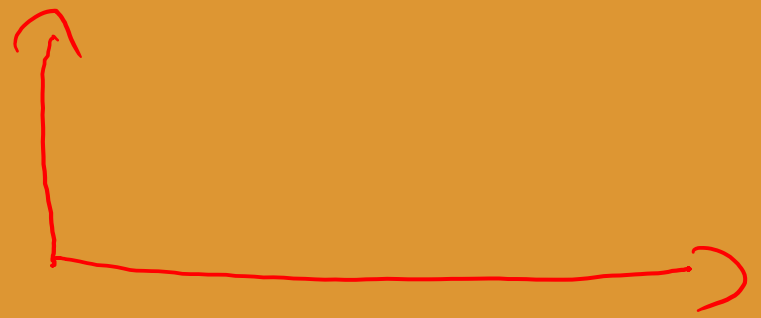
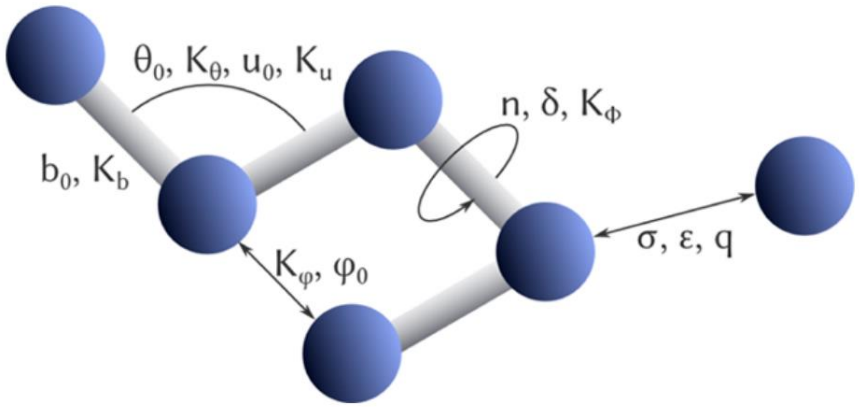
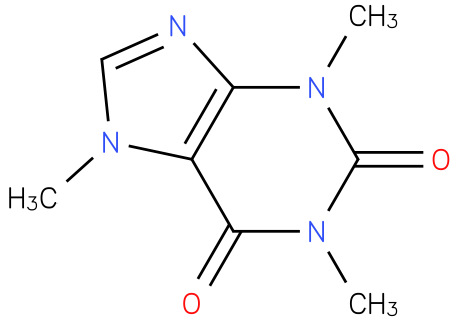
Classical Force Fields



Parameterisation

$$E = \sum_{\text{bonds}} K_b(b - b_0)^2 + \sum_{\text{angles}} K_\theta(\theta - \theta_0)^2$$
$$+ \sum_{\text{dihedrals}} K_\phi(1 + \cos(n\phi - \delta))$$
$$+ \sum_{\text{improper}} K_\varphi(\varphi - \varphi_0)^2 + \sum_{\text{Urey-Bradley}} K_u(u - u_0)^2$$
$$+ \sum_{i<j} 4\varepsilon\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right] + \sum_{i<j} \frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}}$$

