

# Attaching Uncertainties to Predictions from Quantum Chemistry Models

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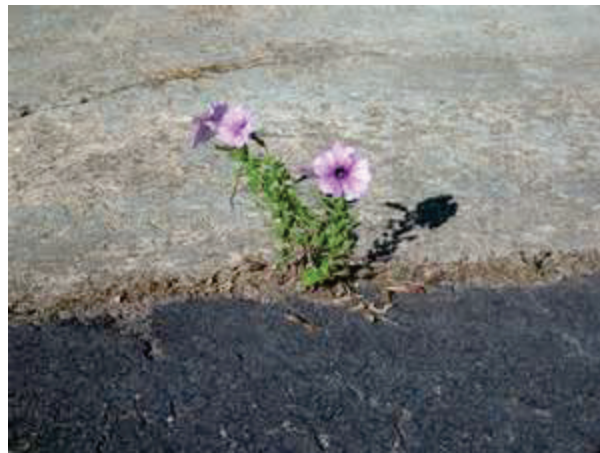
*Chemical Sciences Division*

*MML, NIST*

# Origin in WERB Review

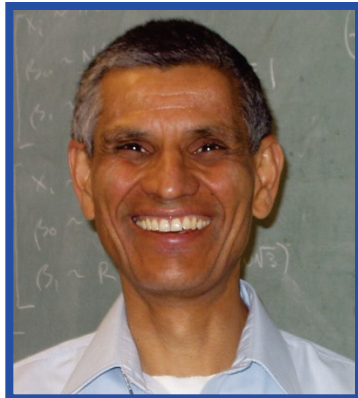
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- By long tradition, quantum chemists (still) do not report uncertainties
- NIST Admin. Manual required uncertainties
  - How bureaucratically unreasonable!
  - ...but maybe it would be a good idea



# Acknowledgments

- Russ Johnson
  - [CCCBDB.nist.gov](http://CCCBDB.nist.gov)



- Raghu Kacker

# Uncertainties are Worth Money

“If you want to make money, give the data away for free. Charge for the error-bars.”

--S.E. Stein (NIST)



When you're building something, uncertainty matters. **Over-design** is expensive and **under-design** is catastrophic.

# Economics Drives Increasing Reliance upon Predictive Models

- Keep getting faster
  - Faster = cheaper
- Keep getting better
  - Better = reliable

Example: CH<sub>3</sub>OH calculation

- Cost in 2015 vs. 1985
- Decrease ~900,000-fold
- That is  $\tau_{1/2} = 18$  months





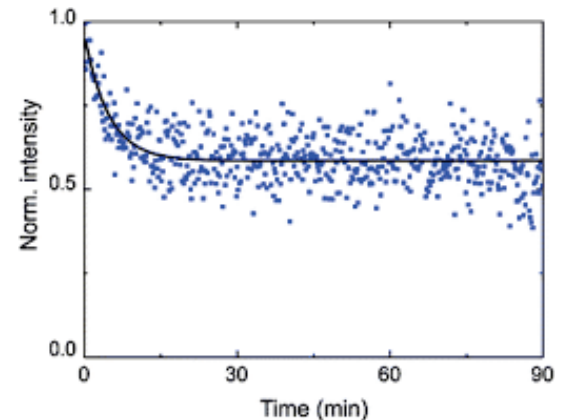
# “Virtual Measurement”


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- Term coined by Walt Stevens (NIST)
- Drop-in replacement for experimental measurement
  - Recommended **value** of measurand
  - Associated **uncertainty** statement
- Why does it matter that it's from a computational model?

# Uncertainties for Experimental Measurements

- Repeatability
  - Measure several times, report stats
- Propagation (linear, MC)
  - Turn it into a math problem
    - Measurement model
  - Run the math
- Why are round robins not unanimous?
  - The real world includes messy ignorance
  - It's very hard to include that mess in the uncertainty, so it's rarely done.





# Uncertainties for Quantum Chemistry Models

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- Interval should be a **probabilistic statement about the true value**
  - This is what people want
  - This is hard to deliver!
- Repeatability is not an issue
  - Non-zero but negligible
- How can we estimate the desired uncertainty interval?



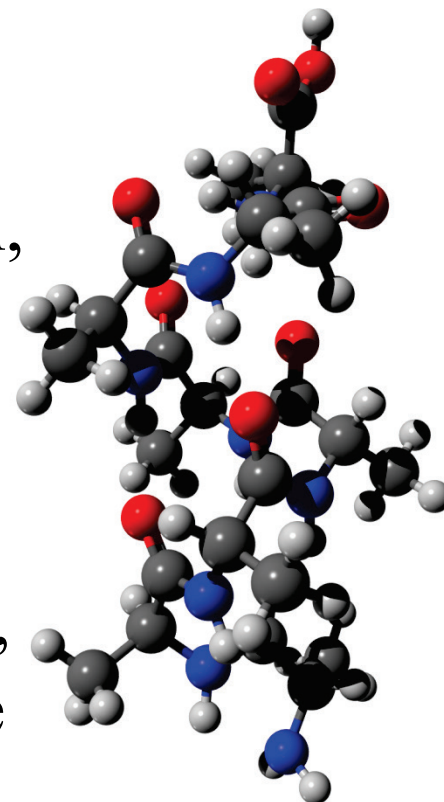
But first:

What is Quantum Chemistry?

