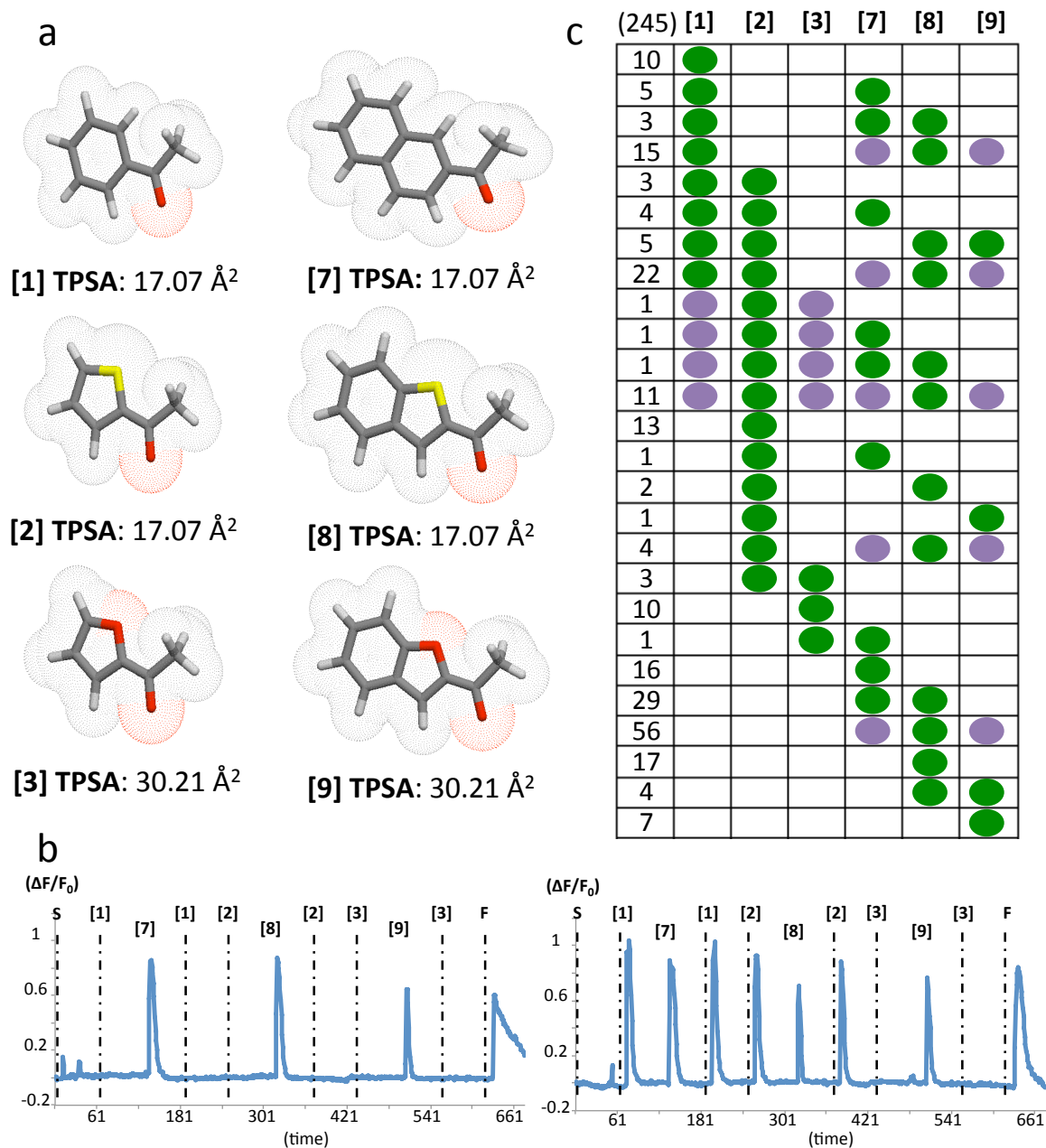


Supplementary Figure 1: Maintenance of the intra-ring PSA rule at high concentrations

