Crystals 2020
The 2nd International Online Conference on Crystals
10–20 NOVEMBER 2020 | ONLINE
crystals MDPI

Quantum chemical modeling of molecular crystal deformations

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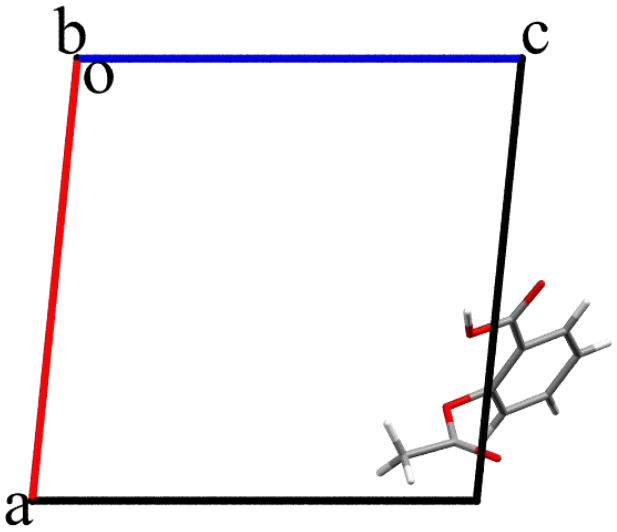
[3] Laboratoire de Spectroscopie pour les Interactions, la Réactivité et L'environnement (UMR CNRS A8516), Université de Lille, 59655, Villeneuve d'Ascq Cedex, France.
* Corresponding author: vakslerea@gmail.com



Université de Lille


Energy-vector diagrams for visualization



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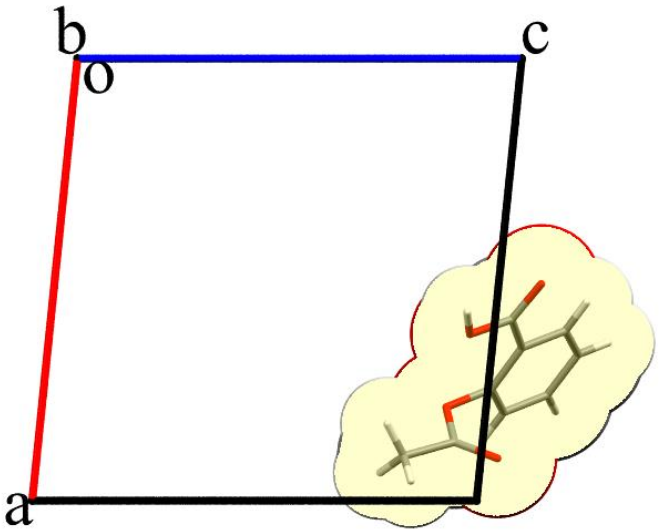

Search for neighbors:

$$D_{ij} \leq VdW_i^{im} + ?$$

where D_{ij} – distance between the i and j atoms of the initial molecule and n*th* neighbor

VdW_i^{im} - van der Waals radius of the i atom of the initial molecule

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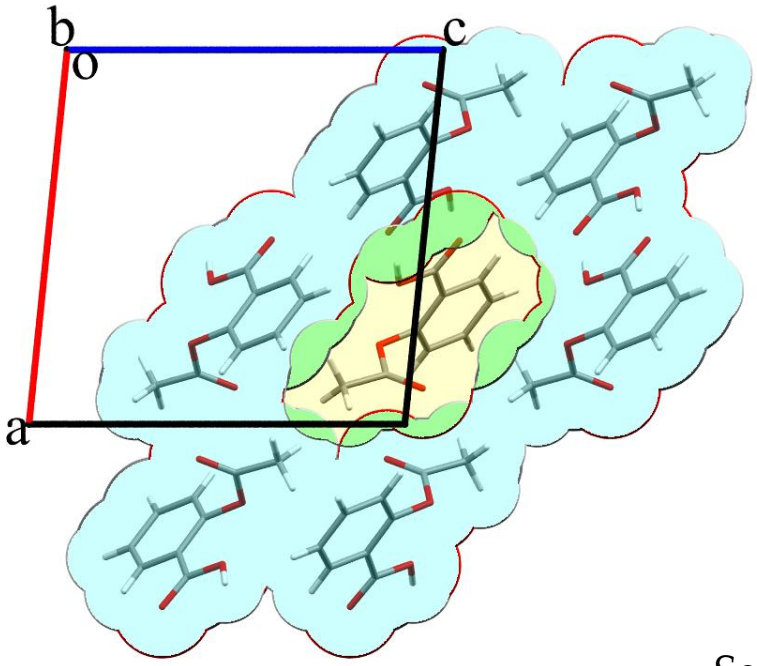

Search for neighbors:

$$D_{ij} \leq VdW_i^{im} + VdW_j^{nm} + 1$$

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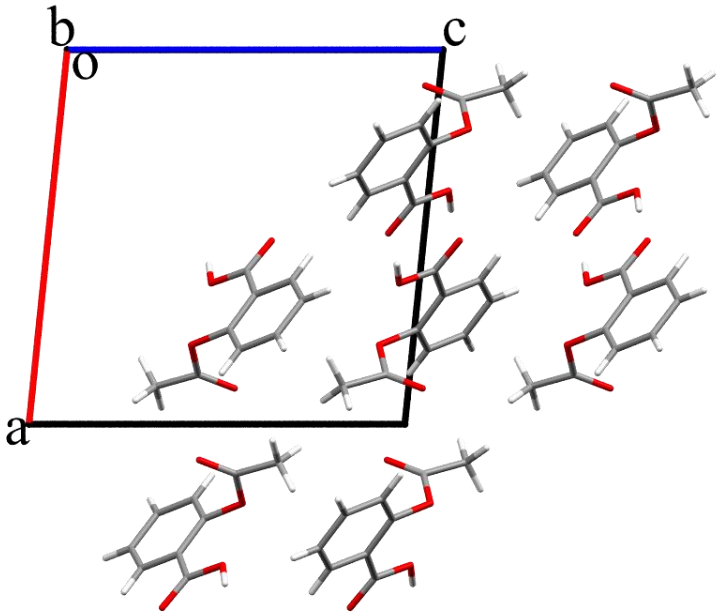

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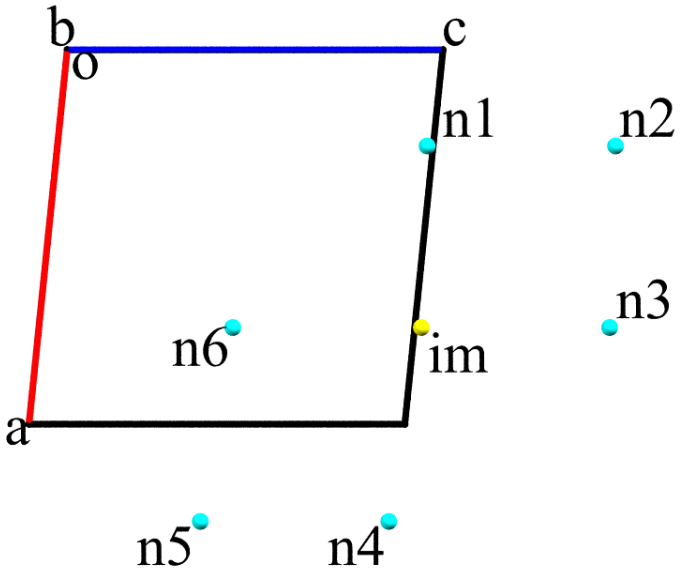

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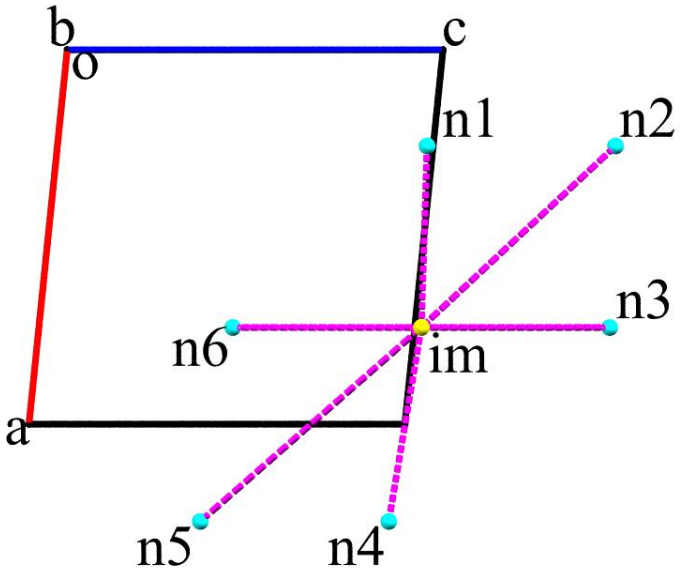

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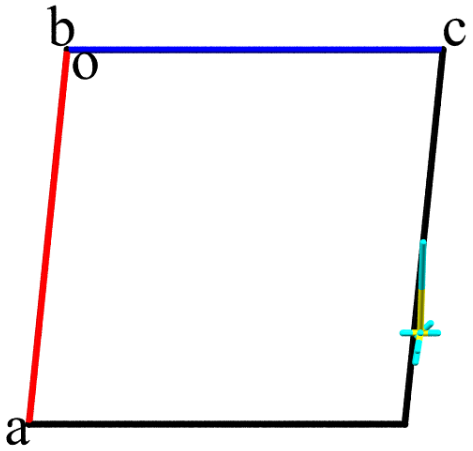
E_n – interaction energy between between n*th* neighbor and the initial molecule