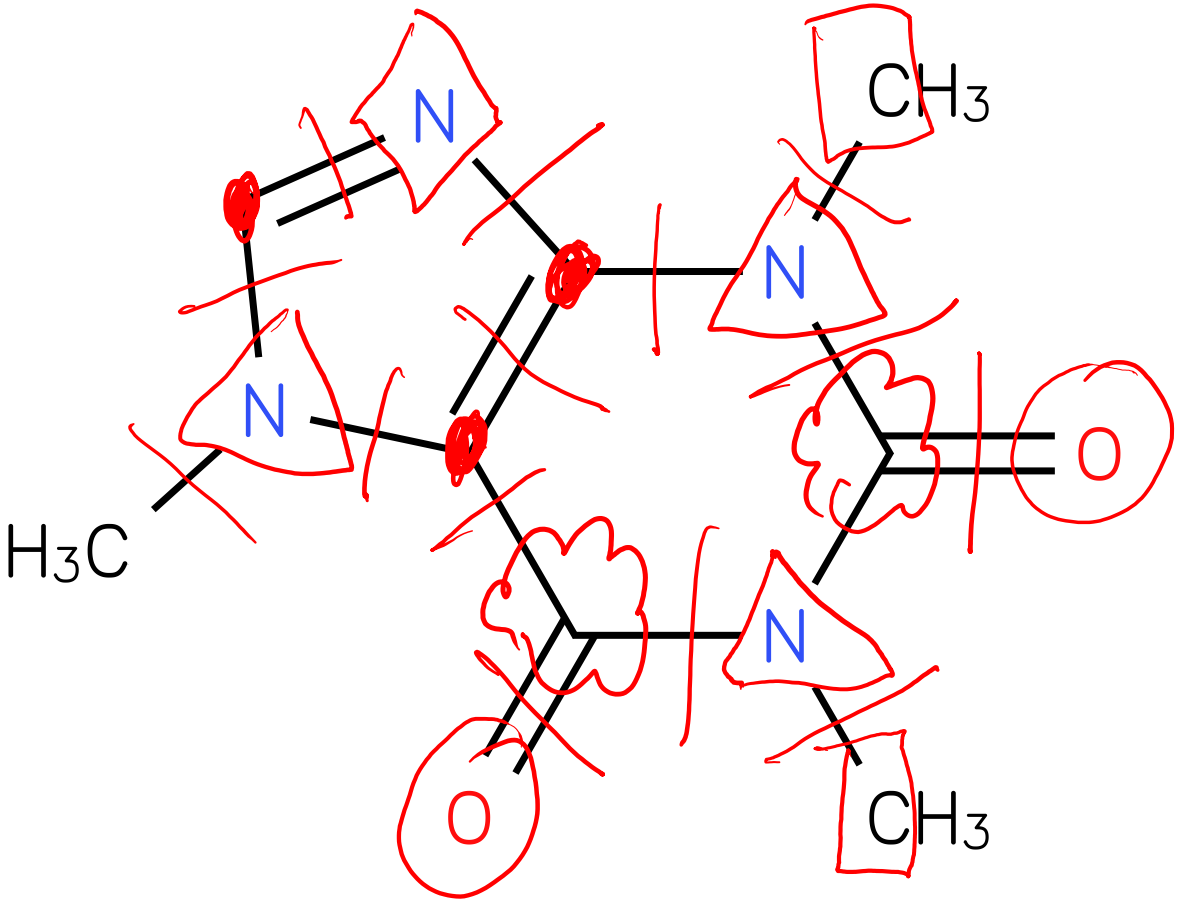


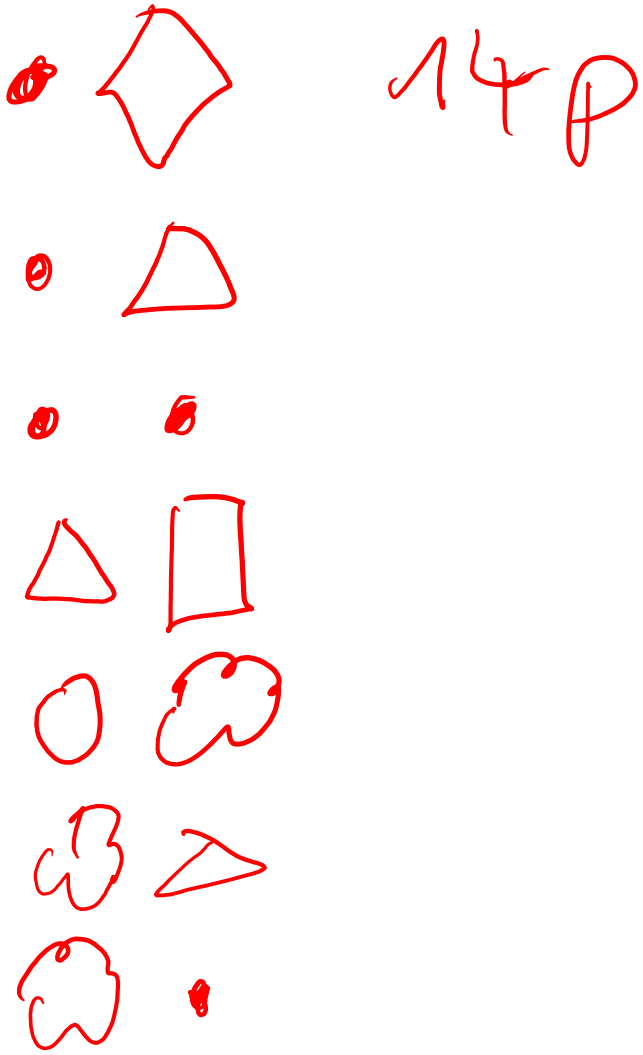


- Elements become *atom types*
- Let's find all unique bonds together...

Parameterisation

Let's find all unique bonds together...

