

Pre-nucleation clusters in liquid benzoic acid

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INTRODUCTION

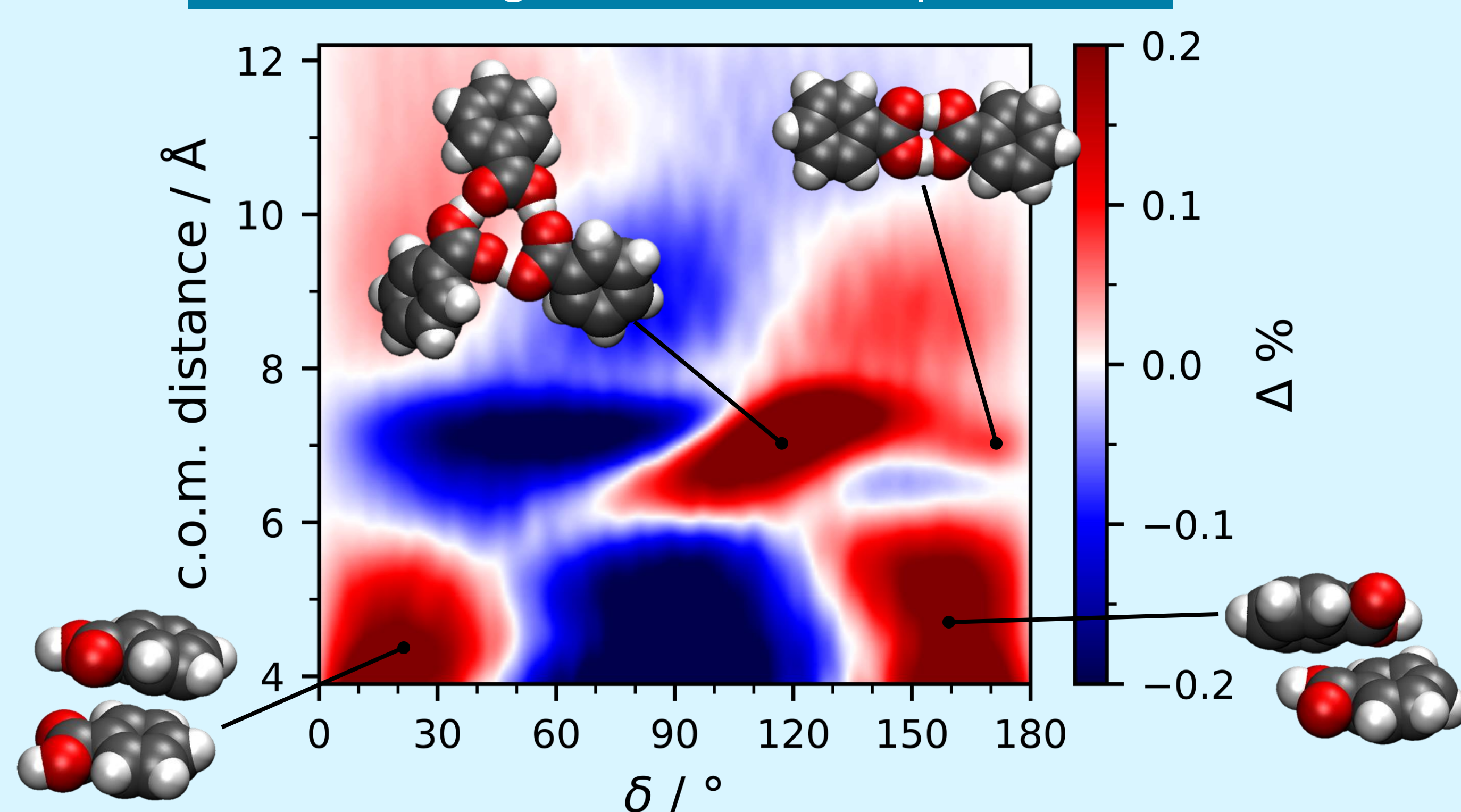
Carboxylic acids play a pivotal role in crystal engineering, owing to their ability to form hydrogen-bonded cyclic dimers, which route the crystallization process. **Benzoic acid (BZA)** is the prototype of aromatic carboxylic acids. Recent results from our group [1] point out that cyclic **dimers**, that are found also in the $P2_1/c$ crystal, are overcome by **trimers** and coexist with greater HB clusters in the liquid. Thus, a question arises – when and why does the structure of the liquid change, so that nucleation of BZA dimers can occur?

