A Computational Screening Method in Deriving New Promising Explosive Molecules: ADD Method-1 and MS-HEMs

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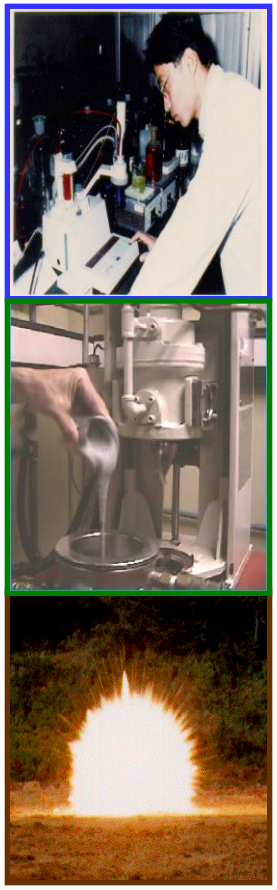
Research Purpose:

Develop Better Warhead/Ammunition for Korean Armed Force

Performance of Warhead/Ammunition Heavily Depends upon Performance of Explosives Used

Development of New Explosives



New Molecules
- ○ Novel Explosive Molecules
- ○ Additives (Binders, Plasticizers, etc.)

New Formulations
- ○ Properly Combining Various Ingredients
- ○ Machining (Casting, Pressing, etc.)

Tests and Evaluation
- ○ Performance, Safety
- ○ Chemical Properties

Feedback

Two Main Issues in Developing Novel Explosive Molecules:

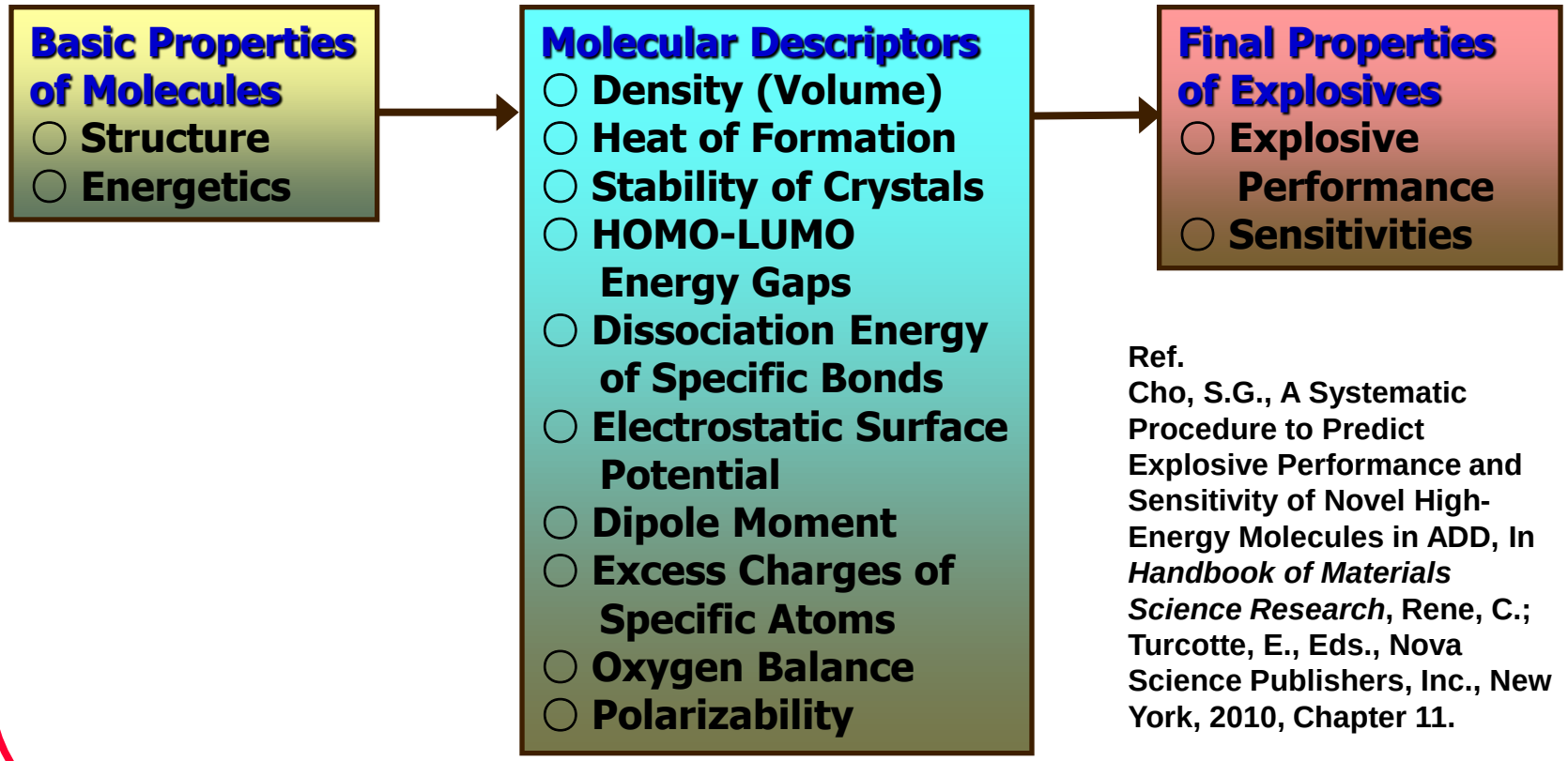
- **(Derive) Where Can We Get Good Candidate Molecules?**
  - A Variety of Scaffolds
  - Pools of Molecules
  - Automatic Generation of Diverse Molecules
  - Best Solution: DB for Virtual Molecules

- **(Screen) How Do We Select the Real Good One?**
  - Accurate Prediction of Performance and Sensitivity
  - Improve ADD Method-1
  - Improve Calculation Speed
  - Other Important Issue: Synthetic Feasibility (pKa Pred.)
  - Other Issues: Decomposition Temp., M.P., …
    (in Drug Design: ADME/Tox)

- ADME/Tox: Absorption, Distribution, Metabolism, and Excretion / Toxicity
  ADME greatly influence the performance of the compound as a drug.

