

**Figure 3**

TNF α /NF- κ B Signaling Pathway. The TNF α /NF- κ B signaling pathway. (a) The network. (b) The Tree of Complexes representation. The flow of action is visually represented by background colors: green for activators (IKKs) and yellow for inhibitors (I κ Bs, and p100). The NIK kinase is in the first functional group (A), together with all three members of the IKK complex and p100. Functional group B includes, in addition to p100, the IKKs and two inhibitors I κ B α and I κ B β . This group is the beginning of interaction between IKKs and I κ Bs. Functional group C loses some of the IKKs, continues to show I κ B and begins to show interaction between I κ Bs and NF- κ B factors. Finally, in group E we see the entrance of NIK-independent Col-Tpl2 kinase.

nected to either D or C. The representation that maximizes the number of leaves is shown in Figure 3(b). One can clearly see the interplay between the activators and inhibitors. Proteins p105 and NF- κ B participate in the same functional groups and thus follow the same path in the tree. The same is true for the pair of proteins I κ B α and I κ B β . The Tree of Complexes captures this by grouping p105 and NF- κ B, and I κ B α and I κ B β .

Pheromone signaling pathway

The yeast *Saccharomyces cerevisiae* may be present in one of two haploid cell types, which are able to mate. Pheromones released by one type of cell bind to a specific receptor

of the other type. This triggers the activation of a scaffold protein-bound mitogen-activated protein kinase (MAPK) cascade and subsequent activation of nuclear proteins that control subsequent cellular events. In a recent paper, Spirin *et al.* [13] identified a subnetwork of proteins involved in this process within a yeast protein interaction network [21]. We analyzed this subnetwork using the COD to see if our method can extract elements of temporal ordering. The subnetwork identified by Spirin *et al.* and its Tree of Complexes representation is given in Figure 4. In this case, the protein network is not chordal. First, the COD method identifies and connects a pair of weak siblings, MKK1 and MKK2. Then, to transform the network to a chordal graph,