E_{str} – energy of the strongest pairwise interaction in crystal



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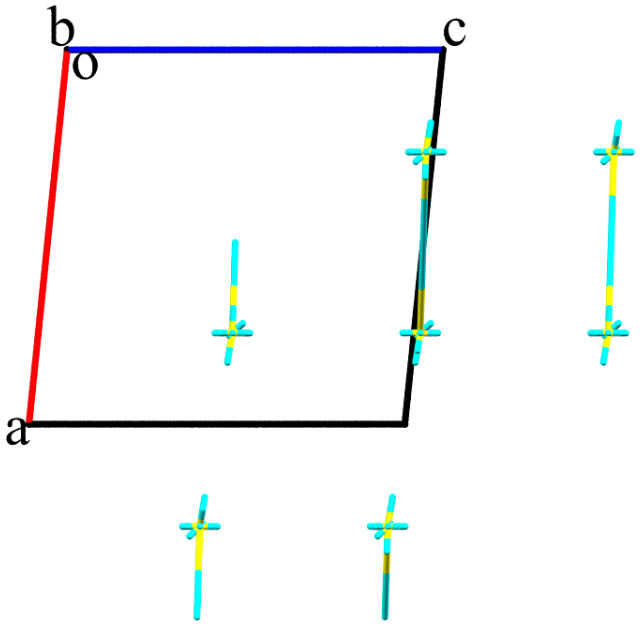

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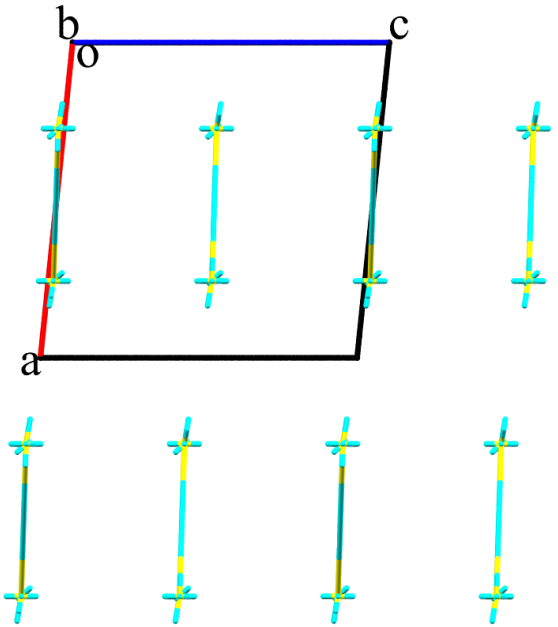

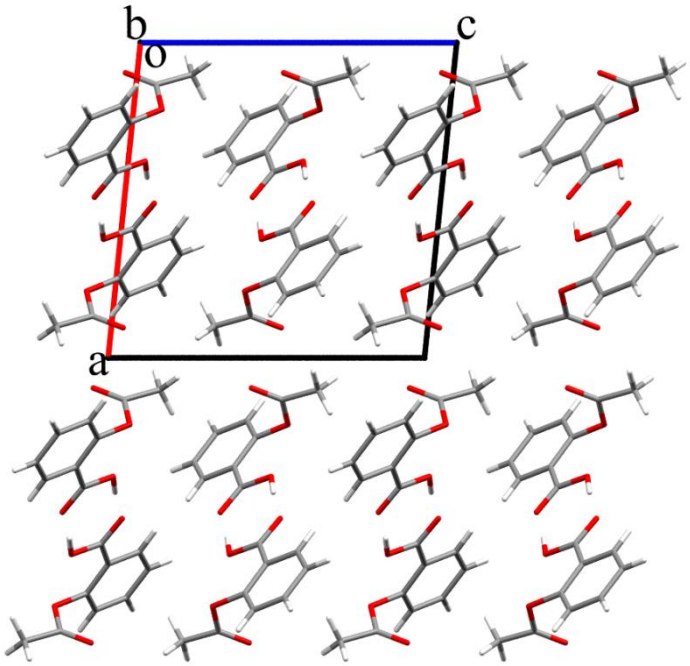

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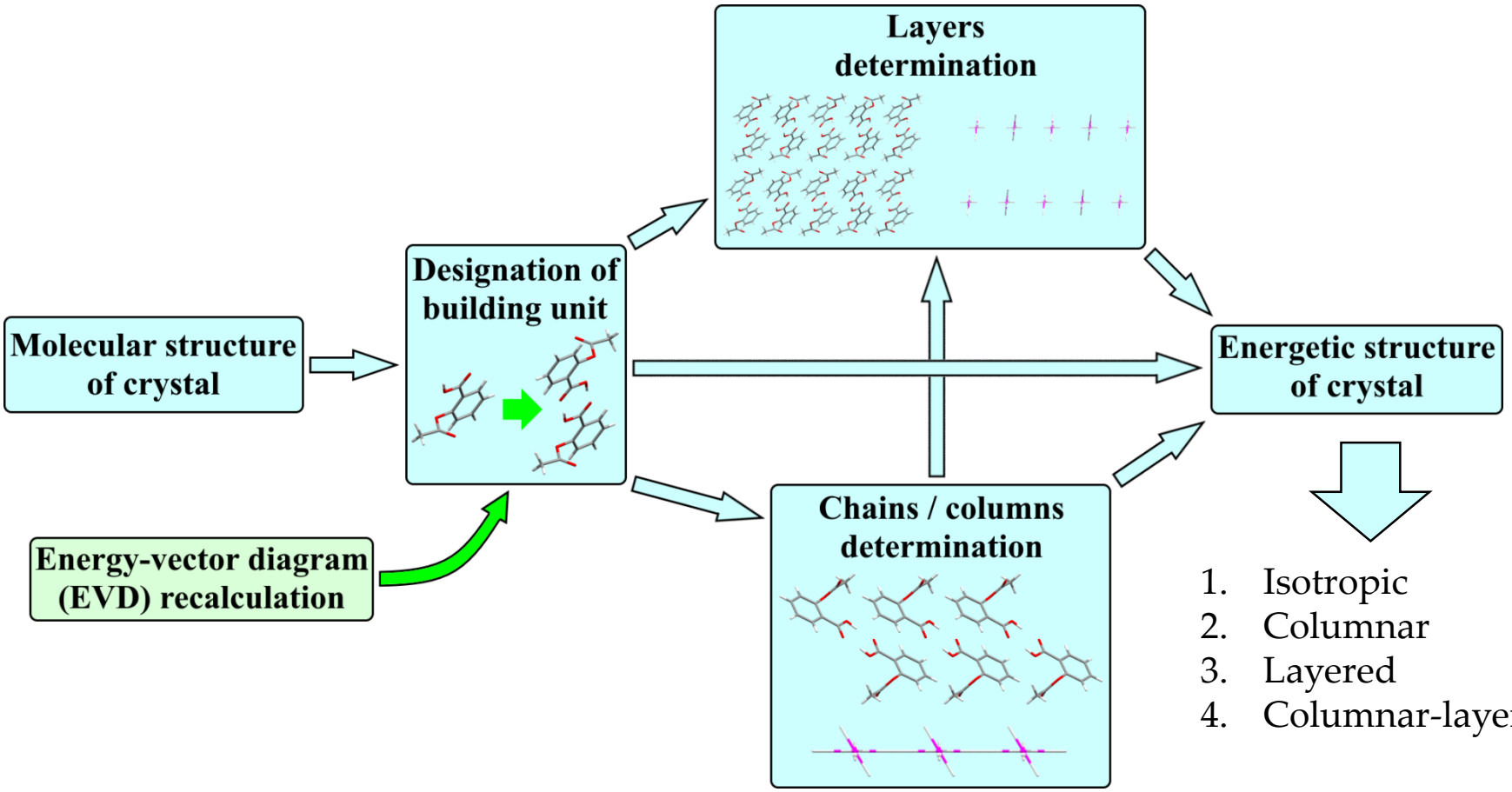
Classification of molecular crystals



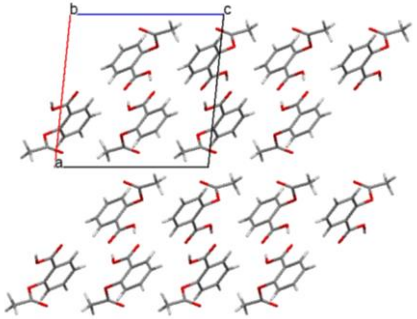
- **Relationship between anisotropy of physical properties and anisotropy of crystal packing**
- **Different properties of polymorphs due to different systems of intermolecular interactions**

Shishkin O. V. , Zubatyuk R. I., Shishkina S. V., [et al.] (2014). *Phys. Chem. Chem. Phys., 16, 6773-6786.*

Aspirin's polymorphic forms

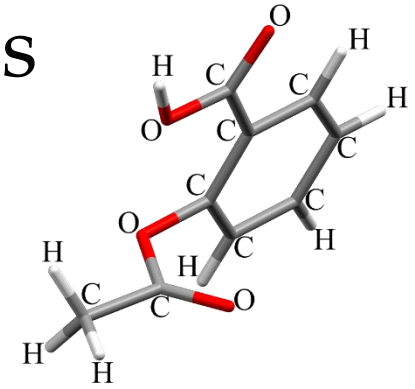
P21/c: a= 11.2776, b= 6.5517, c= 11.2741 β= **95.837**

I



2.0 GPa

III

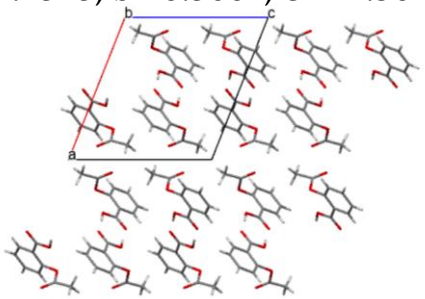


Grinding*

Bond A., Boese R., Desiraju G. (2007).
Angew. Chem. Int. Ed., 46(4), 615-617

P21/c: a= 12.1515, b= 6.5064, c= 11.3677 β= **111.574**

II

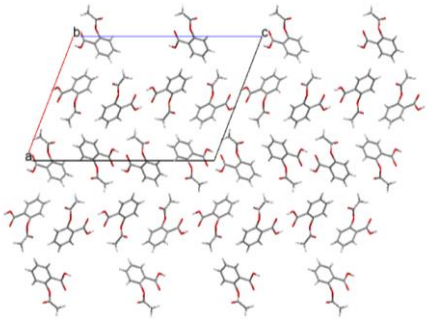


2.2 GPa

III

P21/c: a= 16.741, b= 4.795, c= 23.802 β= **111.08**

III



Pressure drop

Metastable

Unknown form

Shtukenberg A., Hu C., Zhu Q., [et al.] (2017).
Cryst. Growth Des., 17(6), 3562-3566