METHODS

To gain insights on the problem, we investigate liquid benzoic acid as a function of T by means of **molecular dynamics**, with the free **MiCMoS** platform [2-5]. 3 ns long NpT simulations are performed on pre-equilibrated simulation boxes composed of 432 BZA molecules, below, close to, and above the melting point (395 K), and the last 0.5 ns are analyzed. We propose novel structure-free energy-based **criteria** to highlight relevant **sub-critical clusters (SCCs)** that might precede nucleation [6].

RESULTS AND DISCUSSION

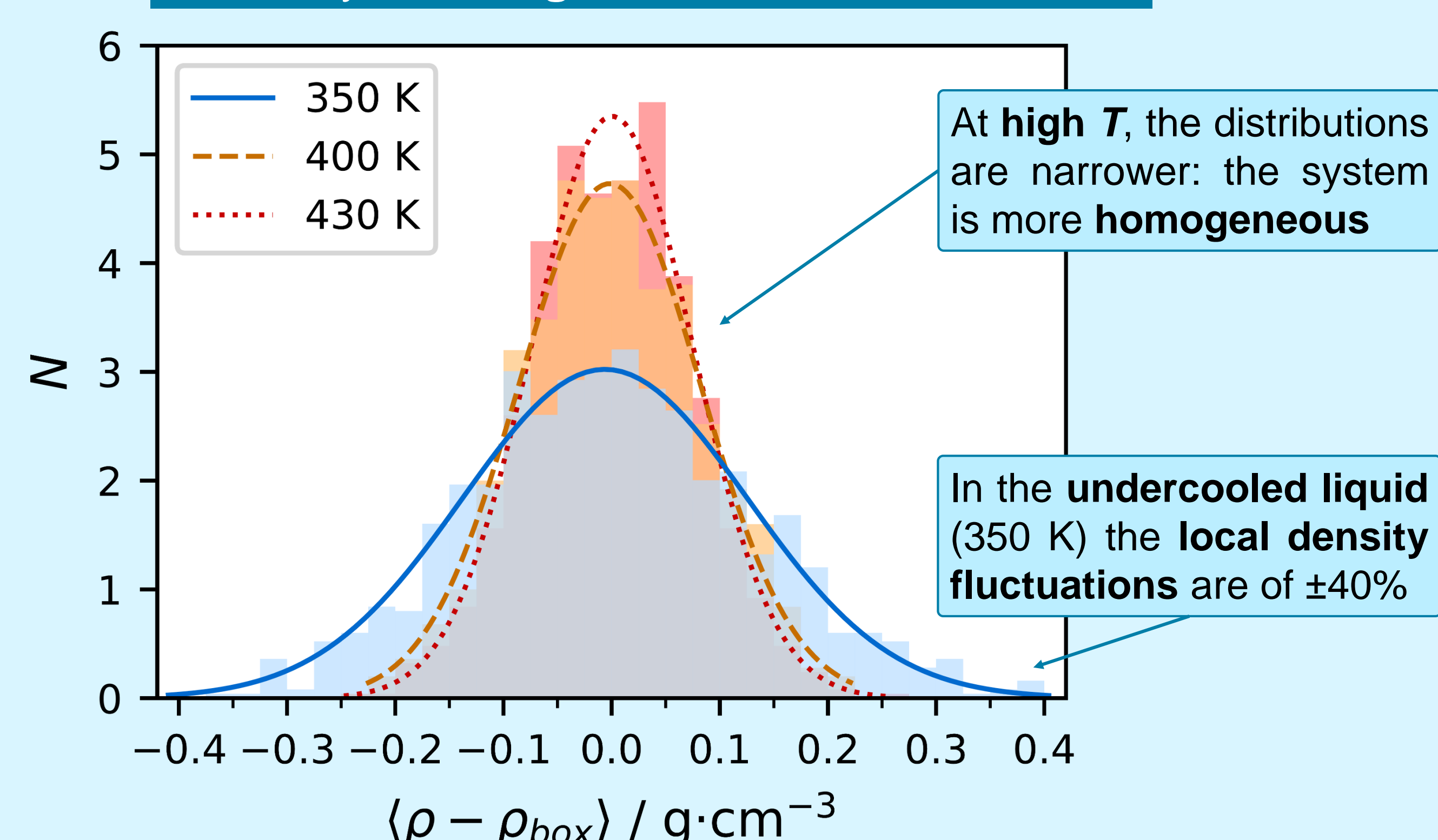
Average structure of the liquid



Red regions indicate **interaction modes** with a higher frequency than a random distribution

However, the heatmap doesn't capture nanoscale inhomogeneities of the system like SCCs

Density inhomogeneities at the nanoscale



At **high T**, the distributions are narrower: the system is more **homogeneous**

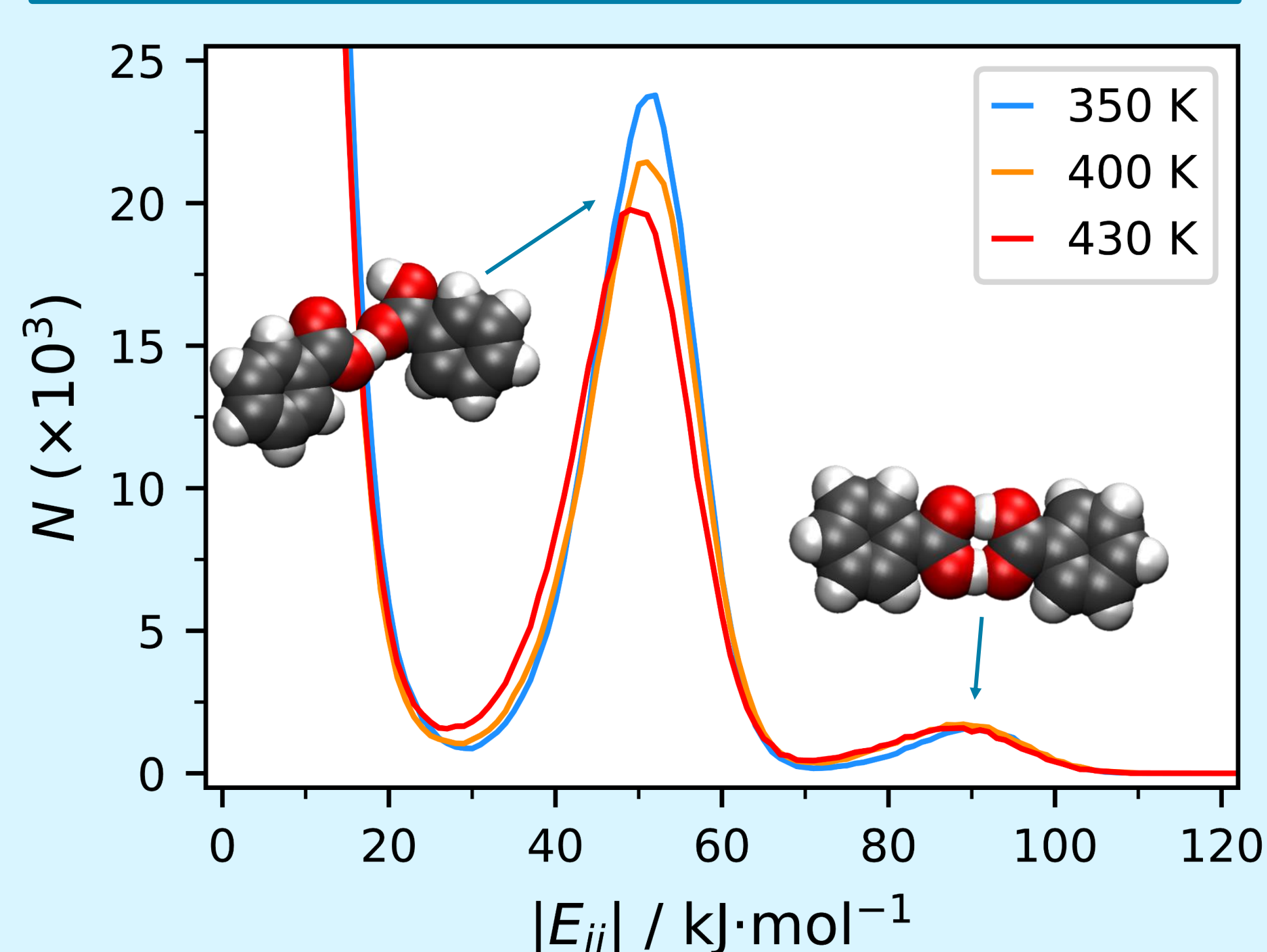
In the **undercooled liquid** (350 K) the **local density fluctuations** are of $\pm 40\%$