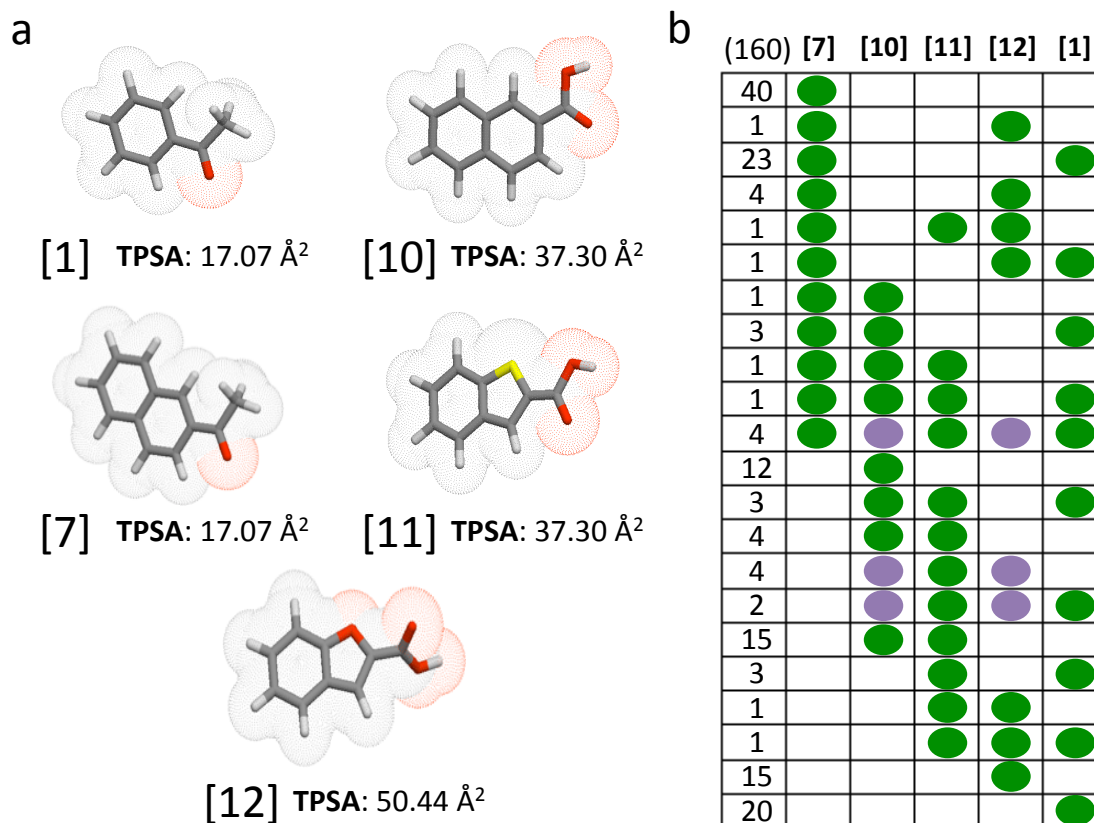
(a) Venn-Diagram of OSNs responding to 30µM each of the single-ring ketones [1], [2], and [3]. (b) Venn-Diagram of OSNs responding to 150µM each of [1], [2], and [3]. Even at the higher concentration, if an OSN responds to [1] and [3] it always responds to [2]. OSNs were counted and converted into surface area for each response combination using the eulerAPE free software. The number of OSNs responding with that pattern is indicated in that sector. [1]: acetophenone, [2]: 2-acetylthiophene, [3]: 2-acetylfuran. Nb: total number of viable OSNs screened.



Supplementary Figure 2: Responses of dissociated OSNs to P2 odorants in Calcium Imaging.

(a) 3D-representation of Panel 2 odorants, following the scheme outlined in Figure 1. (b) Calcium imaging traces of three different OSNs responding to Panel 2 odorants. (c) 245 OSNs out of 926 viable OSNs responded to at least one

Panel 2 odorant, leading to 26 distinct binary response patterns. The numbers indicate how often a particular response pattern was observed. Green dot: activation of the OSN by the corresponding odorant. The OSNs that respond to [1] and [3] always respond to [2] (Purple dot). The OSNs that respond to [7] and [9] always respond to [8] (Purple dot) S: dimethyl sulfoxide, F: forskolin, [1]: acetophenone, [2]: 2-acetylthiophene, [3]: 2-acetylfuran, [7]: 2-acetonaphthone, [8]: 2-acetyl benzothiophene [9]: 2-benzofuranyl methyl ketone.