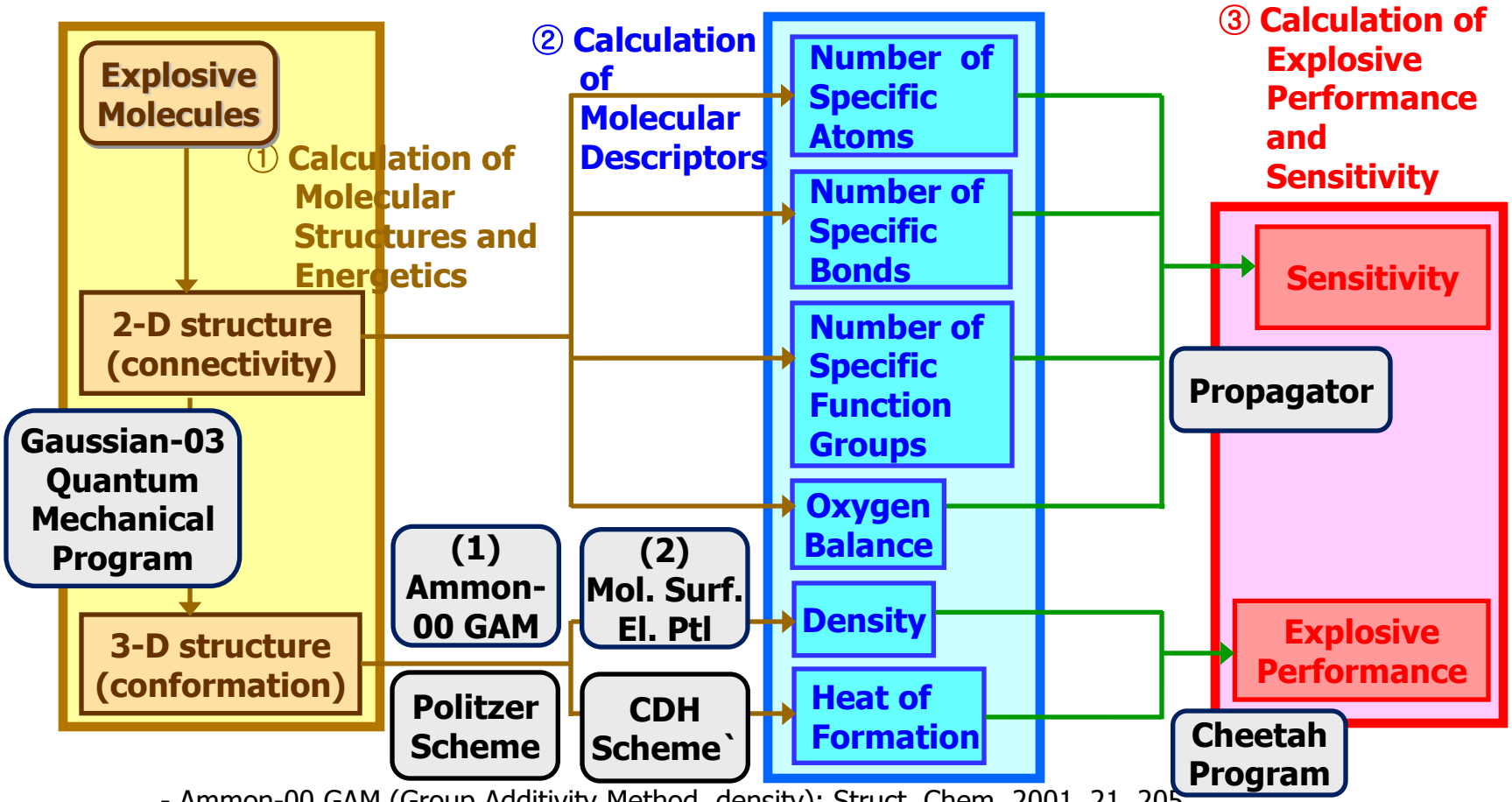
- **Screening**
  - **ADD Method-1**
- **Deriving**
  - **MS-HEMs**

General Procedure in Explosives Modeling



Ref.
Cho, S.G., A Systematic Procedure to Predict Explosive Performance and Sensitivity of Novel High-Energy Molecules in ADD, In *Handbook of Materials Science Research*, Rene, C.; Turcotte, E., Eds., Nova Science Publishers, Inc., New York, 2010, Chapter 11.

Screening New Explosive Molecules:
ADD Method-1

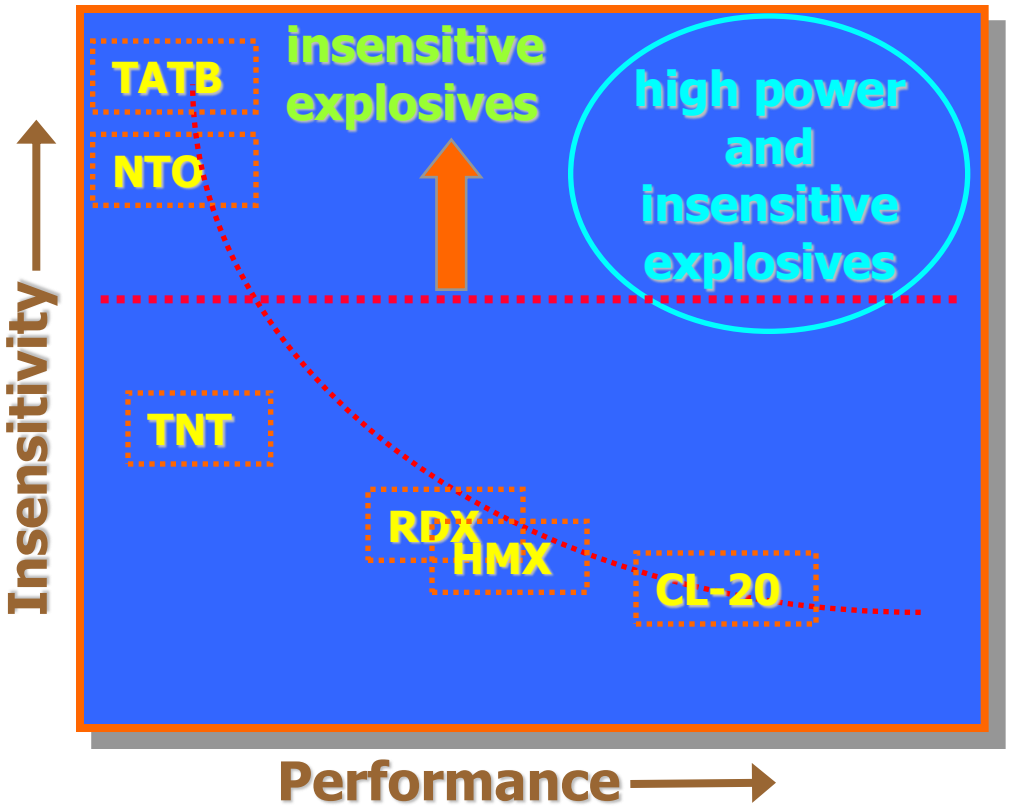


- Ammon-00 GAM (Group Additivity Method, density): Struct. Chem. 2001, 21, 205.
- Mol. Surf. El. Ptl. (density): B3LYP/6-31G* Opt., J. Comput. Chem. 2004, 25, 2073.
- Politzer Scheme (heat of formation): BP86/6-31G** Opt., J. Comput. Chem. 1995, 16, 654.
- CDH Scheme (sublimation energy): J. Chem. Soc. Perkin Trans. 2 1995, 2023

