Energy-Structure-Function maps for functional molecular crystals

UK-QSAR & MGMS, Structure-Activity Relationships
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Crystal engineering

Understanding relationship between molecular structure and crystal packing

molecule
(1,4-bis-p-cyano-styrylbenzene)

crystal structure

property: Fluorescence
Single crystal under UV (365 nm)

“design” of materials with targeted properties

Structure-property relationships

and
The challenge of design in molecular crystals

Target property (e.g. luminescence)

$\lambda_{\text{emission}}^{\text{max}}$ 532 nm

generally a function of intrinsic molecular properties

The challenge of design in molecular crystals

target property (e.g. luminescence)

\[ \lambda_{\text{emission}}^{\text{max}} = 532 \text{ nm} \]

\[ \lambda_{\text{emission}} = 462 \text{ nm} \]


generally a function of intrinsic molecular properties

and

solid state arrangement
The challenge of design in molecular crystals

Our challenge

- Molecular synthesis is well developed, relatively reliable, and transferable routes to creating chemical functionality
  - But what should we synthesise?

- Unpredictability of crystallisation - self-assembly process
  - What will be the solid state structure of molecule X?

- Structure-function relationship can be complex
  - What packing arrangement do we want?

\[
\lambda_{\text{emission}}^{\text{max}} \quad 532 \text{ nm} \quad 462 \text{ nm}
\]

(target property (e.g. luminescence)


generally a function of intrinsic molecular properties and solid state arrangement
Crystal structure prediction (CSP)

What we hope to get out of CSP

- A complete (as possible) set of the possible crystalline structures for a given molecule (or mixture of molecules).
- Their relative stabilities.
  - lattice energies
  - recent progress: quasi-harmonic free energies: P, T-dependence of structures and relative stabilities
- Structures that are “accurate enough”
  - as models for structure determination
  - for property prediction
Crystal structure prediction (CSP)

Generate crystal structures with all low energy conformers
- sample: molecular positions & orientations, unit cell dimensions
- allow different space group symmetries

Lattice energy minimisation
- intermolecular: anisotropic atom-atom force fields
- DFT intramolecular

Low-discrepancy sampling

Global Lattice Energy Explorer

DMACRYS
PCCP, 12, 8478 (2010)
Crystal structure prediction (CSP)

Generate crystal structures with all low energy conformers.

- Sample: molecular positions & orientations, unit cell dimensions
- Allow different space group symmetries

Low-discrepancy sampling

Global Lattice Energy Explorer


Conformer searching with QM methods

Relative lattice energy (kJ/mol)

DFT intramolecular

DMACRYS

PCCP, 12, 8478 (2010)

Density (g/cm³)

Grey = X-ray diffraction determined structure of thermodynamically stable form

Black = global minimum from CSP

Grey = X-ray diffraction determined structure of thermodynamically stable form

Black = global minimum from CSP

Distributions of energy minima

Day et al, PCCP (2007), 9, 1693

Nyman & Day, CrystEngComm (2015), 17, 5154

crystal packing is susceptible to small chemical changes
CSP in materials exploration

Case study: computer-guided discovery of a porous molecular crystal
Target property: **Methane storage**

- Volumetric deliverable capacity is most relevant metric
- **Deliverable capacity** = storage capacity – residual capacity
- Records: 180–190 v STP/v
- > 150 v STP/v is ‘good’

Methane deliverable capacities for the best reported materials (all are metal organic frameworks)

<table>
<thead>
<tr>
<th>Material</th>
<th>Uptake at 65 bar (v STP/v)</th>
<th>Deliverable capacity (v STP/v)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>HKUST-1</td>
<td>262</td>
<td>181</td>
<td>b</td>
</tr>
<tr>
<td>MOF-5</td>
<td>215</td>
<td>185</td>
<td>b</td>
</tr>
<tr>
<td>PCN-14</td>
<td>240</td>
<td>160</td>
<td>b</td>
</tr>
<tr>
<td>Mg-MOF-74</td>
<td>230</td>
<td>143</td>
<td>b</td>
</tr>
<tr>
<td>Ni-MOF-74</td>
<td>259</td>
<td>141</td>
<td>b</td>
</tr>
<tr>
<td>Co-MOF-74</td>
<td>249</td>
<td>136</td>
<td>b</td>
</tr>
<tr>
<td>NU-125</td>
<td>232</td>
<td>183</td>
<td>c</td>
</tr>
<tr>
<td>NU-111</td>
<td>206</td>
<td>179</td>
<td>c</td>
</tr>
<tr>
<td>UTSA-20</td>
<td>230</td>
<td>170</td>
<td>c</td>
</tr>
<tr>
<td>UTSA-80a</td>
<td>233</td>
<td>174</td>
<td>d</td>
</tr>
<tr>
<td>Co(bdp)</td>
<td>203</td>
<td>197</td>
<td>e</td>
</tr>
</tbody>
</table>

*a* The difference in uptake between 65 bar and 5.8 bar [for T2, HKUST-1, MOF-5, & Co(bdp)] or 5 bar (for the rest).  
Design Hypothesis – rigid molecular core + strong, directional interactions to form porous networks

Question – which of a set of candidate molecules is most likely to give properties we require for a given application?