*Varughese S., Kiran M. S. R. N., Solanko K. A., [et al.] (2007).
Angew. Chem. Int. Ed., 46(4), 615-617

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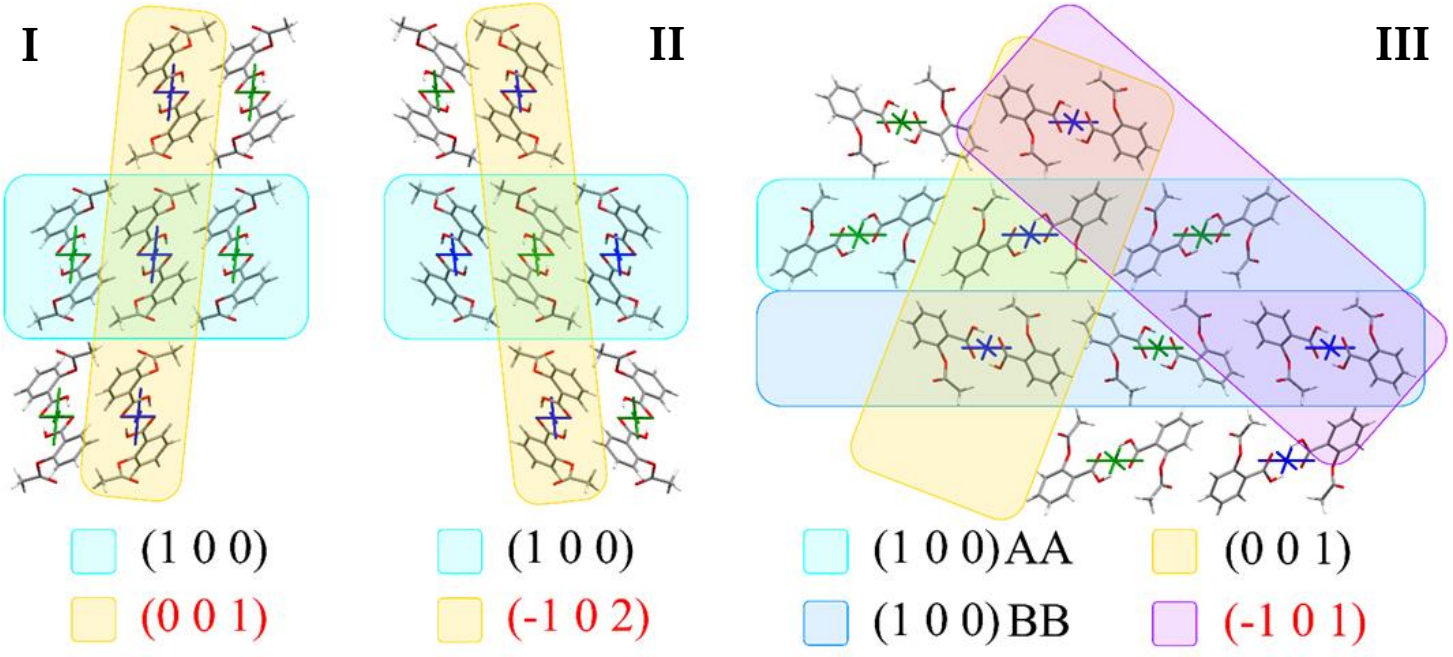
Analysis of energetic structure of **aspirin**'s polymorphs

Interaction energy, kcal/mol	I		II		III AA		III BB	
	(1 0 0)	(0 0 1)	(1 0 0)	(-1 0 2)	(1 0 0)	(0 0 1)	(1 0 0)	(0 0 1)
In chain	-26.8		-26.9		-35.3		-32.9	
Between chains in layer	-32.2	-12.3	-33.6	-13.3	-19.7	-17.4	-20.9	-17.4
In layer	-59.9	-39.0	-60.5	-40.1	-55.0	-52.8	-53.8	-50.3
Between layers	-15.4	-36.3	-14.8	-35.2	-24.6	-26.9	-24.6	-28.1
Chain with all neighbors	-48.6		-48.4		-44.3		-45.5	
Total	-73.5		-73.5		-79.7		-78.5	



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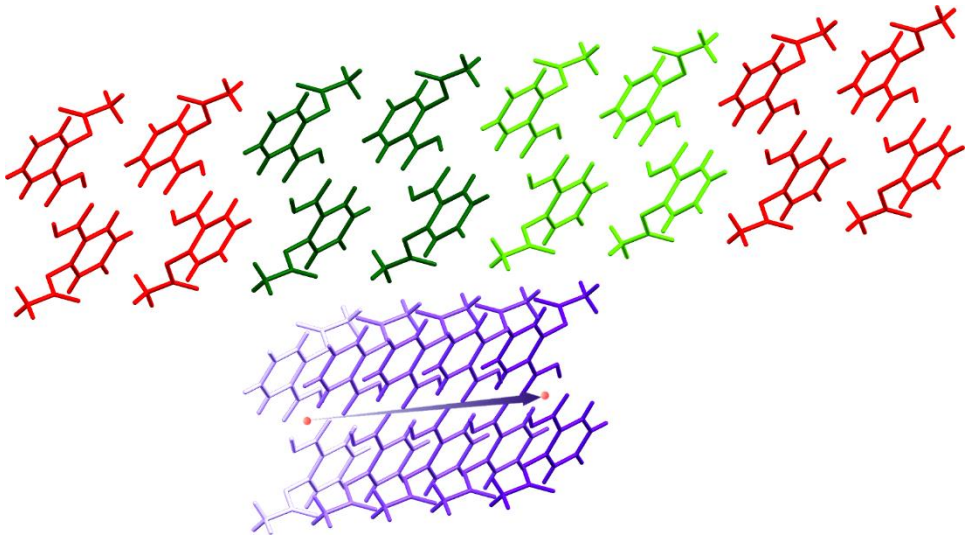
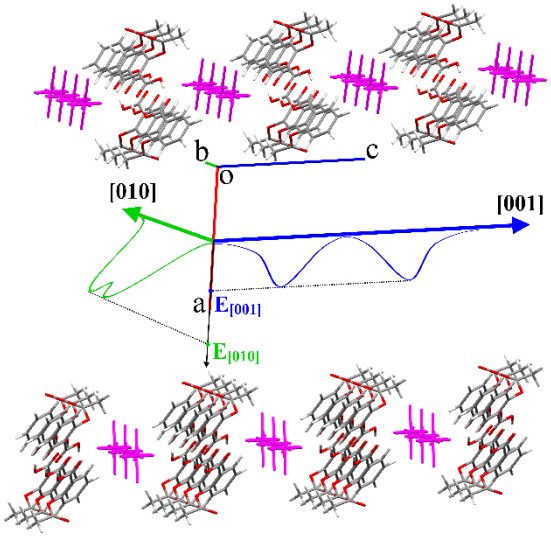
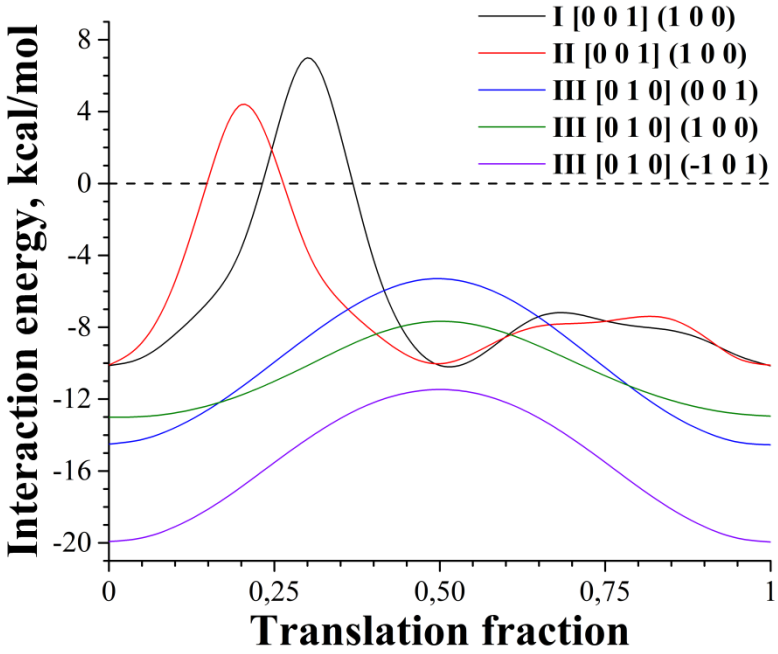
Modelling of shift in **aspirin**'s crystals





Please, take a look at the video "Shift"



	Shift energy barrier, kcal/mol	Minimal distance, Å
I [001] (100)	17.1	1.19
II [001] (100)	14.5	1.27
III [010] (001)	9.2	1.73
III [010] (100)	5.3	1.73
III [010] (-101)	8.5	1.82