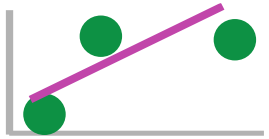




... + angles, + dihedrals

Parametrisation: Challenges

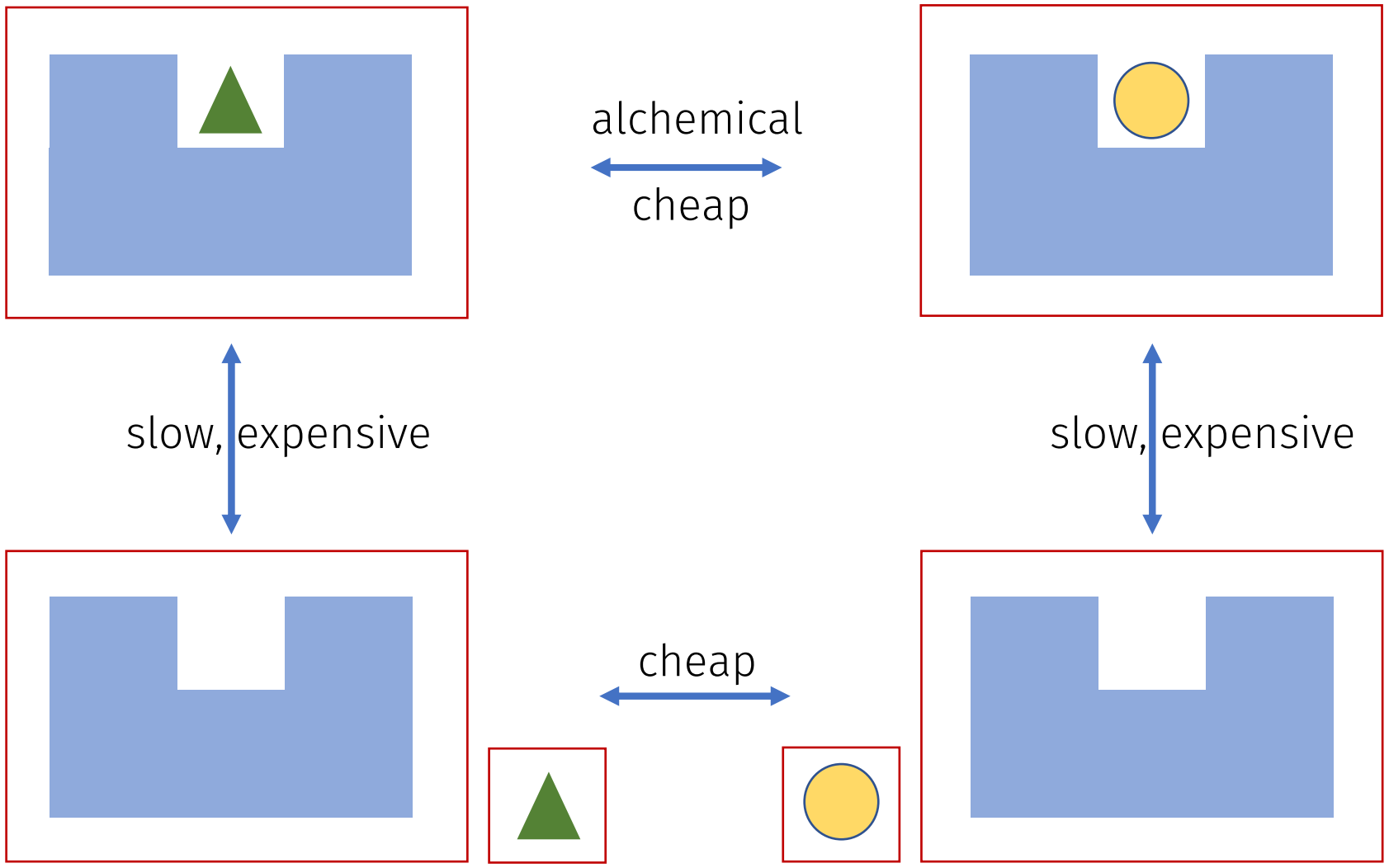
- Fixed, parametric form — High bias, sub-selects chemical space



