



## Non photochemical light induced nucléation

Anne Spasojevic - de Biré, Bertrand Clair, Aziza Ikni, Nicolas Guiblin, Igor Kornev, Xiaoxuan Shi, Jianyao Long, Hongxun Yang, Wenjing Li, Annais Mendre, et al.

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Anne Spasojevic - de Biré, Bertrand Clair, Aziza Ikni, Nicolas Guiblin, Igor Kornev, et al.. Non photochemical light induced nucléation. Journées nationales en nanosciences et nanotechnologies, Nov 2012, Bordeaux, France. hal-02302622

HAL Id: hal-02302622

<https://hal.science/hal-02302622>

Submitted on 28 Sep 2020

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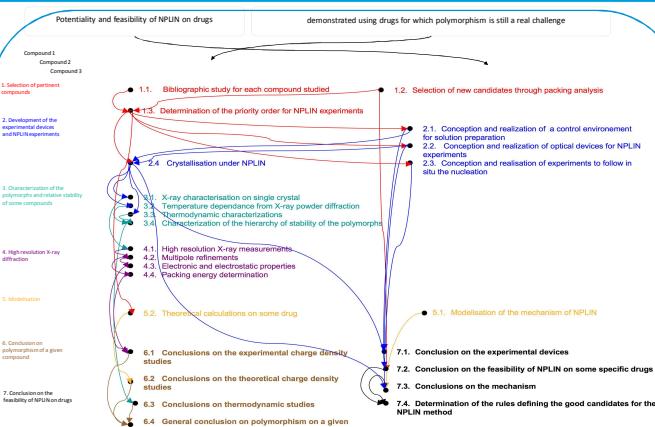
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# NPLIN-4-drug

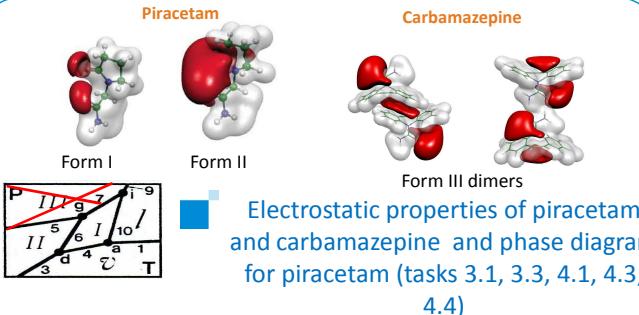
## Non Photophysical Light Induced Nucleation for drugs

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### Journées Nationales en Nanosciences et Nanotechnologies 2012



#### Goals and tasks of the project



#### Polymorphism studies important in the industrial pharmaceutical context

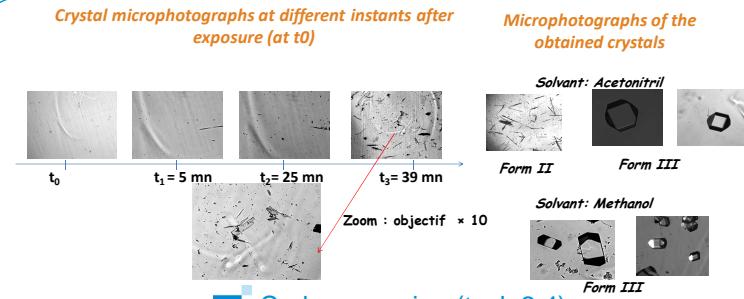
Method developed on urea [1], glycine [2], L-histidine [3], Hen Egg White Lysozyme [4], Bovine P T [5], Pentyl cyanobiphenyl [6], KCl [7] [9], NaClO<sub>3</sub> [8], KBr [9], Acetic acid [10]

[1] Garetz B.A. et al. *Phys. Rev. Lett.* **1996**, 16, 3475-3476; Yoshikawa H.Y. et al. *Jpn. J. Appl. Phys.* **2006**, 45, 303-305; Yoshikawa H.Y. et al. *Jpn. J. Appl. Phys.* **2006**, L23-L26. [2] Zaccaro J., et al. *Cryst. Growth Des.* **2001**, 1, 5-8; Garetz B.A. et al. *Phys. Rev. Lett.* **2002**, 88, 14801-14812; Sun X.Y. et al. *Cryst. Growth Des.* **2006**, 6, 685-689; Sugiyama T. et al. *Chem. Lett.* **2007**, 12, 1480-1481; Sun X.Y. et al. *Cryst. Growth Des.* **2008**, 8, 1720-1722. [4] Lee et al. *Cryst. Growth & Design* vol. 8 n°12, 4255-4261. [5] Li et al. *Cryst. Growth & Design* vol. 8 n°12, 4255-4261. [6] Sun et al. *Phys. Rev. E* vol. 79 2009 021701 [7] Alexander A.J. et al. *Cryst. Growth Des.* **2009**, 9, 958-965; Duffus A.J. et al. *J. Am. Chem. Soc.* **2009**, 131, 11676-11679; Ward M.R. et al. *Phys. Rev. Lett.* **2009**, 102, 25-28. [8] Ward et al. *J. Chem. Phys.* Vol. 135 2011 114508 [9] Ward et al. *Cryst. Growth & Design* vol.12 2012, 4554-4561 [10] Ward et al. *Phys. Chem. Chem. Phys.* **2011** Vol.14