Crystal structure transformation under pressure

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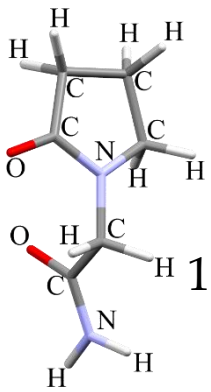
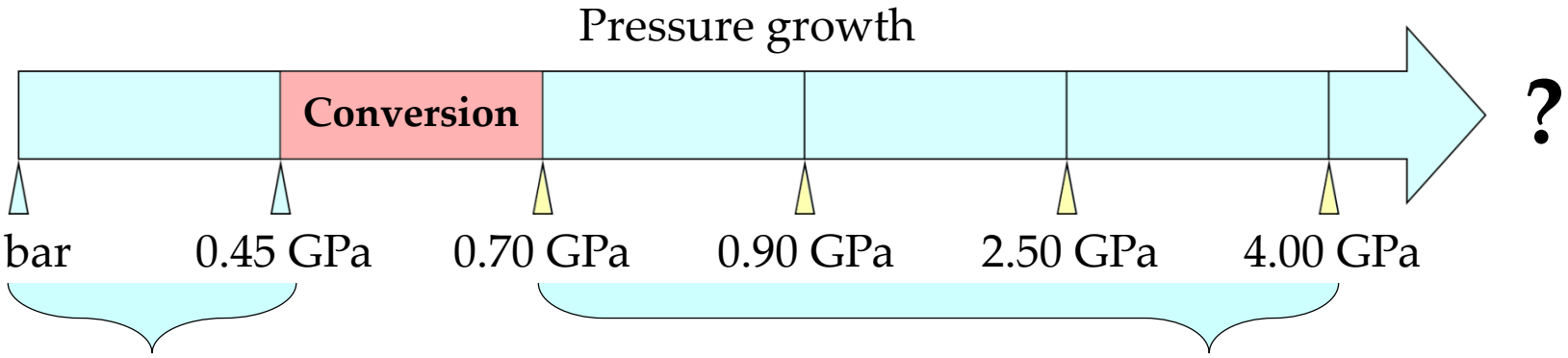
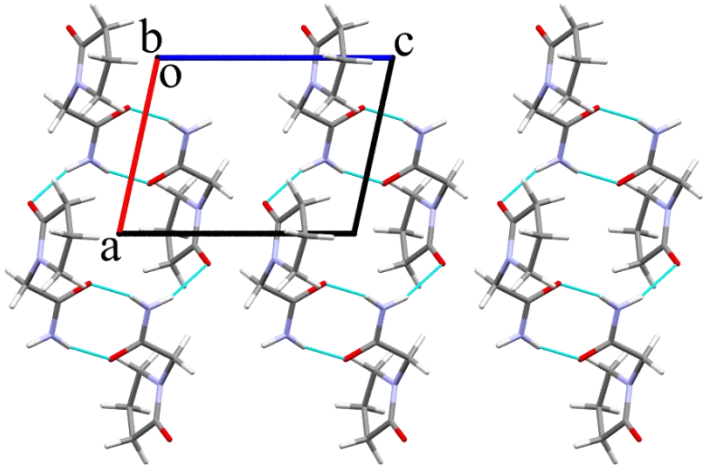
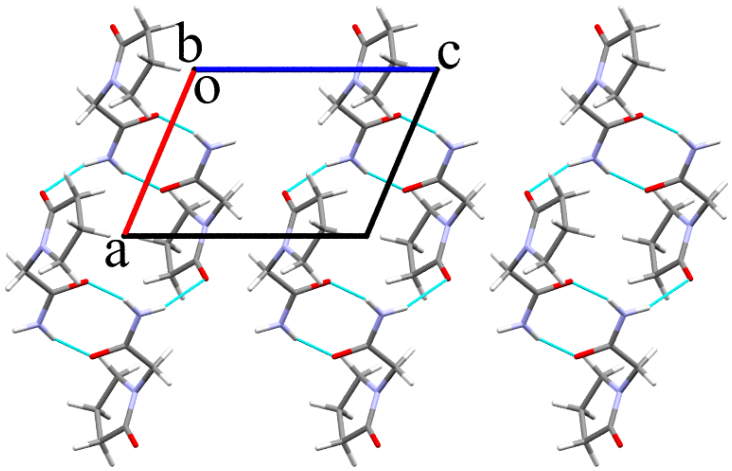
Transformation in **piracetam** under pressure







Tableting



Form II, P-1: a= 6.321, b= 6.5597, c= 8.380
α= 79.82, β= **102.34**, γ= 90.94

Form V, P-1: a= 6.442, b= 6.3530, c= 8.737
α= 81.43, β= **112.88**, γ= 91.38

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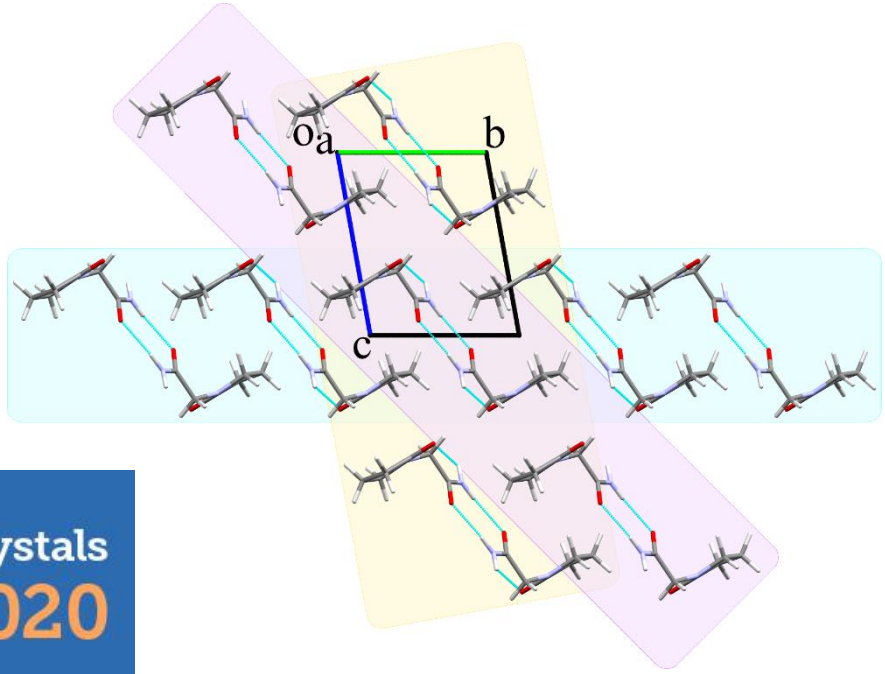
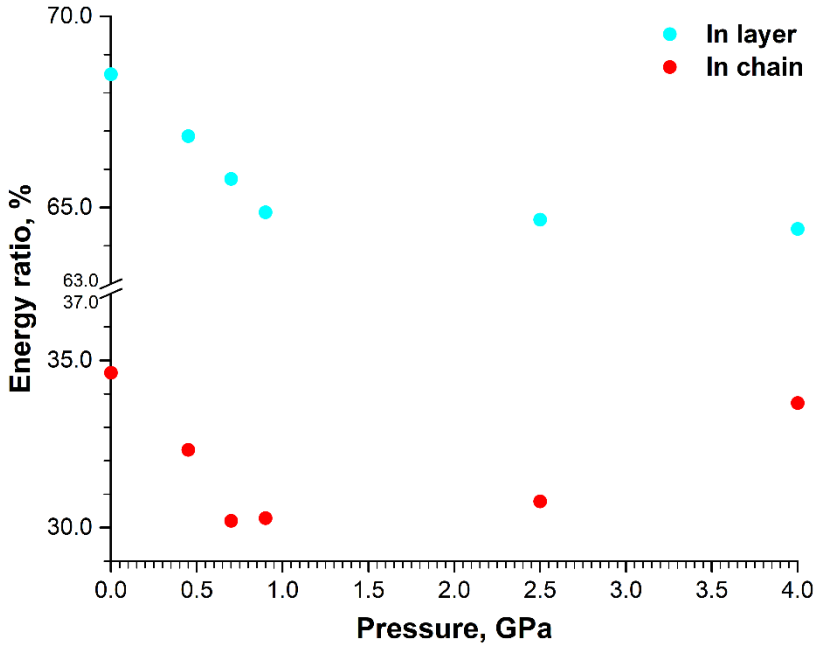
Fabbiani F. P. A., Allan D. R., David W. I. F., [et al.] (2007).
Cryst. Growth Des., 7(6), 1115-1124.

Changes in energetic structure of **piracetam** upon a transition

Interaction energy, kcal/mol	II at 0.45 GPa			V at 0.70 GPa		
	(001)	(010)	(0-11)	(001)	(010)	(0-11)
In chain	-35.9			-34.6		
Between chains in layer	-19.2	-8.8	-9.6	-20.4	-13.2	-12.9
In layer	-74.3	-53.4	-55.2	-75.4	-60.9	-60.3
Between layers	-18.4	-28.8	-27.9	-26.0	-33.2	-33.5
Total	-111.0			-127.4		





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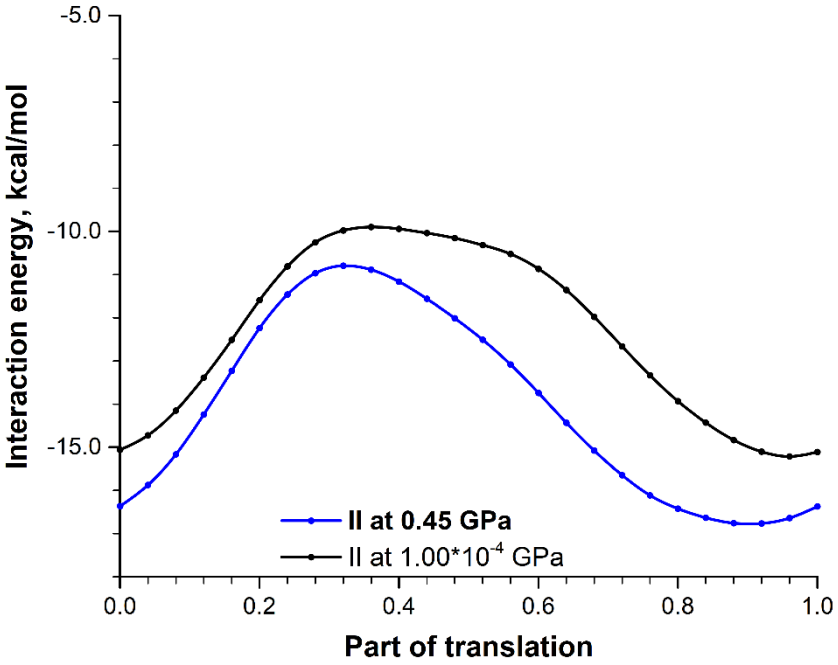
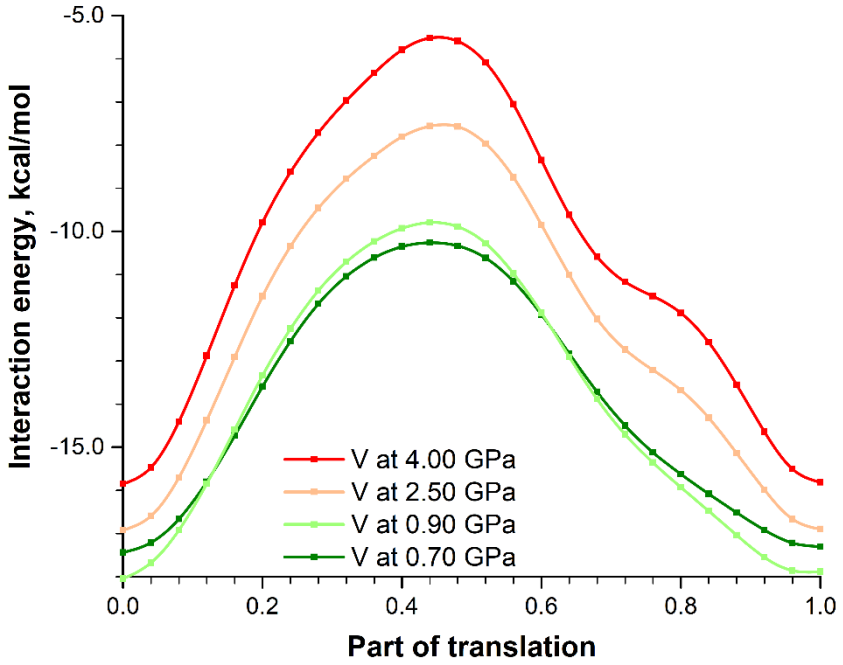
Modelling of shift in **piracetam**'s crystals

