

## Supporting Information

### The landscape of mechanical properties of molecular crystals

Chenguang Wang, and Changquan Calvin Sun\*

Efficient uses of literature nanoindentation data benefit from a clear understanding of indentation principle and possible limitation in calculating  $E$  and  $H$ .<sup>1</sup> For a linear elastic material,  $E$  (calculated by dividing stress with strain) is a time and speed independent material constant. Taking the Berkovich tip as an example, both loading force and the corresponding depth of penetration of the indenter are monitored during the indentation test. The resulting force – displacement curves are analyzed to obtain  $H$  and  $E$  of the indented material.<sup>2</sup> Fitting the upper part of unloading portion of the force– displacement curve leads to stiffness,  $S$  (slope of the line), which is used to calculate reduced modulus,  $E_r$ , using Eq. S1, where  $A(h_c)$  is the projected contact area between indenter tip and sample.

$$E_r = \frac{\sqrt{\pi}S}{2\sqrt{A(h_c)}} \quad (\text{S1})$$

The Young's modulus of the sample can be calculated using Eq. S2 by accounting for the indenter elastic deformation.

$$\frac{1}{E_r} = \frac{(1 - \nu^2)}{E} + \frac{(1 - \nu_i^2)}{E_i} \quad (\text{S2})$$

Where  $\nu$  and  $\nu_i$  are Poisson's ratios of samples and indenter,  $E$  and  $E_i$  are elastic moduli of sample and indenter, respectively.

The true hardness,  $H$ , is an engineering parameter that reflects the resistance to the plastic deformation, which is irreversible. The plastic deformation is time- and speed- independent, or weakly dependent.<sup>1</sup> During a nanoindentation measurement, the first sudden relaxation of load in displacement control mode, or a displacement burst in load control mode, signifies the onset of plastic deformation.<sup>3</sup> The hardness value determined by nanoindentation is contact hardness ( $H_c$ ) given by Eq. S3, i.e., peak load ( $P_{\max}$ ) divided by the projected contact area under load.

$$H_c = \frac{P_{max}}{A(h_c)} \quad (S3)$$

Where  $A(h_c)$  is obtained from the contact depth, obtained by correcting the deflection of surface at the contact perimeter using Eq. S4, and area function of a given indenter tip.

$$h_c = h_m - \frac{3P_{max}}{4S} \quad (S4)$$

Where  $h_m$  and  $h_c$  are the recorded maximum and residual contact displacement, respectively.

The theoretical relationship between  $E_r$  and  $H$  follows Eqs. S5, S6, or S7,<sup>4, 5</sup> where  $R$  is defined as mean contact pressure during the indentation of a rigid perfectly plastic material,  $\beta$  is the equivalent cone angle of indenter,  $\alpha_1$  and  $\alpha_2$  are constants for a defined indenter ( $\alpha_1 = 24.5$  and  $\alpha_2 = 4.4$  for Berkovich), respectively.

$$E_r = 0.6647(HR_s)^{1/2} \quad (S5)$$

$$R_s = \frac{1.7778 * S^2}{P_{max}} \quad (S6)$$

$$H = \frac{R}{\left(1 + \left(\frac{R}{E}\right)^{\frac{1}{2}} * \left(\frac{2}{\tan(\beta)}\right)^{\frac{1}{2}}\right)^2} \quad (S7)$$

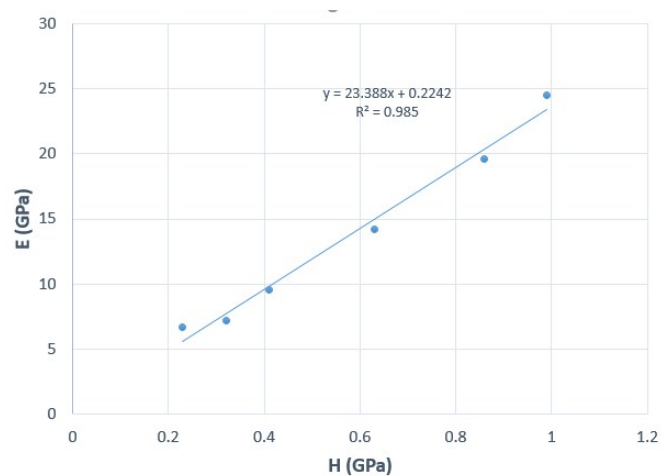
Since both elastic and plastic deformations contribute to the total contact area,  $H_c$  slightly differs from  $H$ . By decoupling the irreversible and reversible deformation during nanoindentation measurement, it was shown that  $H$  and  $H_c$  are related according to Eq. S8 for materials only undergo elastic – plastic deformation.<sup>6</sup>

$$H_c = \frac{1}{\alpha_1((\alpha_2)E)^{-\frac{1}{2}} + (\alpha_1H)^{-\frac{1}{2}})^2} \quad (S8)$$