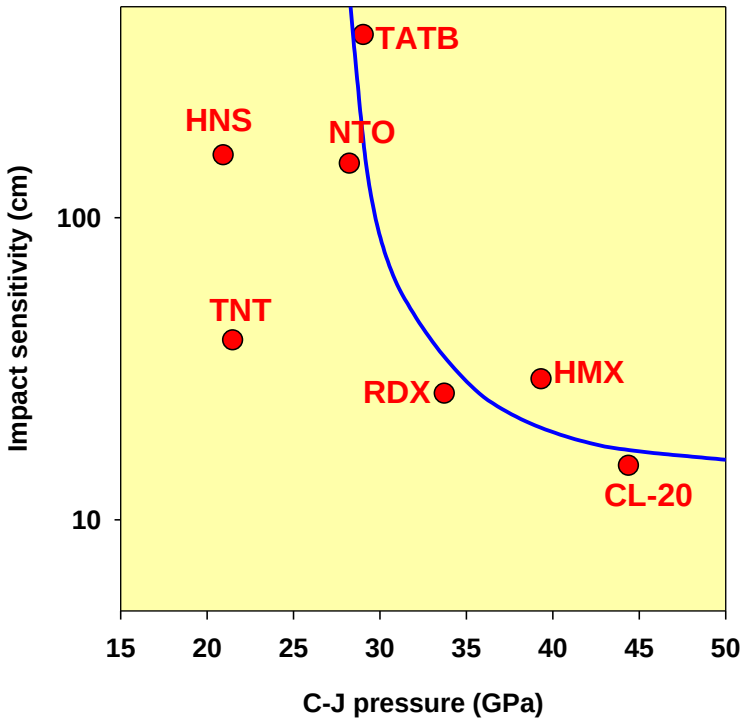
Main Comp. Features of ADD Method-1

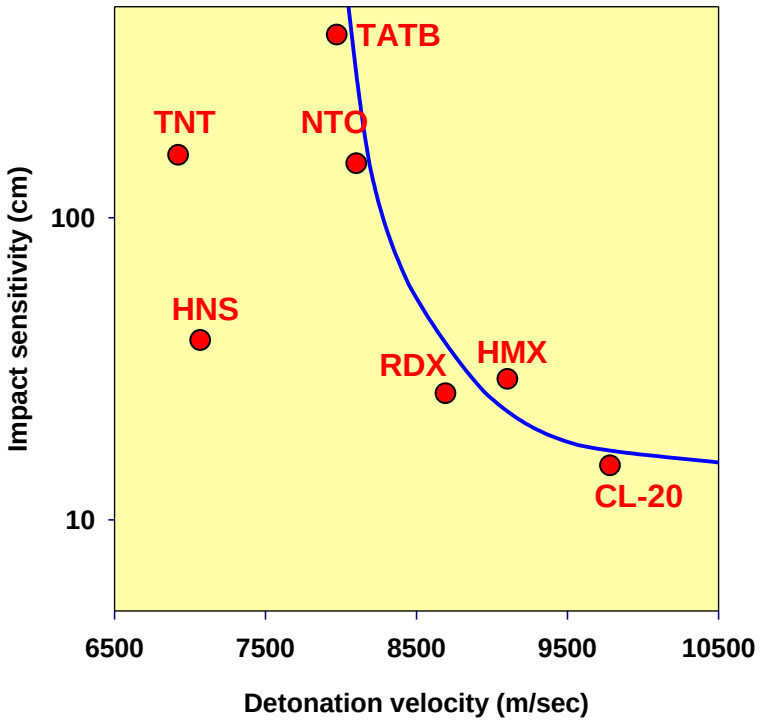
- Density Calculation
  - Very Difficult Problem
  - (1) Group Additivity method or (2) QSPR with Molecular Surface Electrostatic Potential
- Heat of Formation (HoF) Calculation
  - Quantum Mechnics (DFT BP86/6-31G**)
  - Solid State HoF with Sublimation Energy Estimation
- Impact Sensitivity Calculation
  - Probably Insoluble with Scientific Reasoning
  - Artificial Neural Network Approach (Only Choice)
    - Black Box (No Science Behind)
    - Crude Results
- Performance Calculation
  - Cheetah Program (from Dr. Fried, LLNL, USA)
- 2-D Plot between Performance and Insensitivity