[100] direction along (001) layer





Polymorph	Pressure, GPa	Shift energy barrier, kcal/mol	Minimal distance, Å
II	$1.00*10^{-4}$	5.3	1.72
	0.45	6.0	1.84
V	0.70	7.2	2.01
	0.90	8.2	1.96
	2.50	9.4	1.88
	4.00	10.3	1.84

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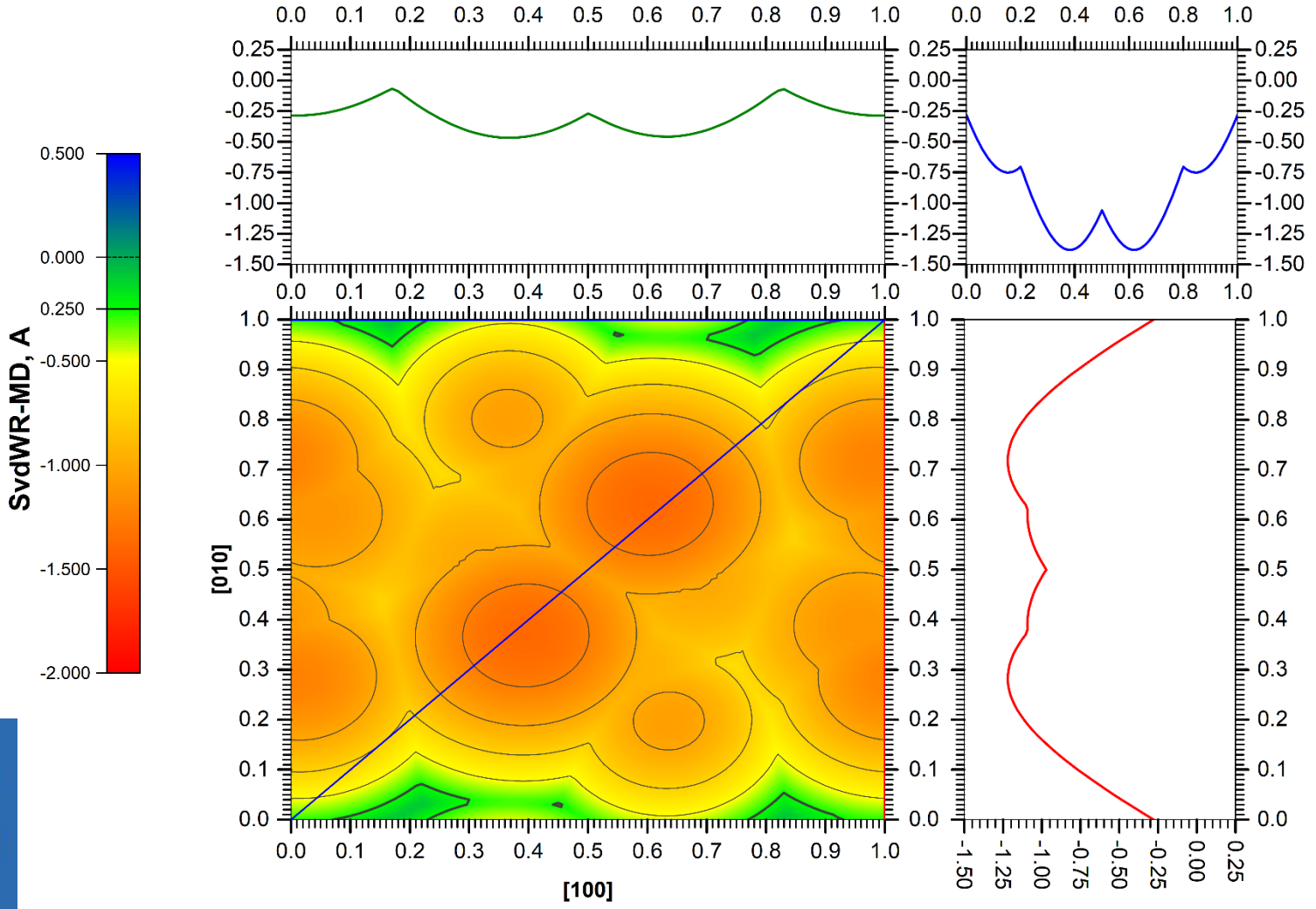
Cavities detection in **piracetam**

Shortening of the van der Waals radii sum at a point:

$$SvdWR\text{-}MD = \min(D_{ij} - R_i^{FP} - R_j^{MP})$$

where D_{ij} – the distance between the atoms of fixed (i) and motile (j) parts

R_i^{FP}, R_j^{MP} – van der Waals radii of the corresponding atoms in fixed (i) and motile (j) parts



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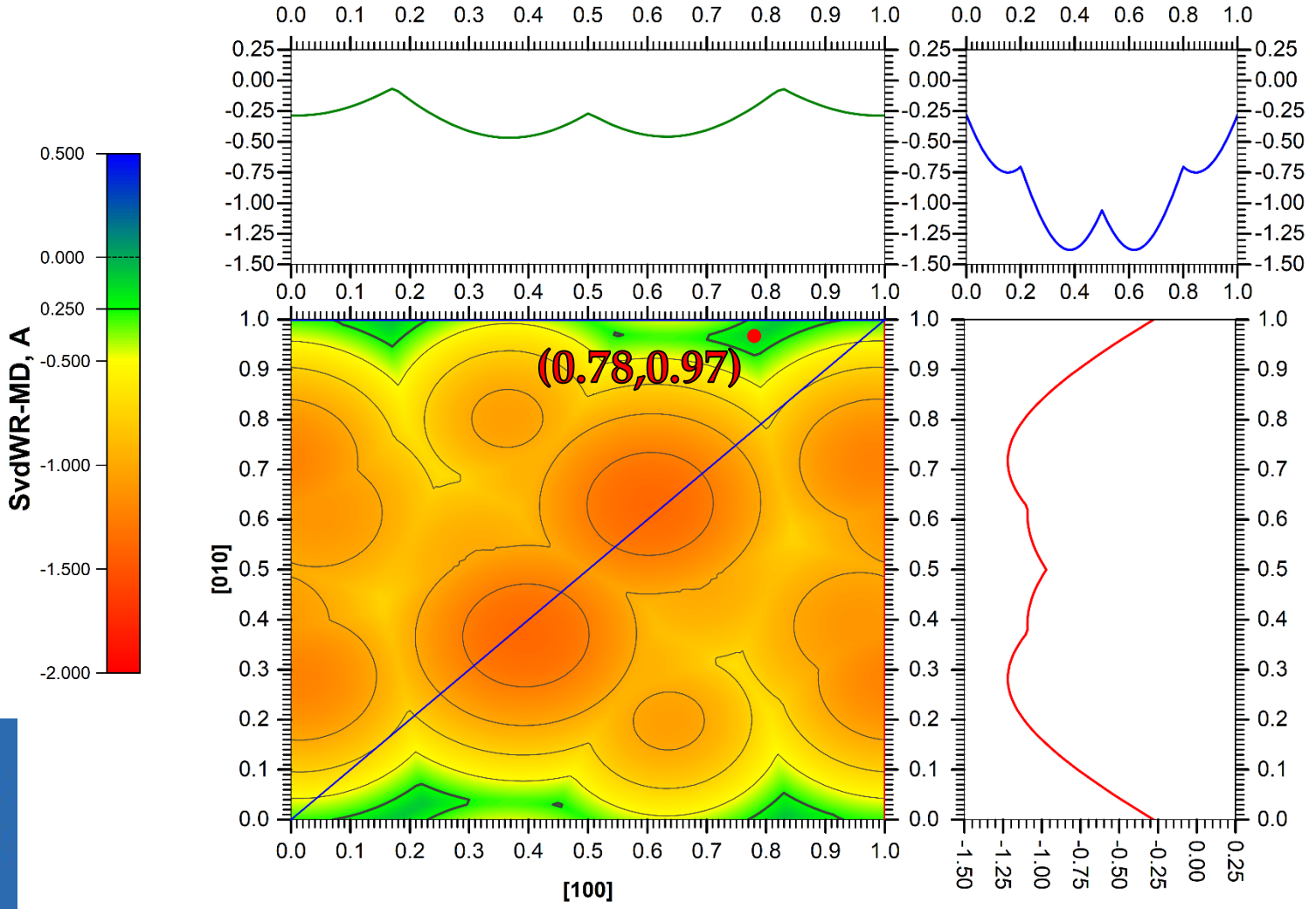