**Table S1.** Ratios of the highest to lowest  $E$  and  $H_c$  values in different groups of molecular crystals

Anisotropy effect				Polymorph effect				Salt or cocrystal			
Compound name	# of facets studied	highest/lowest E	highest/lowest Hc	Compound name	# of phases studied	Highest/lowest E	Highest/lowest Hc	Compound name	# of phases studied (including parent compound)	highest/lowest E	Highest/lowest Hc
Calcium fumarate trihydrate	3	1.99	1.26	Omeprazole	5	1.1	1.98	$\beta$ -Piroxicam	2	1.55	1.19
Aspirin	2	1.6	1.07	Aspirin	2	1.93	1.69	Theophylline	2	1.3	1.7
Caffeine 4-chloro-3-nitrobenzoic acid	2	1.36	1.1	Caffeine 4-chloro-3-nitrobenzoic acid	2	1.59	1.82	Metformin	3	2.18	1.77
Piroxicam	3	1.23	1.6	Famotidine	2	1.16	1.88	Diphenhydramine	4	1.33	2.93
Famotidine	2	1.12	1.19	Felodipine	2	2.44	1.22	Vanillin	4	1.51	1.5
Olanzapine	2	1.12	1.03	Caffeine-glutaric acid	2	1.01	1.06	Voriconazole	7	5.12	3.31
Felodipine	4	1.45	1.25	Febuxostat	2	1.64	1.45	Acetaminophen	2	4.62	2.08
Sucrose	2	1.15	1.09	Curcumin	3	1.99	1.3	Methyl gallate	2	1.61	1.63
Sodium saccharin dihydrate	2	1.16	1.08	Sulfathiazole	4	2.04	3.03	Saccharin	2	2.27	1.29
Sodium saccharin dihydrate dehydrated	2	1.3	1.01	Fluorinated Amide	2	1.35	2.02				
Saccharin	2	1.05	1.11	Glycine	2	1.57	1.32				
Glycine	4	1.69	1.53								
L-alanine	3	1.02	1.5								
1,2,4,5-Tetracya-nobenzene with pyrene	2	1.27	1.19								
1,2,4,5-Tetracya-nobenzene-with phenan-threne	2	1.25	1.04								
1,1-Diamino-2,2-dinitroethylene	3	1.92	1.29								
Mn(2-methylsuccinate)ln	2	1.32	1.37								
$\beta$ -HMX	2	1.12	1.16								
Cyclotrimethylene	3	1.29	1.09								



**Figure S1.** Linear relationship between  $E$  and  $H_c$  values of different molecular crystals from a single study, where potential variations in experimental conditions were minimal.<sup>7</sup>

**References:**

1. M. L. Oyen and R. F. Cook, *J. Mech. Behav. Biomed. Mater.*, 2009, **2**, 396-407.
2. W. C. Oliver and G. M. Pharr, *J Mater Res*, 1992, **7**, 1564-1583.
3. A. M. Minor, S. A. Syed Asif, Z. Shan, E. A. Stach, E. Cyrankowski, T. J. Wyrobek and O. L. Warren, *Nat. Mater.*, 2006, **5**, 697.
4. Y. W. Bao, W. Wang and Y. C. Zhou, *Acta Materialia*, 2004, **52**, 5397-5404.
5. D. Labonte, A.-K. Lenz and M. L. Oyen, *Acta Biomaterialia*, 2017, **57**, 373-383.
6. M. L. Oyen, *J Biomech*, 2006, **39**, 2699-2702.
7. M. R. Taw, J. D. Yeager, D. E. Hooks, T. M. Carvajal and D. F. Bahr, *J Mater Res*, 2017, **32**, 2728-2737.