Supplementary Figure 3: Responses of dissociated OSNs to Panel 3

odorants in Calcium Imaging.

(a) 3D-representation of Panel 2 odorants, following the scheme outlined in

Figure 1. (b) 160 OSNs out of 308 viable OSNs responded to at least one

Panel 3 odorant, leading to 22 distinct binary response patterns. The

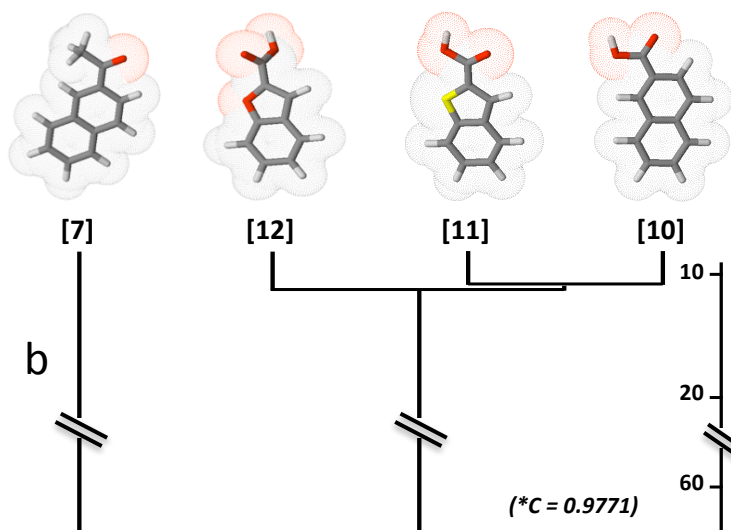
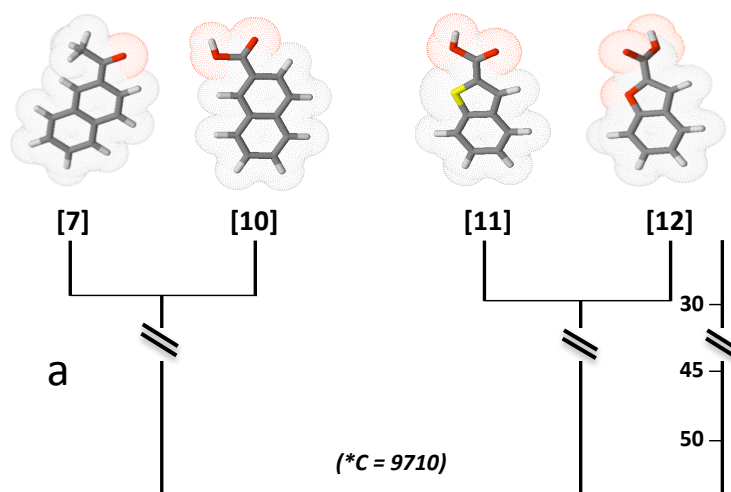
numbers indicate how often a particular response pattern was observed.

Green dot: activation of the OSN by the corresponding odorant. The OSNs

that respond to [10] and [12] always respond to [11] (Purple dot). [1]:

acetophenone, [7]: 2-acetonaphthone, [10]: 2-naphthoic acid, [11]:

benzo[b]thiophene-2-carboxylic acid, [12]: benzo[b]furan-2-carboxylic acid.



Supplementary Figure 4: Hierarchical Clustering Analysis of Panel 3

odorants

(a) Panel 3 odorants clustered according to chemical similarity as evaluated by 1,666 molecular descriptors downloaded through the e-dragon applet. Normalized descriptors were used for calculating Euclidian distances. (b) Panel 3 odorants clustered according to biological response similarity as based on calcium imaging of dissociated OSNs. *Cophenetic correlation coefficient. See online methods for details of dendrogram generation. [7]: 2-

acetonaphthone, [10]: 2-naphthoic acid, [11]: benzo[b]thiophene-2-carboxylic acid, [12]: benzo[b]furan-2-carboxylic acid.