Schematic 2-D Plot of Performance vs. Sensitivity

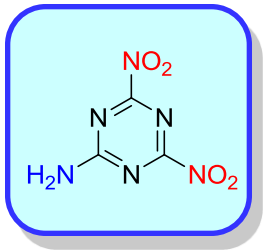


Real 2-D Plot of Performance vs. Sensitivity



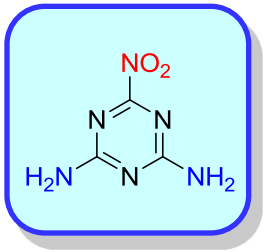


Nitrated or Azido Triazines



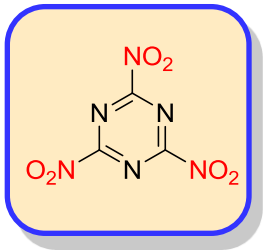
2-amino-4,6-dinitro-
1,3,5-triazine

ADNTRZ



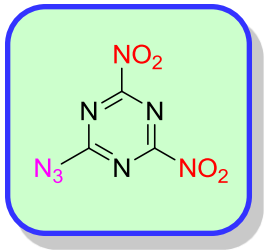
2,4-diamino-6-dinitro-
1,3,5-triazine

DANTRZ



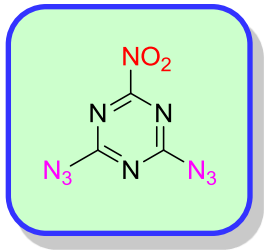
2,4,6-trinitro-
1,3,5-triazine

TNTRZ



2-azido-4,6-dinitro-
1,3,5-triazine

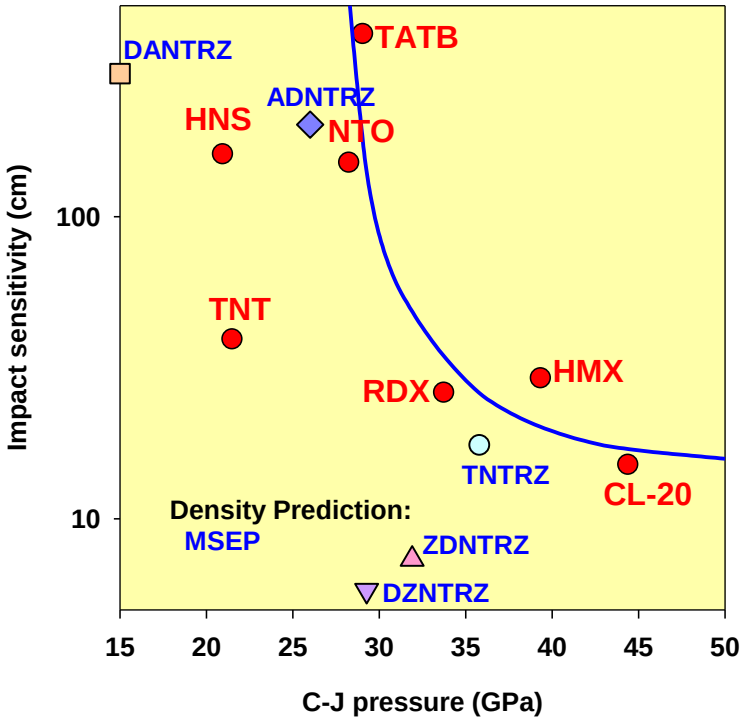
ZDNTRZ

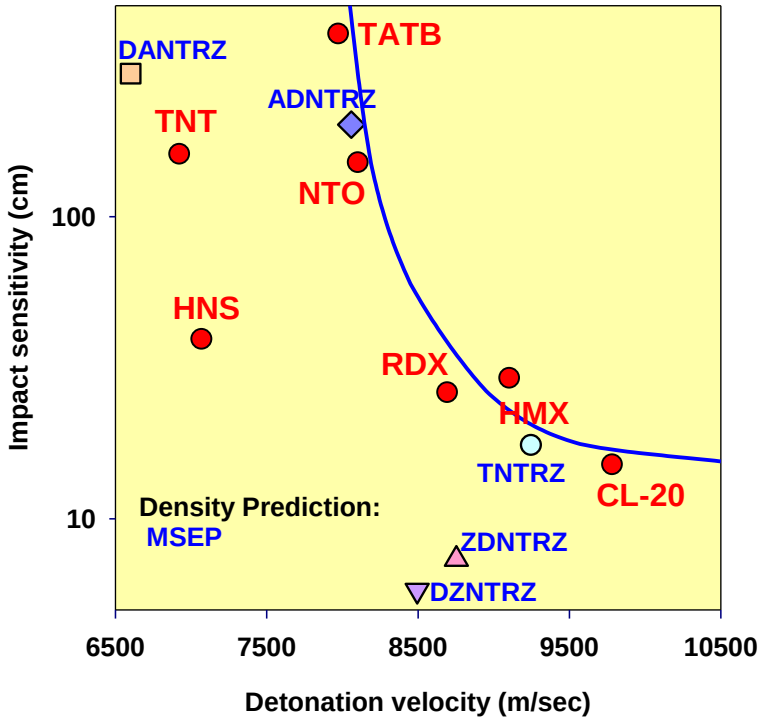


2,4-diazido-6-dinitro-
1,3,5-triazine

DZNTRZ

2-D Screening Plots of Explosive Performance vs. Impact Sensitivity



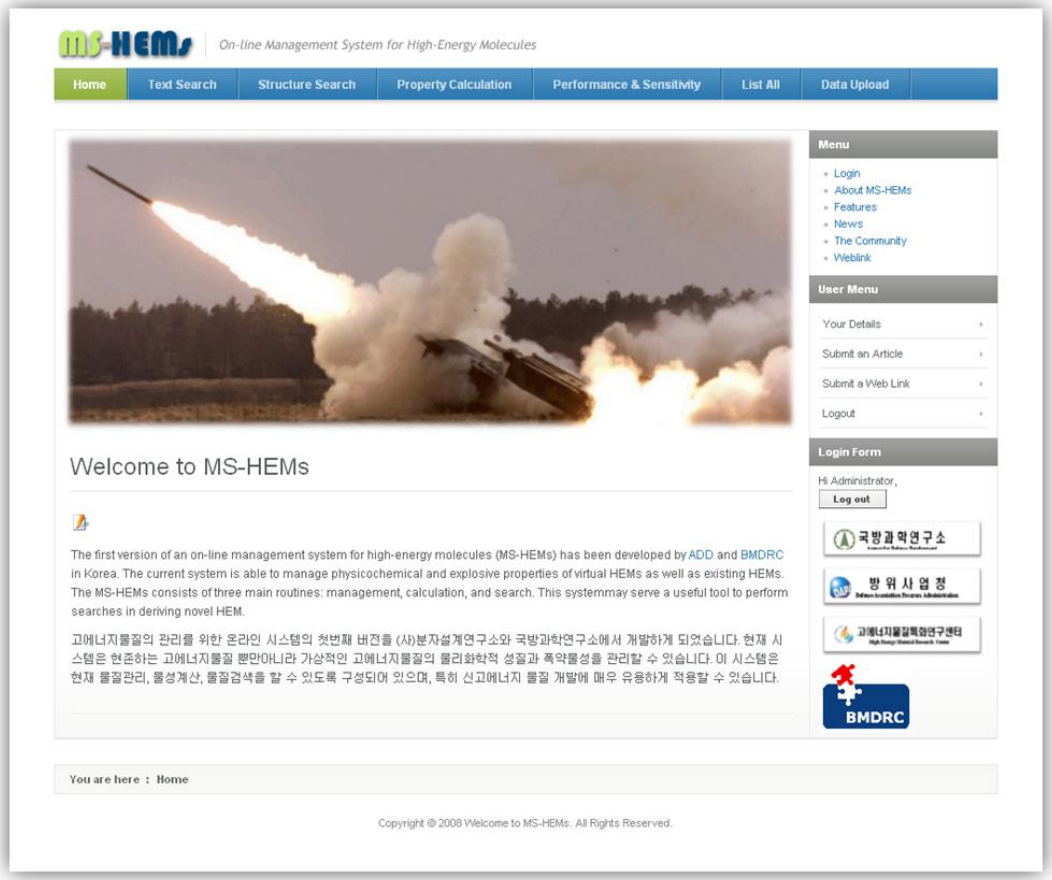


Future Direction of ADD Method-1

- **Fast Screening of Numbers of Target Compounds**
  - Deal with Lots of Compounds at One Time
    - Combinatorial Approaches
    - Synthetic Data from Others
- **Skip 3-D Calculations in Molecular Structures**
  - Total Procedure : Very Fast
    (Heat of Formation: Benson's Group Additivity)
  - Accuracy : Not High, yet Reasonable
  - Ready to Predict
- **Extend Scope to Molecules and Mixtures**
  - Salt, Inorganic, Polymeric …
  - Explosive Formulations

- **Screening**
  - **ADD Method-1**
- **Deriving**
  - **MS-HEMs**

MS-HEMs System (Main Page)