Nature (2017), 543, 657-664
Porous crystal discovery: energy – density distributions

Porous crystal discovery: energy – density distributions


Grand canonical Monte Carlo on each structure: CH$_4$ uptake at storage and depletion pressures
Energy-structure-function maps: methane deliverable capacity

At a glance, these show that T2 and P2 are more promising for methane storage than T0, T1, S1, P1, P1M, S2, P2M (not shown).
Porous crystal discovery: **T2 solvent stabilisation**

Some, *but not all*, porous structures can be stabilised with respect to the global minimum. Stabilising influence of different solvents varies between porous structures → possible solvent selectivity.
T2 synthesis and crystallisation screening

Structures found during crystallisation screening:
- T2-α
- T2-β
- T2-γ
- T2-δ

All can be desolvated, if done carefully.

predicted (red) vs X-ray structure (blue)

Density (g cm⁻³):
- T2-α: 0.412 g cm⁻³
- T2-β: 0.412 g cm⁻³
- T2-γ: 0.412 g cm⁻³
- T2-δ: 0.412 g cm⁻³

Pore size: 1.99 nm

Relative lattice energy (kJ mol⁻¹):
- T2-α
- T2-β
- T2-γ
- T2-δ

post-publication
Sublimation at
P = 1 x 10⁻³ hPa (10⁻⁶ bar)
T= 700 °C

RMSD₃₀ = 0.135 Å

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Cambridge Structural Database density distribution
Molecular crystals, C, N, O, H

Nature (2017), 543, 657-664
Sorption isotherms can be predicted \textit{a priori}.

\textbf{T2 experimental vs predicted properties}

Increasing pressure

\textit{expt vs grand canonical Monte Carlo}

![Graph showing CH$_4$ uptake vs pressure for different T2 structures.](image)
ESF maps for gas selectivity

Energy-Structure-Function maps can be produced for any target property that is calculable from crystal structure.

$C_3H_8 / CH_4$ selectivity prediction

![Graph showing energy vs density for $C_3H_8/CH_4$ selectivity and IAST selectivity](image-url)
Electron or hole transport in molecular crystals

High mobility organic semiconductors

High mobilities often seen in polyaromatic hydrocarbons, *eg.* pentacene.

**hoping rate**

\[
k = \left(\frac{t^2}{\hbar}\right)\left(\frac{\pi}{\lambda kT}\right)^{\frac{1}{2}}e^{-\frac{\lambda}{4kT}} \rightarrow \text{mobility}
\]

\(\lambda = \text{molecular reorganisation energy: molecular property}\)

\(t = \text{electronic coupling (transfer integral): depends on packing}\)
Pentacene hole mobility landscape

Extracting structure-property relationships

Effects of substitution on the packing landscape

Recall pentacene mobility results:

Effects of substitution on the packing landscape

The mobility landscape is very sensitive to molecular and crystal structure.

Towards higher-throughput ESF map generation

- CSP calculations on rigid, pentacene-sized molecules now < 1 day (using ~200 CPUs)
- Property predictions become the limiting step
- Machine learning looks promising for accelerating property predictions.

\[ k = \left( \frac{t^2}{\hbar} \right) \left( \frac{\pi}{\lambda kT} \right)^{\frac{1}{2}} e^{\left( -\frac{\lambda}{4kT} \right)} \]

\[ \text{Prediction MAE for the TI [eV]} \]

Percentage of Training Dimers

SOAP descriptor and structural similarity

$$\rho_{\chi^\alpha}^A(r) = \sum_{k \in A^\alpha} \exp \left( \frac{(r - r_k)^2}{2\sigma^2} \right) f_{r_k}(|r_k|).$$

$$k\left(\chi^A_i, \chi^B_j\right) = \int_{\text{SO}(3)} \left| \sum_{\alpha} \int_{\mathbb{R}^3} \rho_{\chi^\alpha}^A(r) \rho_{\chi^\beta}^B(r) dr \right|^2 d\hat{R},$$

$$C_{ij}(A, B) = k\left(\chi^A_i, \chi^B_j\right) / \sqrt{k\left(\chi^A_i, \chi^A_i\right) k\left(\chi^B_j, \chi^B_j\right)}.$$
Summary

• Crystal structure prediction methods are finding an increasing role in materials discovery, particularly where combined with property prediction calculations.

• Energy-structure-function maps: at-a-glance assessment of possible properties for a molecule

• Based on predictive calculations (CSP + property simulations).
  • Can study hypothetical molecules → helps prioritise synthesis

• Could be used for any calculable property
  • Use for pharmaceutical materials: property variability across the polymorphic landscape (mechanical properties, crystal habit)
  • Crystal structure landscapes are rich with structure-property relationship information: many crystal structures of the same molecule.
  • Structure classification methods (SOAP, HDBSCAN*) will help develop solid-state structure-property relationships.
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