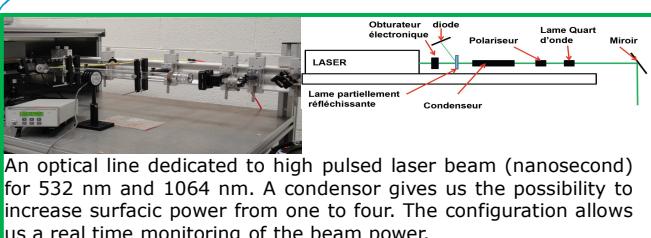
#### Context

**Co-existence of clusters of polarisability tensors of different symmetry: « disk-like » or « rod-like »**  
**Role of the induced dipolar moment depending on the clusters type**  
**Dipole moment induced of the cluster aligned itself on the laser polarization. Minimization of energy.**

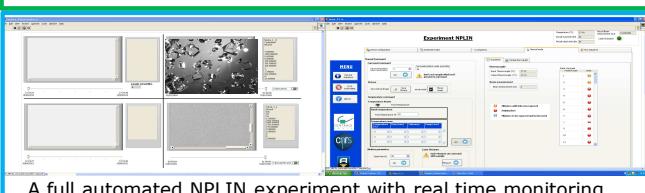
#### Possible mechanism : Kerr effect



#### Carbamazepine (task 2.4)



An original way to maintain a constant temperature in the rotative carrousel with a continuous water flow



#### Conclusions and apertures

- The device allows us to expose and survey till 90 samples during several days and it is fully automated.
- In a near future, the device will permit to study solubility according to temperature and to determine metastable zone.
- This device can probe a huge number of solutions using NPLIN method.
- Interesting results come from Carbamazepine, Glycine and glutamic acid.



#### NPLIN new experimental device (task 2.1, 2.2, 2.3)

#### Production scientifique (publications, brevets)

- B. CLAIR, A. IKNI, H. YANG, F. DUMAS, P. SCOUFLAIRE, A. SPASOJEVIC – DE BIRÉ « Non Photophysical Light Induced Nucleation. A tool to crystallize polymorphs on demand ? » CPOSS meeting, London (UK), Grande-Bretagne, 30 mars 2011  
 A. IKNI, B. CLAIR, H. YANG, F. DUMAS, P. SCOUFLAIRE, A. SPASOJEVIC – de BIRÉ « Non Photophysical Light Induced Nucleation. A tool to crystallize polymorphs on demand ? » IV congrès algérien de cristallographie, Kechelaïa, (Algérie), 14-16 mai 2011  
 A. SPASOJEVIC – de BIRÉ, A. IKNI, B. CLAIR, N. GUERIN, I. KORNEV, Y. SHI, J. LONG, H. YANG, W. LIU, A. MENDRE, P. SCOUFLAIRE, E. JEAN-BART, J. BEAUNIER, F. SAIG, R. ESPEAU, Y. CORVIS, C. ALZINA, N-E GHERMANI, N. EL HASSEN, F. DUMAS, S. VEELE, Z. HAMMADI « Non Photophysical Light Induced Nucleation» Journées nationales en nanosciences et nanotechnologies, Strasbourg (France) 7 – 9 novembre 2011  
 A. SPASOJEVIC – de BIRÉ, A. IKNI, B. CLAIR, F. DUMAS, P. SCOUFLAIRE, A. SPASOJEVIC – de BIRÉ « Non Photophysical Light Induced Nucleation (NPLIN). A tool to crystallize polymorphs on demand ? Application to carbamazepine » GFCC-2011, Paris, novembre 2011  
 A. IKNI, B. CLAIR, P. SCOUFLAIRE, S. VEELE, A. SPASOJEVIC – de BIRÉ, « A Method to probe NPLIN on glycine and histidine : a new path to understand nucleation? » CPOSS meeting, London (UK), 3 avril 2012  
 A. IKNI, B. CLAIR, P. SCOUFLAIRE, A. SPASOJEVIC – de BIRÉ, « Non Photophysical Light Induced Nucleation (NPLIN). Application to carbamazepine (CBZ) » CPOSS meeting, London (UK), 3 avril 2012  
 B. CLAIR, A. IKNI, P. SCOUFLAIRE, A. SPASOJEVIC – de BIRÉ, « NPLIN of glycine and carbamazepine » Serbian Crystallographic Meeting, Bela Crkva (Serbie), 31 mai – 2 juin 2012  
 A. IKNI, B. CLAIR, P. SCOUFLAIRE, A. SPASOJEVIC – de BIRÉ, « NonPhotophysical Light Induced Nucleation of Carbamazepine in Polar protic and aprotic solvents » 2012 Collaborative Conference on Crystal Growth, Orlando (USA), 11-14 décembre 2012  
 B. CLAIR, A. IKNI, P. SCOUFLAIRE, A. SPASOJEVIC – de BIRÉ, « Understanding photophysical effects : NPLIN on glycine and L - glutamic acid » 2012 Collaborative Conference on Crystal Growth, Orlando (USA), 11-14 décembre 2012

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