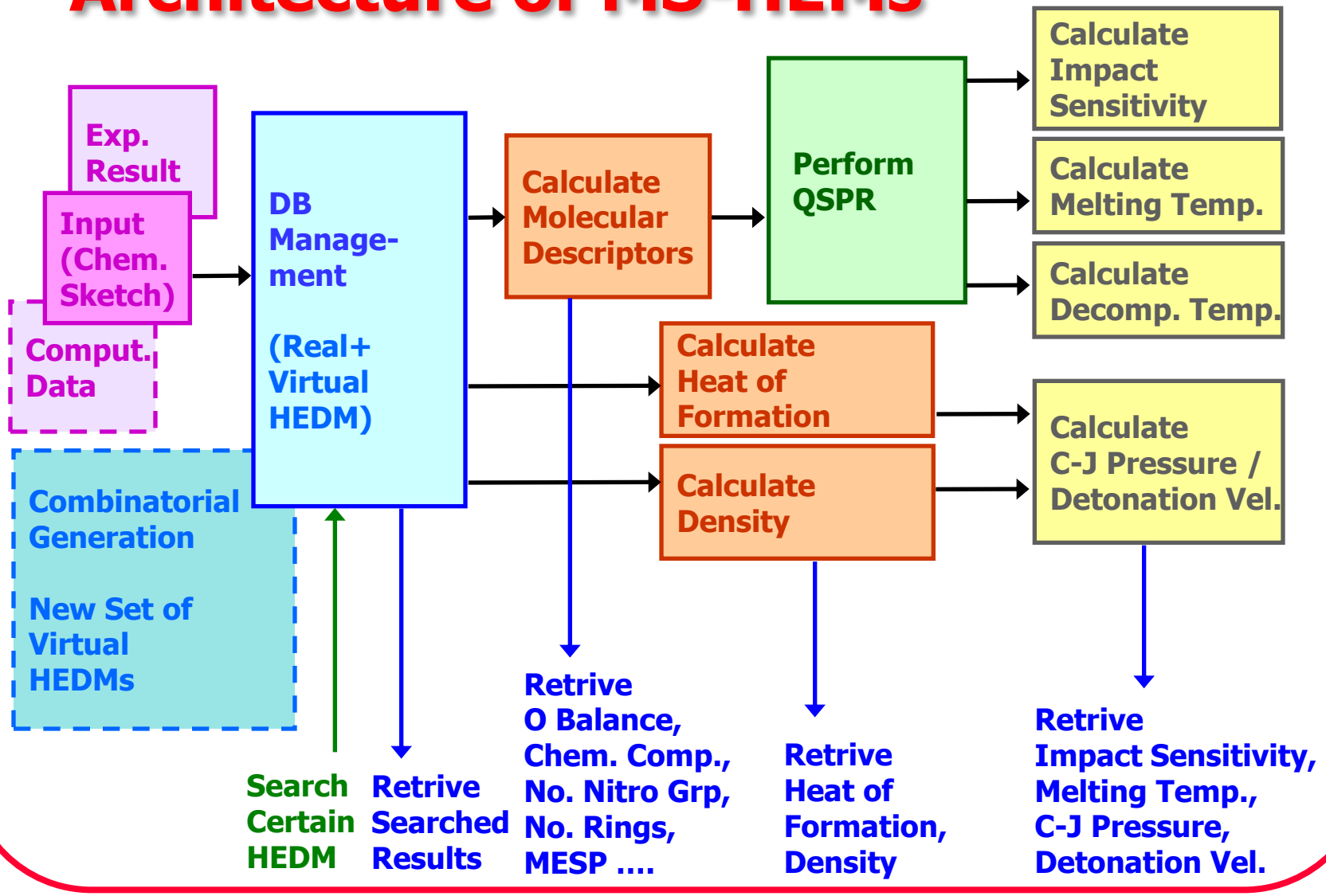


- CMS
  - Login
  - Banner
  - News
  - Community
  - Search
- Login
  - Admin
  - User
  - Super User
  - Manager

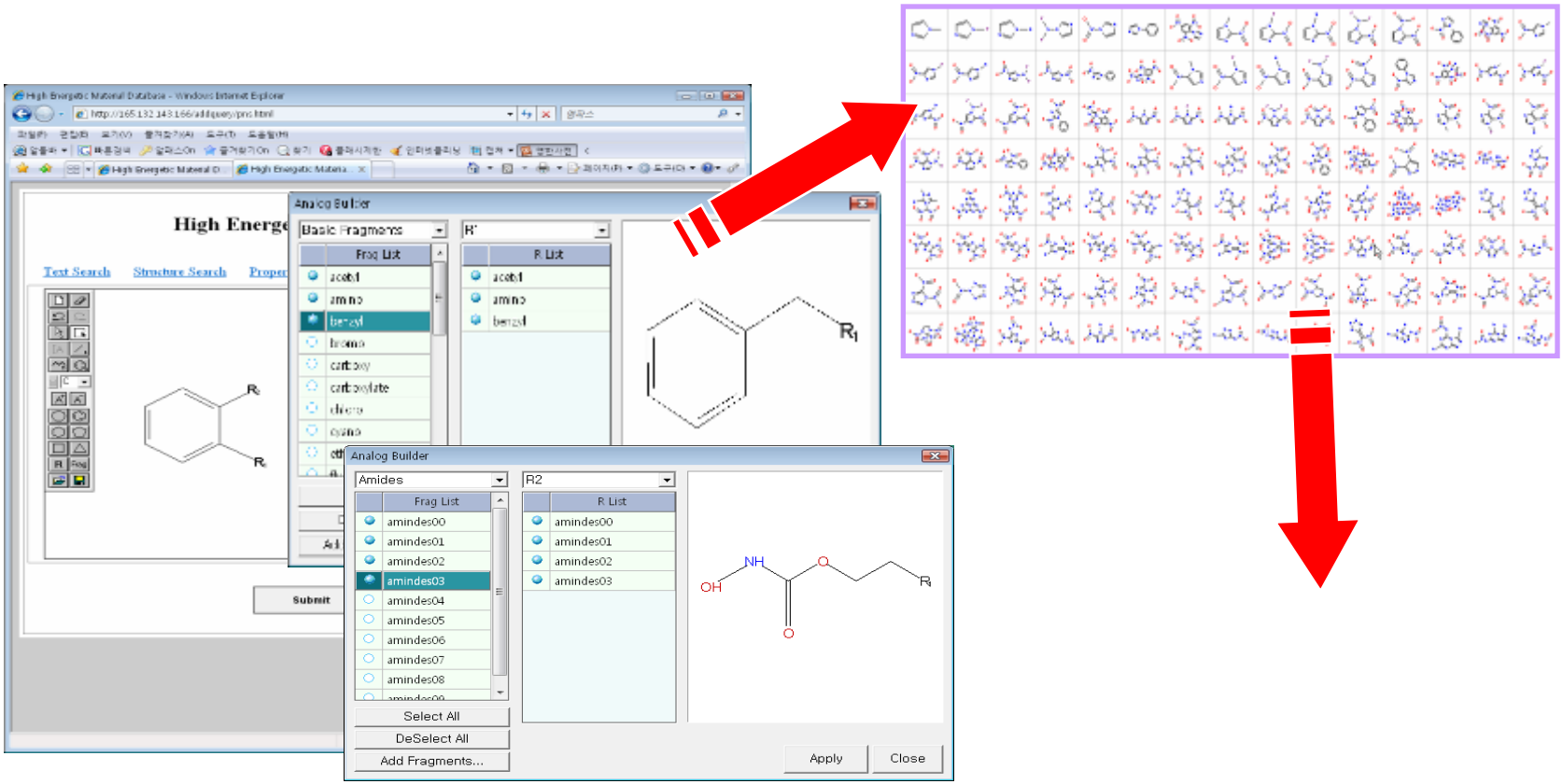
※ MS-HEMs: Management System for High-Energy Molecules