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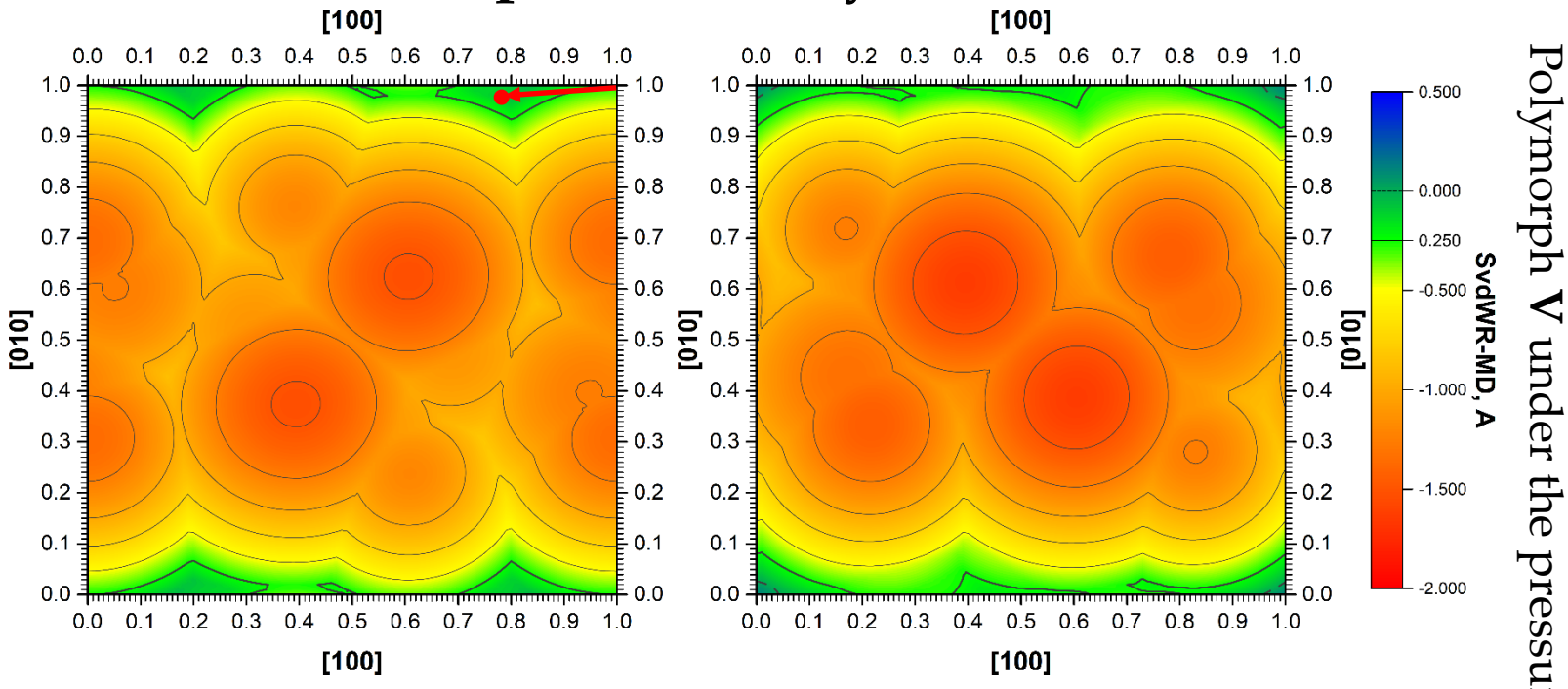
Comparison of structure and energy assessment of the transition in **piracetam** crystals

Polymorph **II** under the pressure of **0.45** GPa



Polymorph **V** under the pressure of **0.70 GPa**

Comparison of structure and energy assessment of the transition in **piracetam** crystals

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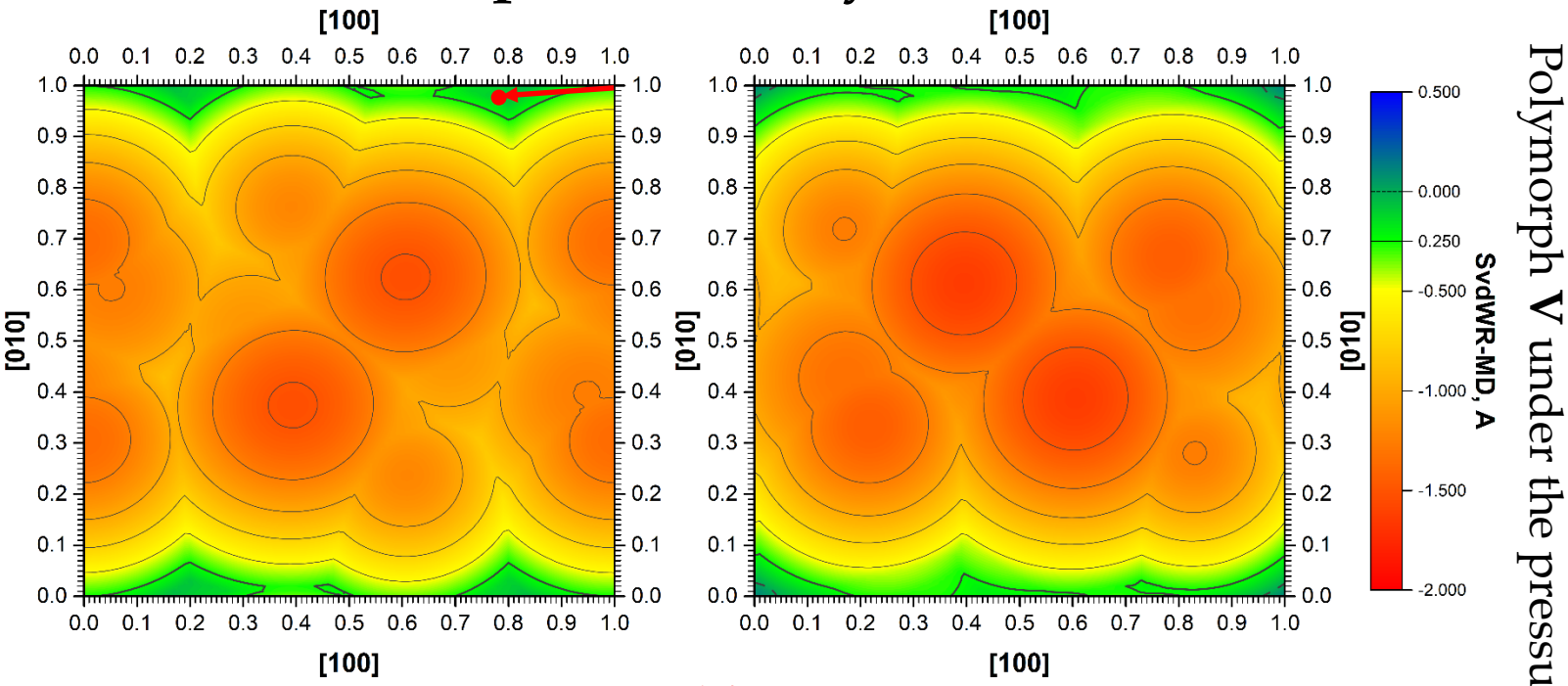

(0,0): -16.4 kcal/mol **No repulsion!** (0.78,0.97): -9.0 kcal/mol

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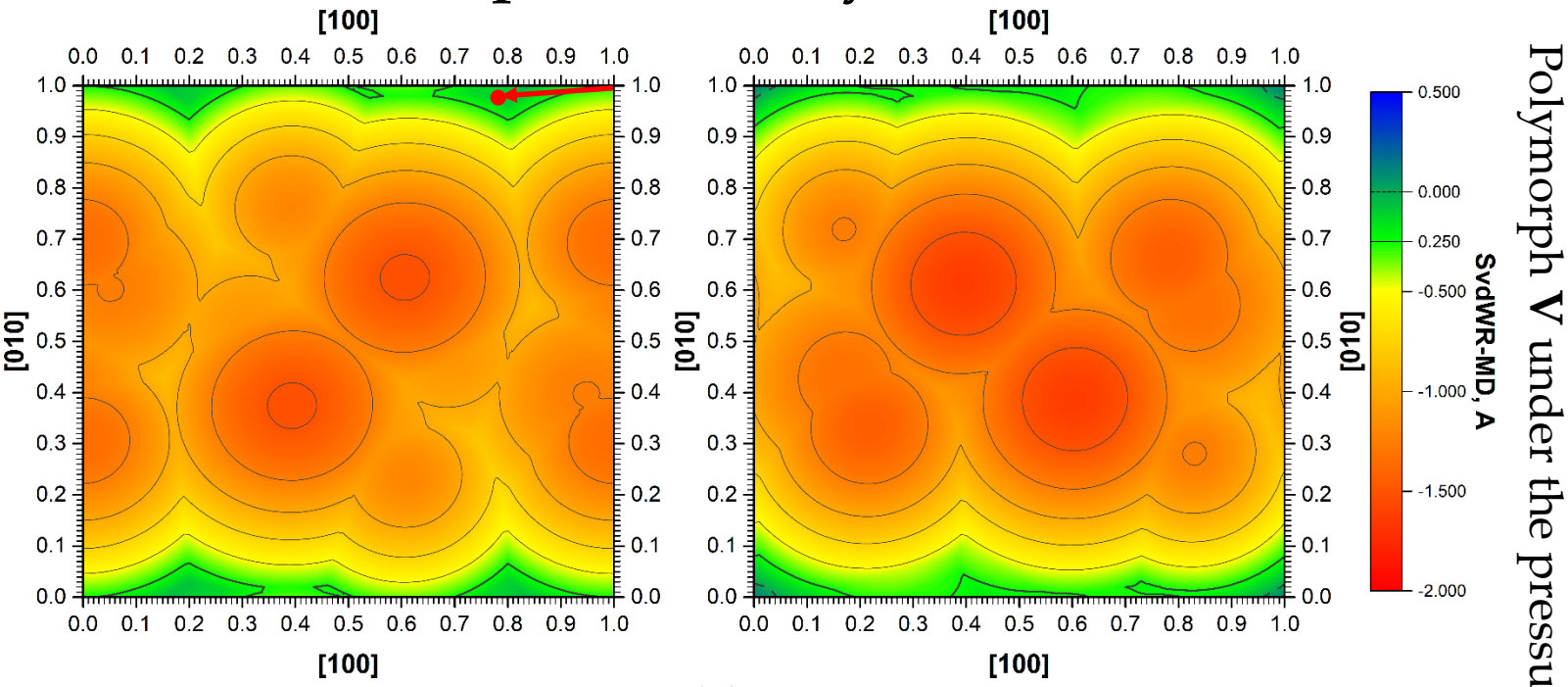