Average of the difference between the density of each of the **1000 voxels** within the simulation box, ρ , and the global density, ρ_{box}

1 $E_{ij} \leq E_{\text{cut}}$

SCCs are **aggregates** of bonded molecules. Two molecules are considered bonded if their **interaction energy** is more negative than a cutoff threshold E_{cut}

Distribution of pair interaction energies



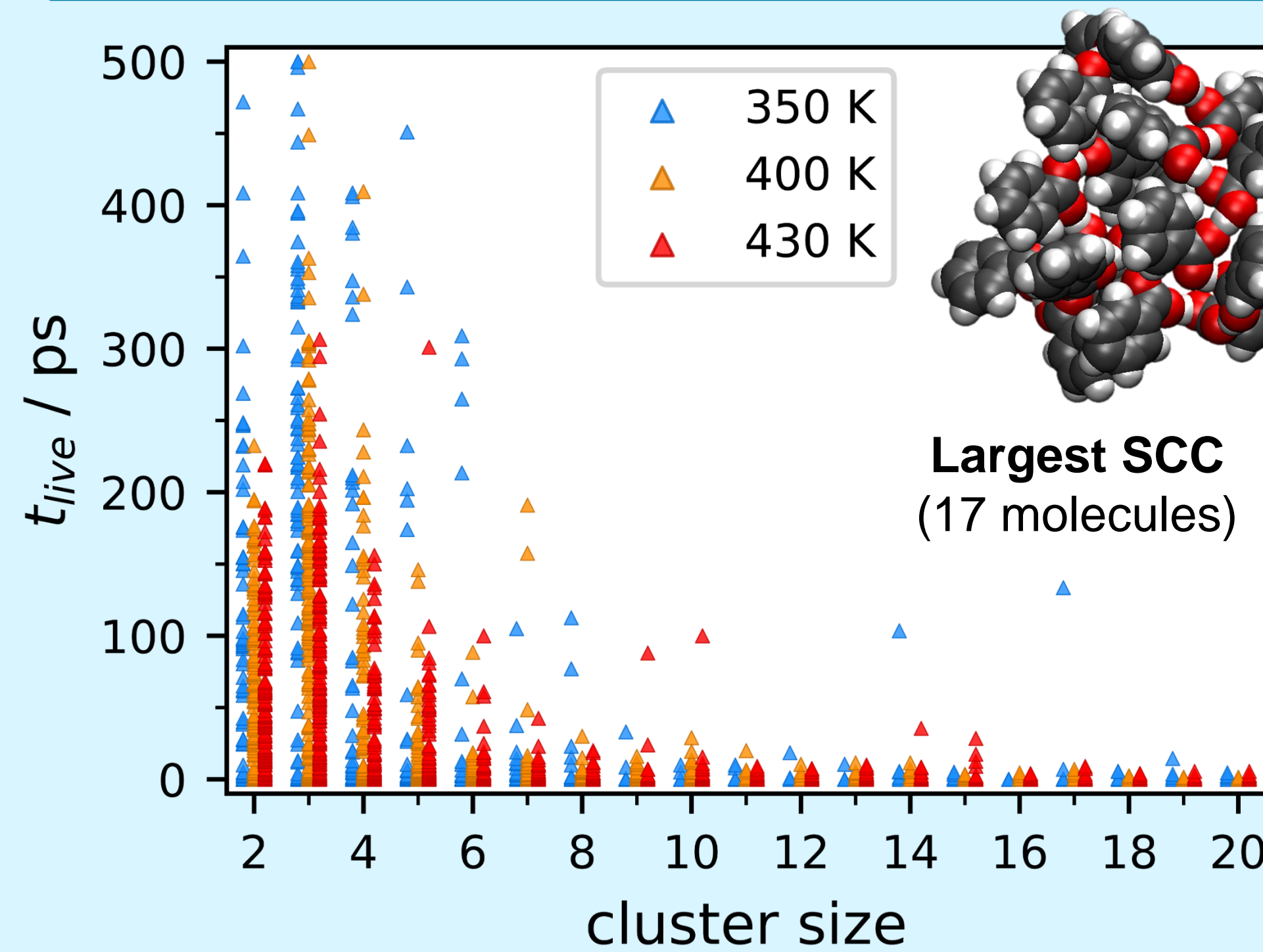
$$E_{\text{cut}} = -25 \text{ kJ mol}^{-1}$$

E_{cut} was chosen to take into account both single and double HBs between BZA molecules

2 $t_{\text{live}} > \Delta t$

SCCs must be **persistent**. Their **lifetime** t_{live} should be greater than **thermal fluctuations**, estimated by averaging the duration of molecule-molecule interactions