Ref. Lee, S.K; Cho, S.G.; Park, J.S.; In, Y.Y.; No, K.T. *Bull. Korean Chem. Soc.* 2012, *33*, 856.

Architecture of MS-HEMs

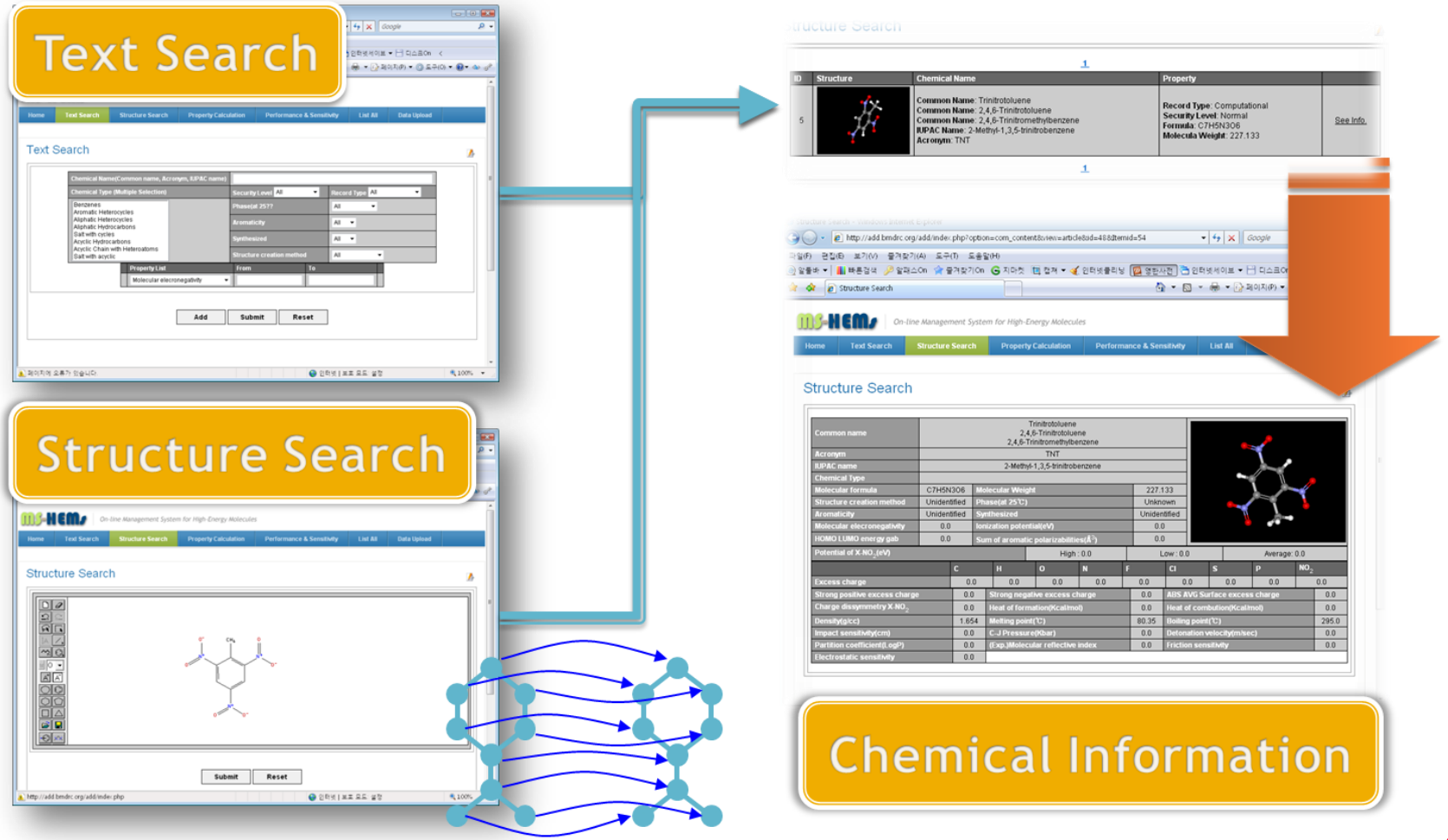


Combinatorial Generation of Virtual HEDM Candidates

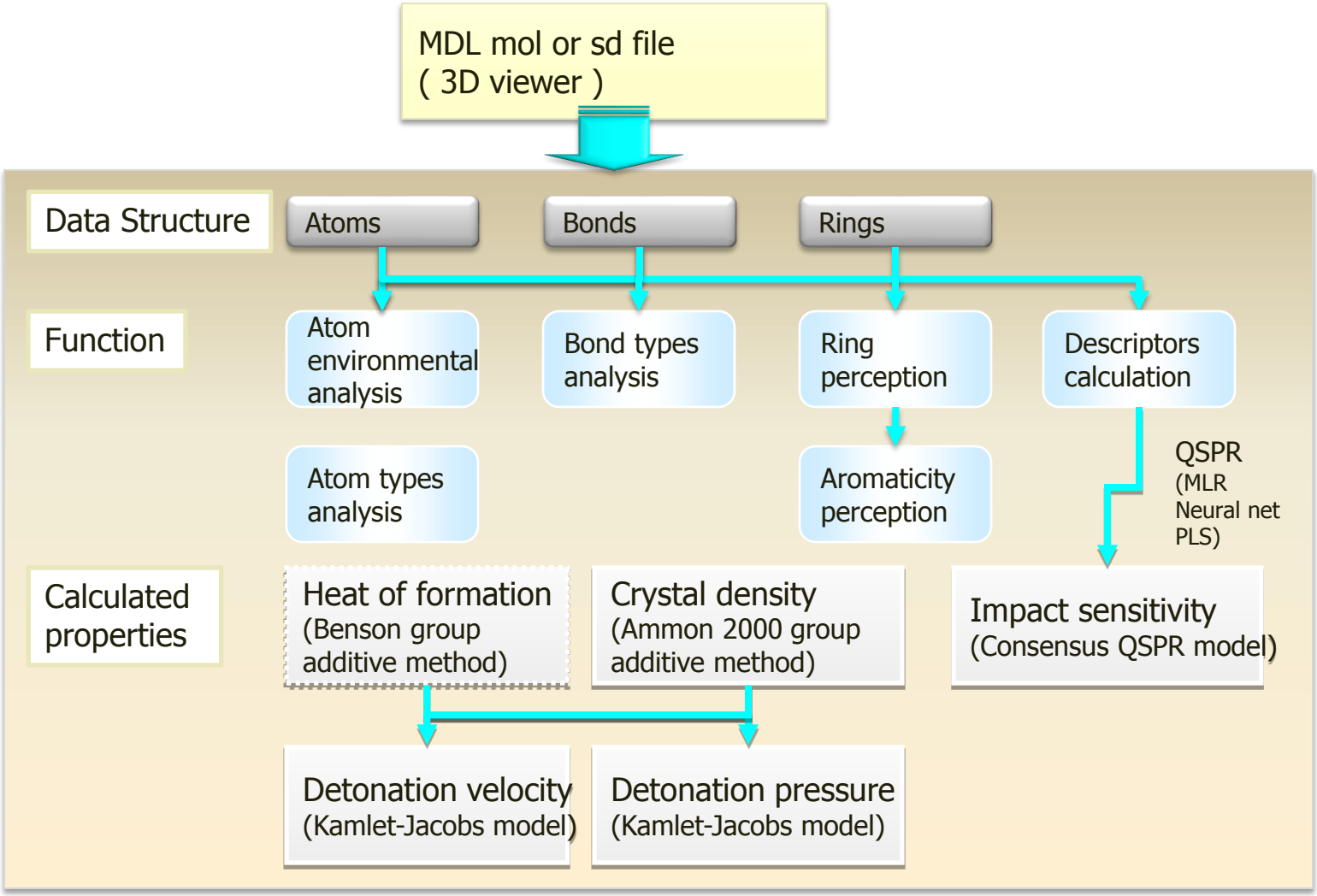


※ Adopted a Feature from PreADME program (http://www.bmdrc.org)

Data Search


Text Search
Text Search
Add
Submit
Reset
Structure Search
Structure Search
Submit
Reset
Structure Search
Chemical Information

Automatic Calculation Routines

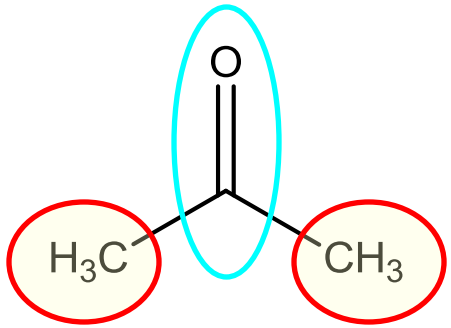


Heat of Formation Prediction Routine

Benson method (group additive method)
- about 4000 second order types (combination of 39 types)

Atom types : 39 types

H	CN	O	S
C	CS	F	SO
C_d	N	Cl	SO_2
C_a	N_I	Br	B
C_t	N_A	I	BO_3
C_B	NO	P	
C_{BF}	NO_2	PN	
CO	NP	PO	



$\Delta H_f = 2 \times C\text{-}(H)_3(C) + 1 \times CO\text{-}(C)_2$
$= 2 \times -10.08 - 31.5 = -51.66$ kcal/mol
(obs. -51.70 kcal/mol)

S.W.Benson, *Thermochemical Kinetics*, Wiley, 1976.
N. Cohen, S.W. Benson, *Chem. Rev.* 1993, 93, 2419.
N. Cohen, *J. Phys.Chem.Ref.Data*, 1996, 25,1411.