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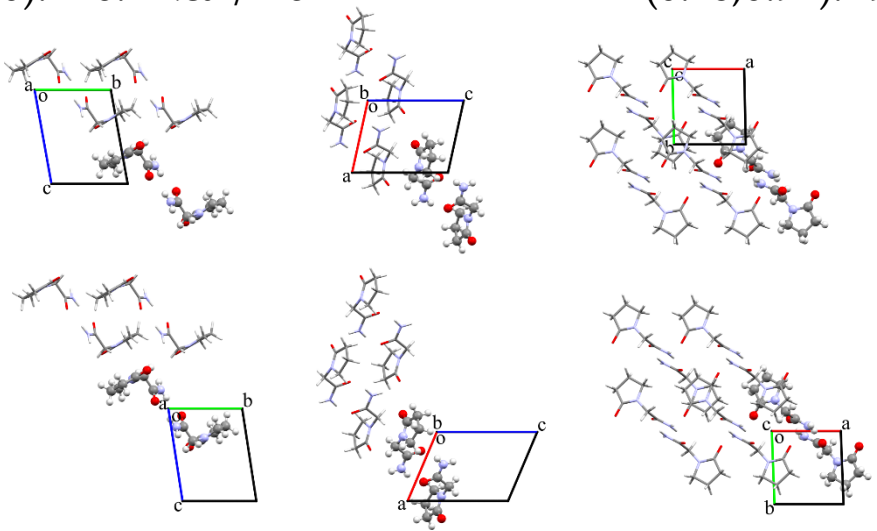

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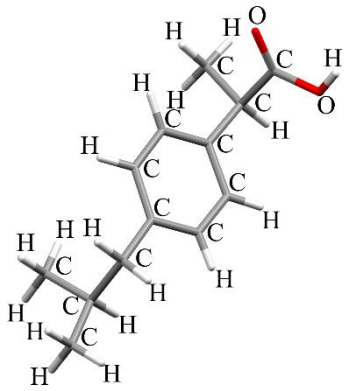
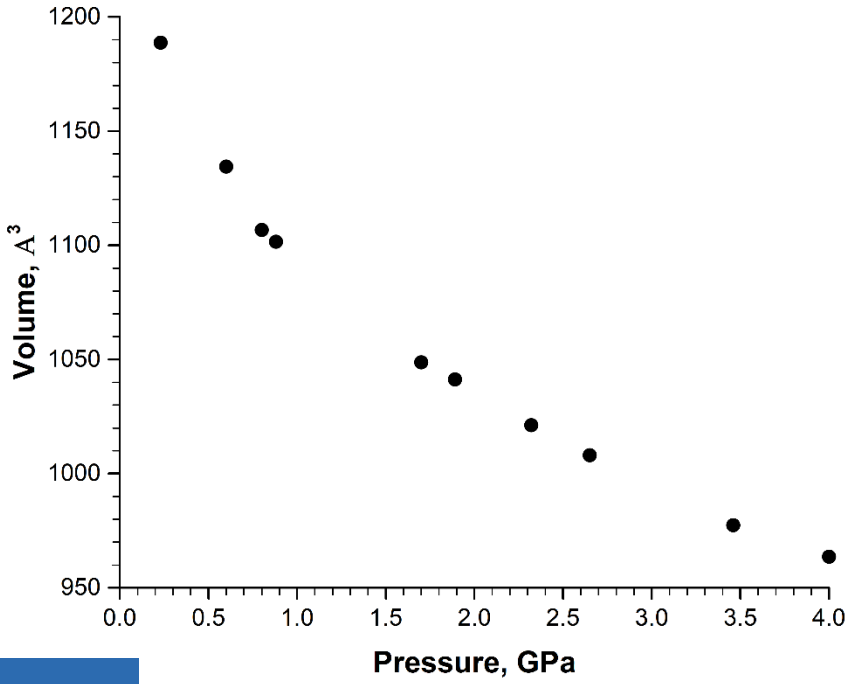
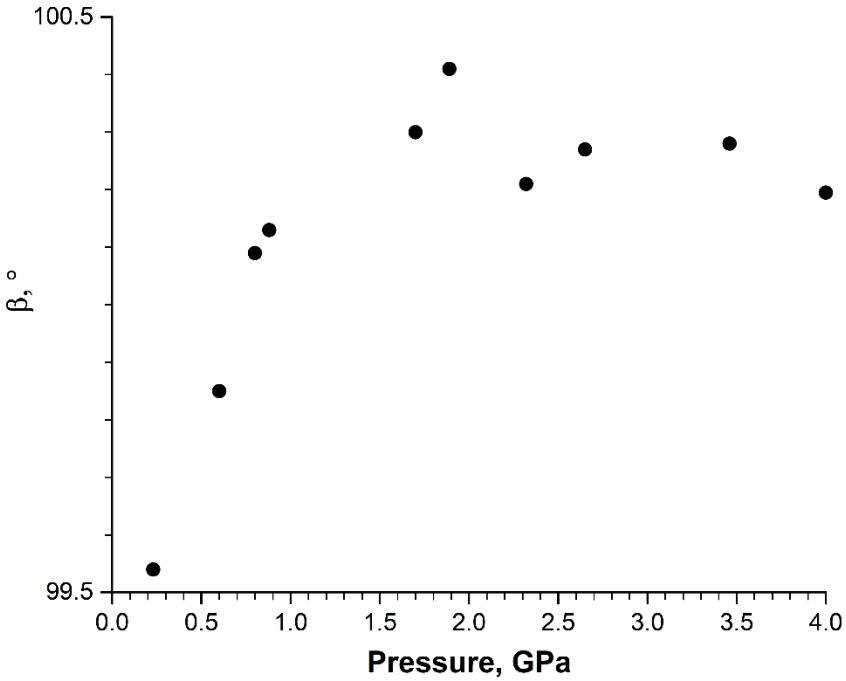
Consistency of **ibuprofen**'s structure



Compression up to 4 GPa

No conversion under pressure!





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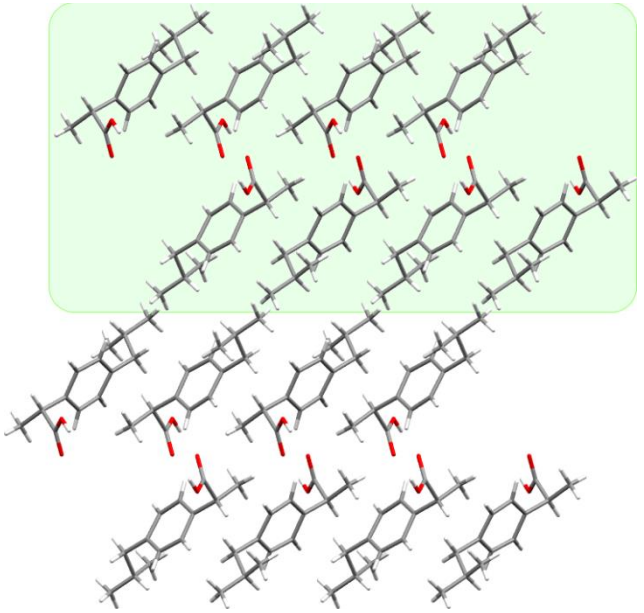
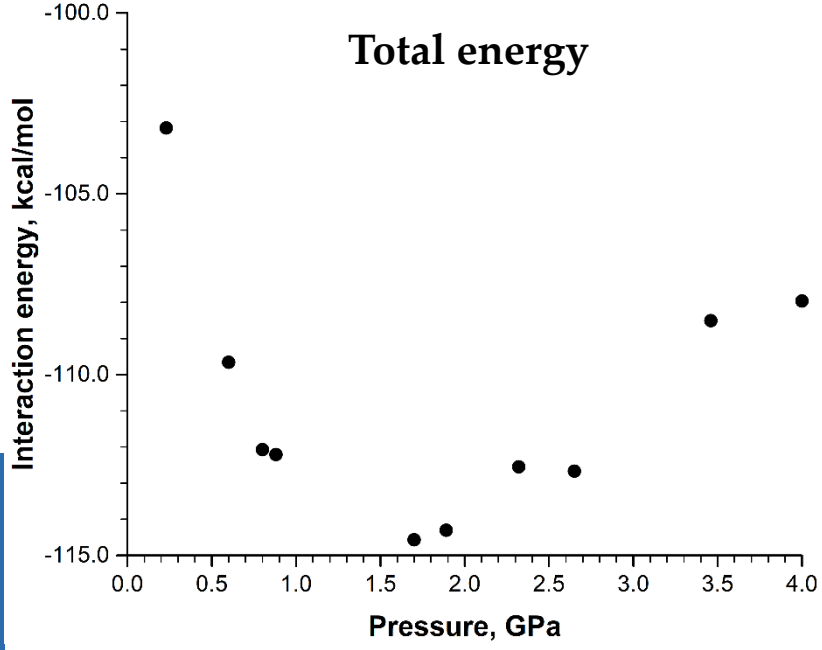
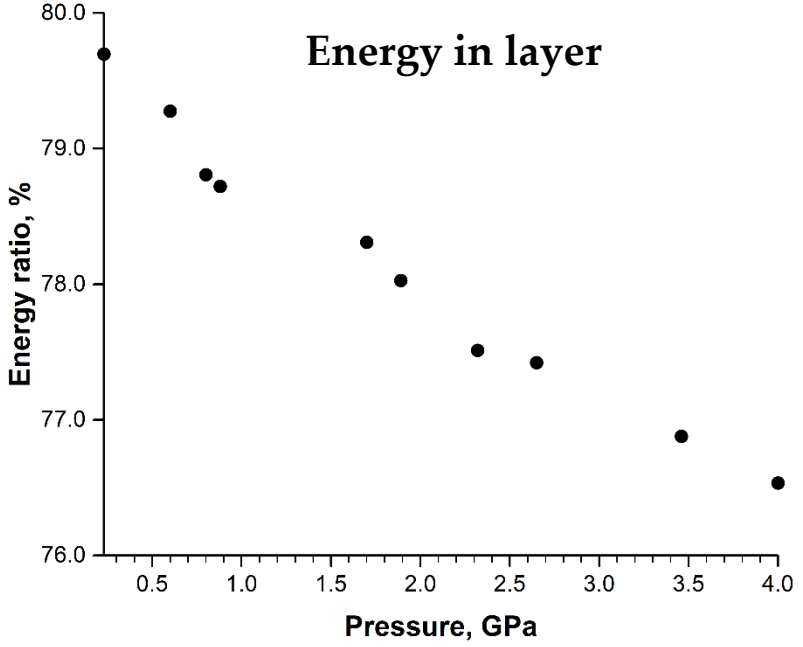
Ostrowska K., Kropidłowska M., Katrusiak A. (2015)
Cryst. Growth Des., 15(3), 1512-1517.

