two cells further differentiate into other types of cells, and so on. Following the above process until the fetus is fully developed yields the complex network shown in this figure. Each node, plotted as a circle, corresponds to a cell type and the edges to a differentiation step. The entire network originates from the fertilized egg (denoted by a red square) and leads to the specialized cells of a developed human. Filled circles correspond to nodes that survive at the end of the development process, while empty circles correspond to non-surviving cell types. Nodes in communities of known functions from the literature are indicated by different colors, except for those cell types with no functional annotation (see SI-Table I for association to the known functions $C1$ to $C19$ extracted from the literature).

Fig. 2. Detection of modules and the network of modules at different scales. **a**, Demonstration of the box-covering algorithm for a schematic network, following the Maximum Excluded Mass Burning algorithm in [13, 29] (see SI-Section III for full details). We cover the network with the smallest possible number of boxes for a given ℓ value. This is done in a two-stage process: *(i)* We detect the smallest possible number of box origins (shown with cyan color) that provide the maximum number of nodes (mass) in each box, according to the following optimization algorithm: We calculate the mass associated with each node, and pick the first center as the node with largest mass and mark the nodes in this box as ‘tagged’. We repeat the process from the remaining non-center nodes to identify a second center with the highest mass, and so on. *(ii)* We build the boxes through simultaneous burning from these center nodes, until the entire network is covered with boxes. For example, at $\ell = 3$ there are four boxes, where the maximum distance between any two nodes in a box is smaller than ℓ . Similarly, we can cover the same network with two boxes at $\ell = 6$. These two boxes are the result of merging two of the four boxes at $\ell = 3$. **b**, Detail of NHCD modules detected by the above box-covering algorithm for two particular functions. The algorithm detects a hierarchy of sub-modules, known functions and super-