Explosive Performance Prediction Routine

- Kamlet-Jacobs Equation

Detonation velocity

$$D(km/s) = 1.01(1+1.3\rho_0)\Phi^{1/2}$$

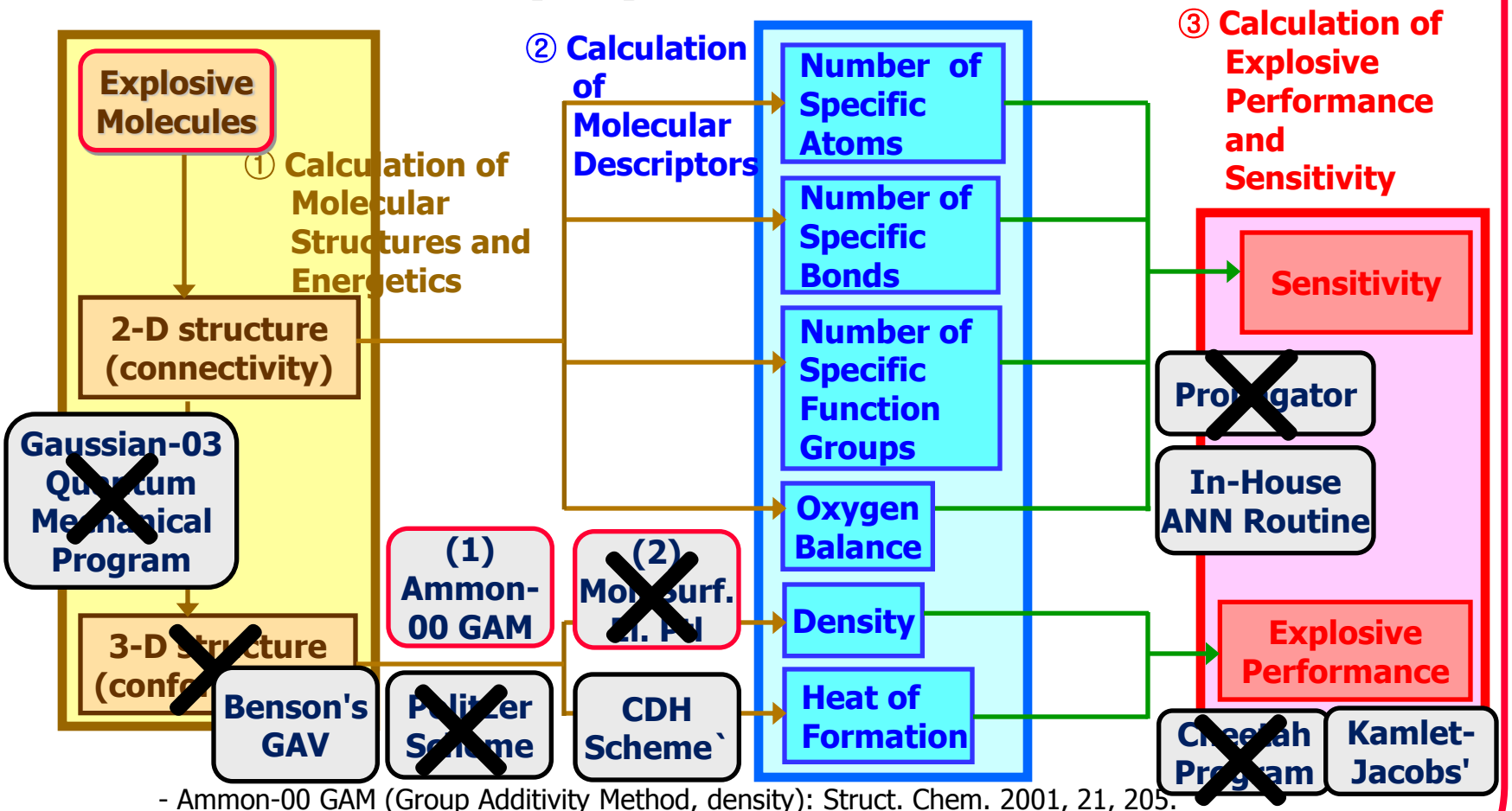
C-J pressure

$$p_{C-J}^{(KJ)} = 15.58\rho_0^2\Phi, \quad \Phi = NM^{1/2}Q^{1/2}$$

N : number of moles of gaseous detonation products per gram of explosive
M : average weight of these gases in gram of gas per mole of gas
Q : chemical energy of the detonation reaction in calories per gram
P_0 : density of the undetonated explosive in gram per cubic centimeter

M. J. Kamlet, S. J. Jacobs, *J. Chem. Phys.* 1968, 48, 23.
M. J. Kamlet, J. E. Ablard, *J. Chem. Phys.* 1968, 48, 36.

Screening New Explosive Molecules:
ADD Method-1(2D)



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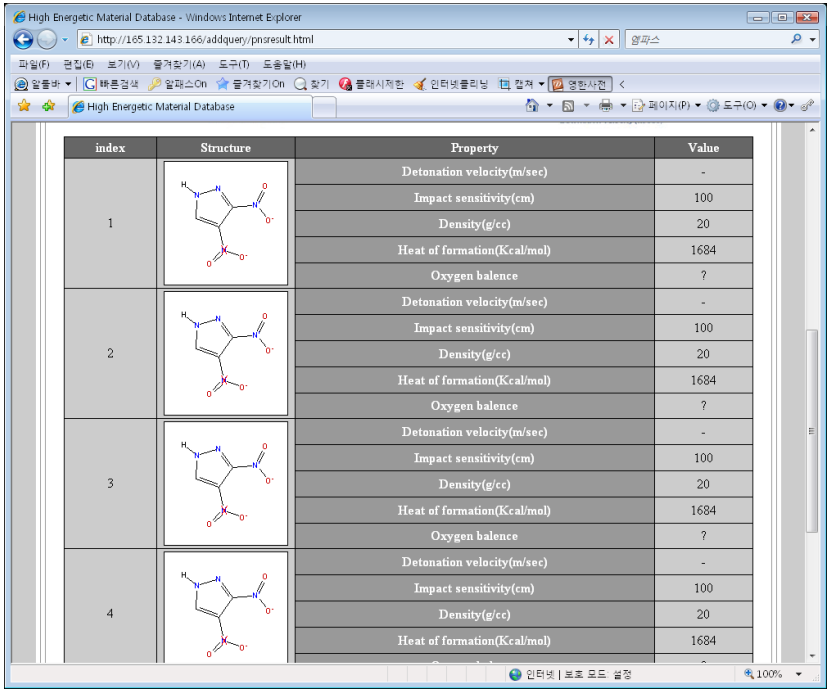
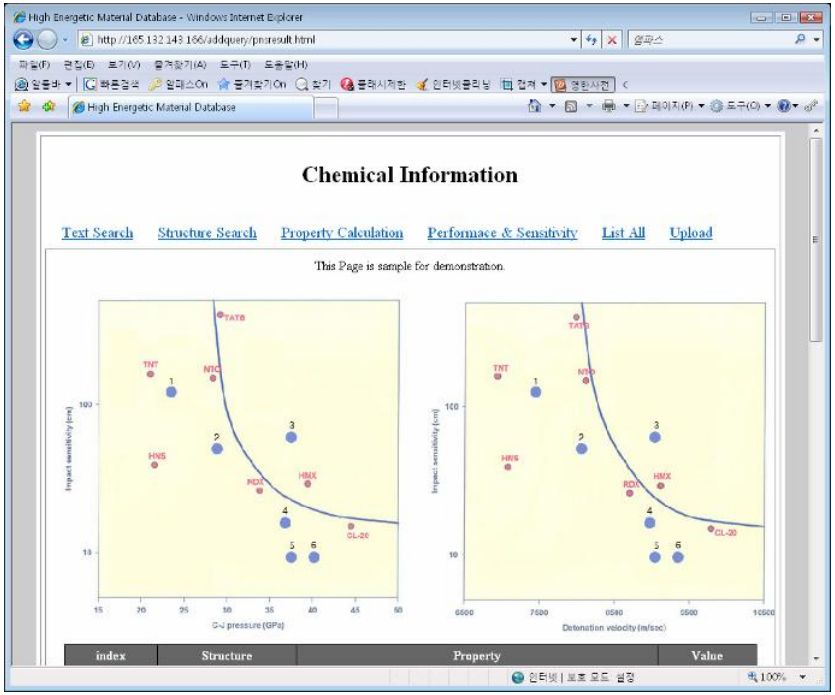
Quick Screening Based on Performance / Sensitivity with ADD Method-1(2D)





Current Status and Future Direction

- **High energetic materials database system**
  - Collection of high energetic materials (fact + virtual)
  - Search for HEM with a certain range of performance / sensitivity
  - Design of novel HEM with virtual molecules in DB
  - Combinatorial design of novel HEM with DB and ab initio calculation
  - Managing computational results of HEM
- **Prediction of HEM properties**
  - Group additivity method : Density, Heat of formation
  - QSPR model : Impact sensitivity, Detonation velocity (under construction)
    - 2D descriptors, GFA, MLR, PLS, Rprop NN and consensus model
    - Validation by large independent external set (high predictability)
    - Rapid prediction of impact sensitivity for new HEM (100 compds/sec)
  - The prediction model permit high throughput experiments of molecules which are not yet synthesized to organic chemists.

Acknowledgment

- Members in High Explosives Team

- Prof. K.T. No (Yonsei Univ, Seoul)
  Prof. S.K. Lee (Hannam Univ., Daejeon)
  Impact Sensitivity Prediction
  MS-HEMs Design

- Prof. C.K. Kim (Inha Univ.)
  Density Prediction

- High Energy Material Research Center (Inha Univ.)
  Next-Generation Converged Energy Research Center (Yonsei Univ.)