- Atom typing — Non-unique, rarely fully automatic
  - e.g. sp2, sp3 carbons – but how to detect them? It's a (vague) quantum definition…
- New compound, new parametrization — Restricts curiosity
  - More of the same: easy, try something new: hard
- Manually but assisted fitting against
  - DFT — Hard to match geometries, hardly possible to get ensembles
  - Experiment — Rarely possible to match both ensemble and geometries

Classical Use Case: Alchemical changes

Alchemical changes



Theory

- Two states: i, j
- NVT ensemble, equilibrated

$$\Delta A_{ij} \equiv -k_B T \ln \frac{Q_j}{Q_i}$$

$$Q_i \equiv \int_{\Gamma_i} \exp\left[-\frac{U_i(\vec{q})}{k_B T}\right] d\vec{q}$$

Helmholtz free energy

Temperature

Partition function

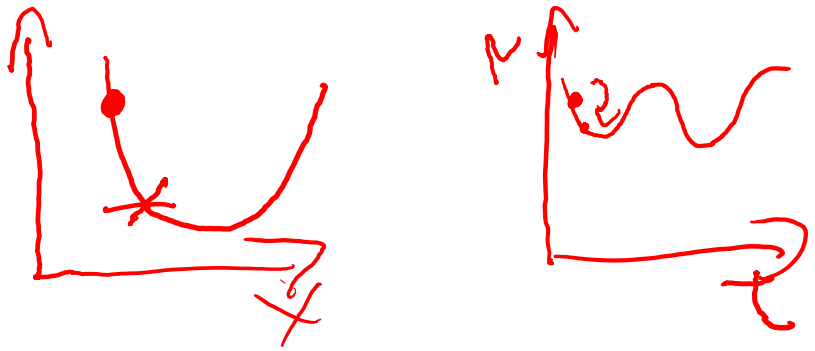
Phase space

Potential energy

Theory: Molecular dynamics

- Need: ensemble average
- Ergodicity: Time average = Ensemble average
- Propagate in small steps (~fs) explicit positions from repeated force evaluations

- Challenges
  - Numerically stable
  - Time reversibility
  - Thermostats / Barostats
  - Equilibration



Questions:

- Why are classical calculations typically time-reversible but quantum mechanical calculations are not?
- What does it mean if a setup is lacking time-reversibility?