Sustainability of **ibuprofen**'s energetic structure

Interaction energy, kcal/mol	0.23 GPa		
	(100)	(001)	(102)
In chain	-21.6		
Between chains in layer	-30.3	-6.0	-4.5
In layer	-82.2	-33.6	-30.5
Between layers	-10.5	-34.8	-36.3
Total	-103.2		







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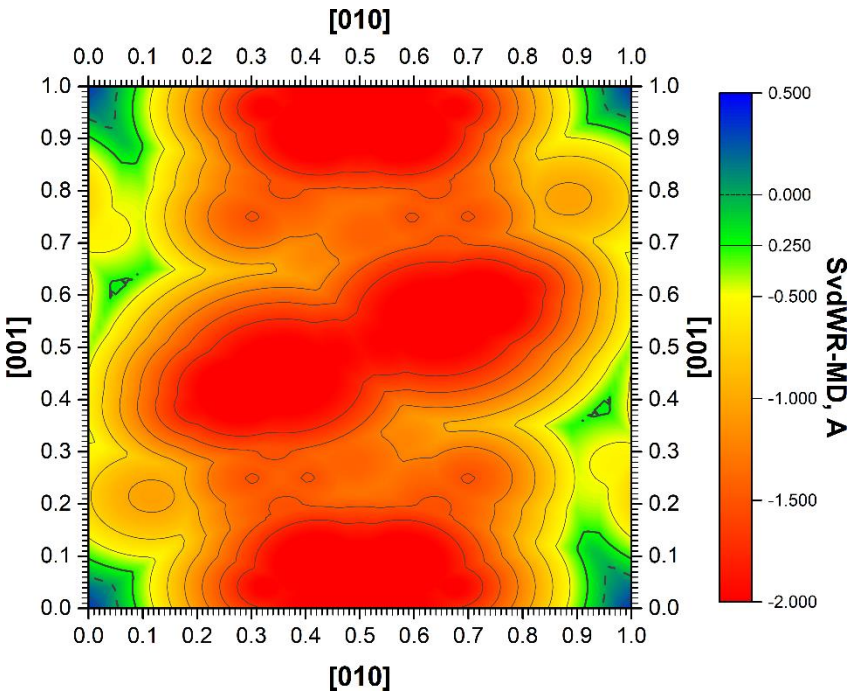
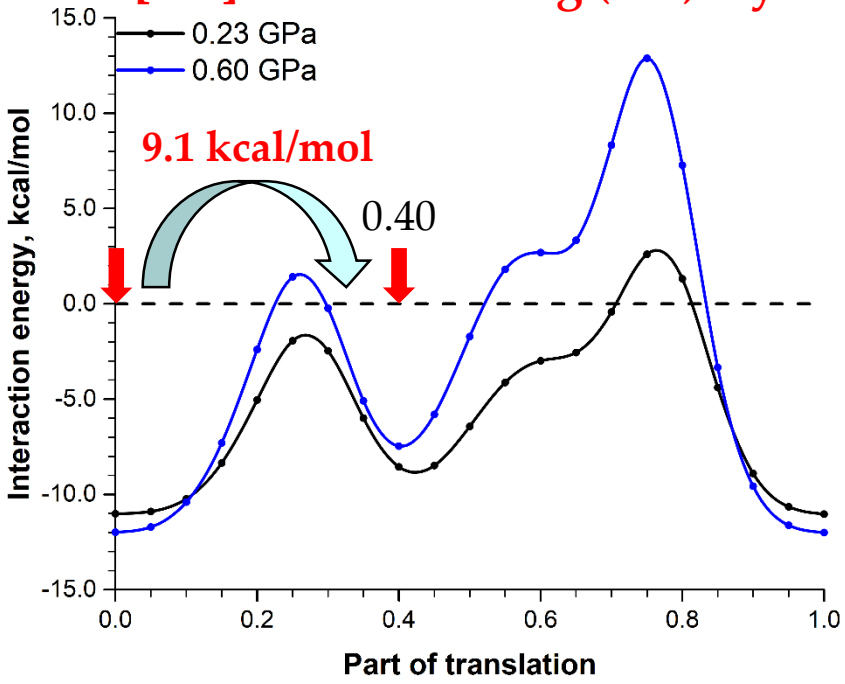
Modelling of shift in **ibuprofen**'s crystals



[001] direction along (100) layer



Pressure, GPa	Shift energy barrier, kcal/mol	Minimal distance, Å
0,23	13,6	1,46
0,60	24,9	1,30
0,80	34,8	1,18
0,88	34,7	1,20
2,65	104,6	0,86
4,00	190,7	0,70

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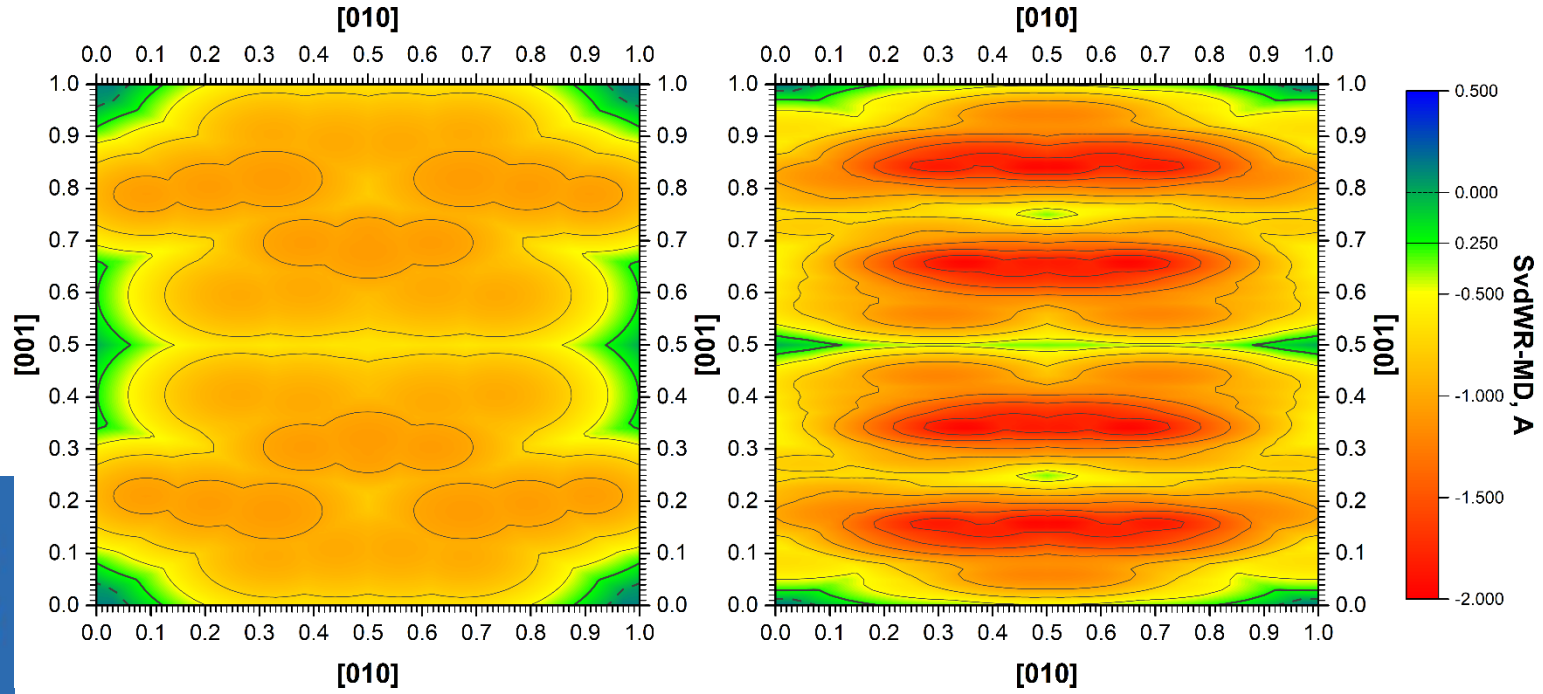
Conclusions

- On the base of a study of pairwise interactions energies in crystals **the new quantum-chemical method** able to describe **shear-based transformations** of crystal structures was proposed.
- The new **cheap express method for the 2d-detection of cavities** in structure was offered and applied for the preliminary assessment of the molecular slips probability in crystals.
- **Testing** with experimental results showed a **good match** within the simulated and real properties and transformations for three pharmaceutic compounds: **aspirin, piracetam and ibuprofen**.



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