Maximum lifetime of independent clusters



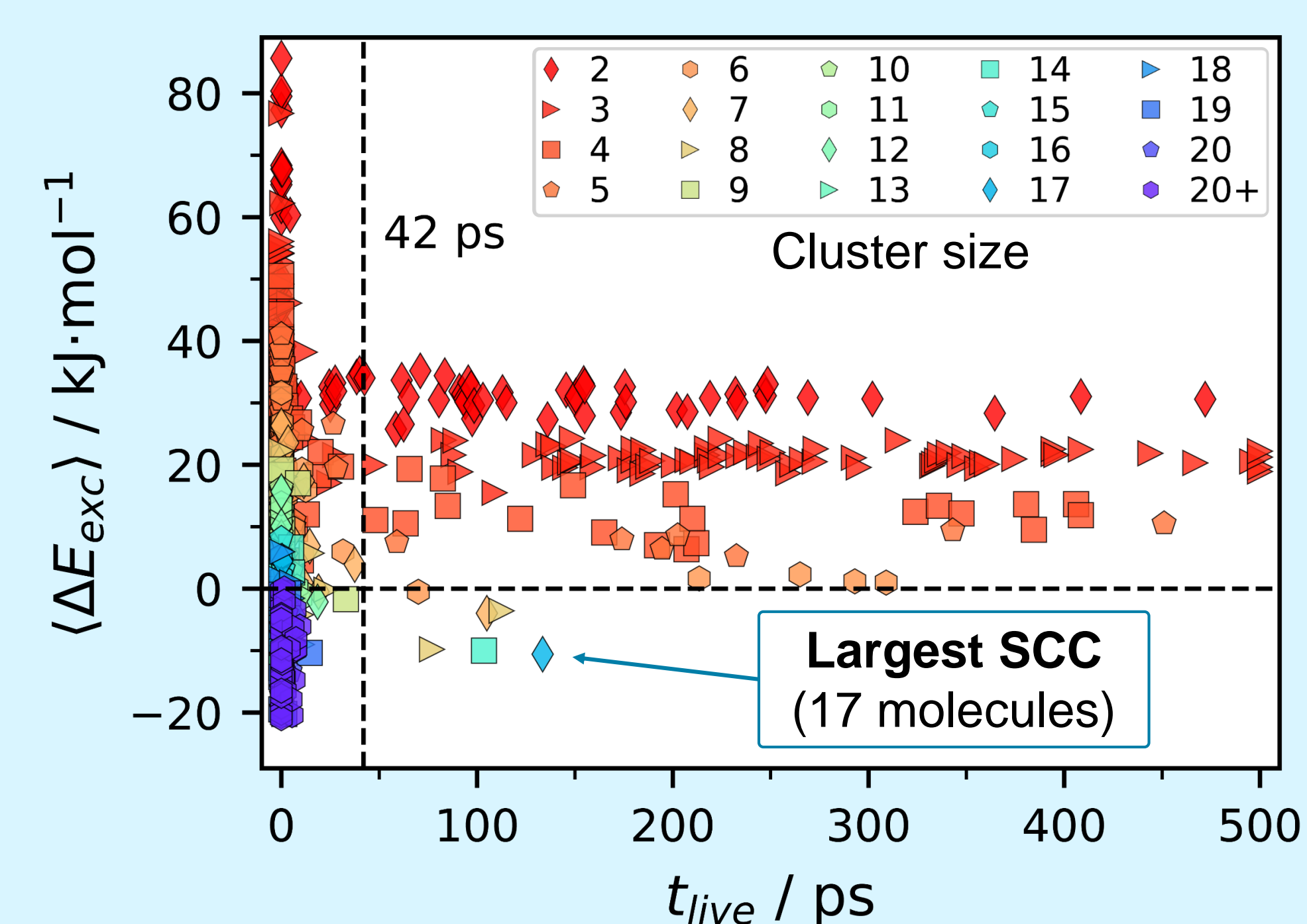
$$\begin{aligned} \Delta t(350 \text{ K}) &= 42 \text{ ps} \\ \Delta t(400 \text{ K}) &= 30 \text{ ps} \\ \Delta t(430 \text{ K}) &= 22 \text{ ps} \end{aligned}$$

The lifetime of thermal fluctuations is longer at low T and shorter at high T

3 $\langle \Delta E_{\text{exc}} \rangle < 0$

SCCs must be **stable**. We introduce the concept of **excess energy**, that must be negative, on average, over the entire lifetime of the aggregate.

Average excess energy and lifetime of independent clusters



$$\Delta E_{\text{exc}} = E_A - E_{AO}$$

Cohesive energy of the aggregate

Interaction energy with other molecules

CONCLUSION

Our tool allows to single out **nanoscale inhomogeneities** that impact on the average structure of the liquid. We find **sub-critical clusters** as large as **17 molecules**, that persist for more than **100 ps** in undercooled BZA and display an inner structure intermediate between the liquid and the crystal, with **HB chains** and intermittent **stacking interactions**. We hypothesise that, on longer time scales, persistent nanoscale inhomogeneities could set up a favourable environment that enhances the probability of nucleation, in agreement with non-classical theories [7].

REFERENCE

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- [7] Zhang, X. (2020) *Crystallization via Nonclassical Pathways*