(aka Electronic Structure Theory)

# Quantum Chemistry Predicts...

- Molecular structure (chemical bonds, molecular shape, dynamics)
- Molecular spectroscopy (**infrared**, Raman, visible, nmr, microwave, THz)
- Chemical reactions (kinetics, **thermodynamics**, mechanisms)
- Many other properties (solubility, acidity, electric, magnetic, semiconductors, phase change)



helical



# Quantum Chemistry is Physics

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- “Ab initio” modeling of collection of atoms
  - Atomic nuclei
  - Electrons
  - Quantum mechanics
    - Time-independent Schrödinger (differential) equation
    - Hamiltonian ( $H$ ) contains the **physics**
    - Eigenvectors ( $\Psi$ ) are wavefunctions
    - Eigenvalues ( $E$ ) are energy levels

$$H\Psi = E\Psi$$



# Physical Approximations

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- Non-relativistic
  - Relativistic effects, if treated, usually by...
    - perturbation theory and/or
    - effective potentials
- Born-Oppenheimer approximation
  - Nuclear motion ignored, then
  - Vibrations considered separately
    - double-harmonic approximation, usually



# Mathematical Approximations

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- First solve a corresponding one-electron problem
  - Mean-field approximation for inter-electron repulsion
  - 1e basis functions describe molecular orbitals
    - atom-centered (non-orthogonal Gaussians)
    - plane waves (orthogonal)
  - Density functional theory (DFT): many-body effects are implicit in the 1e problem
- Wavefunction theory (WFT)
  - Products of 1e solutions comprise basis set for many-e wavefunction
  - Space must be truncated severely to be tractable



# Input Parameters

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- Physics
  - Fundamental constants ( $h$ ,  $e$ , etc.)
  - Initial positions of atomic nuclei
- Math
  - 1e basis set (from literature)
  - Treatment of **electron correlation**
    - the instantaneous repulsion among electrons
    - [more of this on next slide]



# Correlation Choices/Parameters

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- Density functional theory (DFT)
  - Choose **functional** (all are flawed!)
  - Grid density
- Wavefunction theory (WFT)
  - **Method and truncation order**
    - Configuration interaction *or*
    - Perturbation theory *or*
    - Coupled-cluster theory
- Various convergence parameters—defaults OK

# “Computational Model”

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- Refers to choice in the **two main decisions**:
  - 1e basis set
  - Method for coping with electron correlation
- Many are included in the **CCCBDB**
  - “Computational Chemistry Comparison and Benchmark DataBase”
  - Online comparison with experiments
  - <http://cccbdb.nist.gov/>
  - by Russ Johnson (NIST)





# Awkwardnesses Proliferate

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- Error depends upon model
- Error depends upon molecule
- Error depends upon the minor choices, too
- How to measure the error?
  - True error is unknowable
- Hopeless??

# Do It Anyway!

- Do our best
  - Better than user's guess
- It won't be elegant



Engineers get things done.  
If a number is missing,  
they guess.




# Our Strategy (Pragmatic Optimism)

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- Compare model predictions with true values
  - **Experimental** values as **surrogates for true values**
  - Use as many as sensible
    - Errors average out; like a round robin
- Assume errors transferable among molecules
  - Reasonable only for similar molecules
  - “Similar” evades definition
    - Rely upon chemical **classifications** by default

# Simple Approach


$$y_{i \in \kappa} = x_i \circ c_{\kappa}$$

What we  
want

$i$  = molecule

$\kappa$  = class of molecules

$y$  = true value of property

$x$  = model prediction

$c$  = correction for bias

# Choose a Model and Run It

$$y_{i \in \kappa} = x_i \circ c_{\kappa}$$

What we want      What we compute

$i$  = molecule

$\kappa$  = class of molecules

$y$  = true value of property

$x$  = model prediction

$c$  = correction for bias

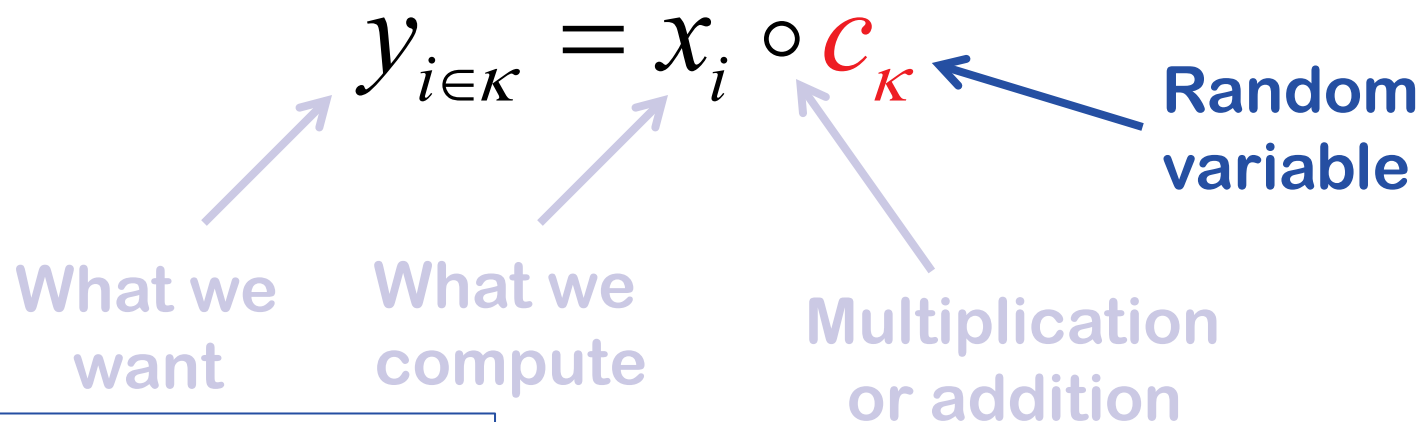
# Additive or Multiplicative Correction for Bias

$$y_{i \in \kappa} = x_i \circ c_{\kappa}$$

What we want      What we compute      Multiplication or addition

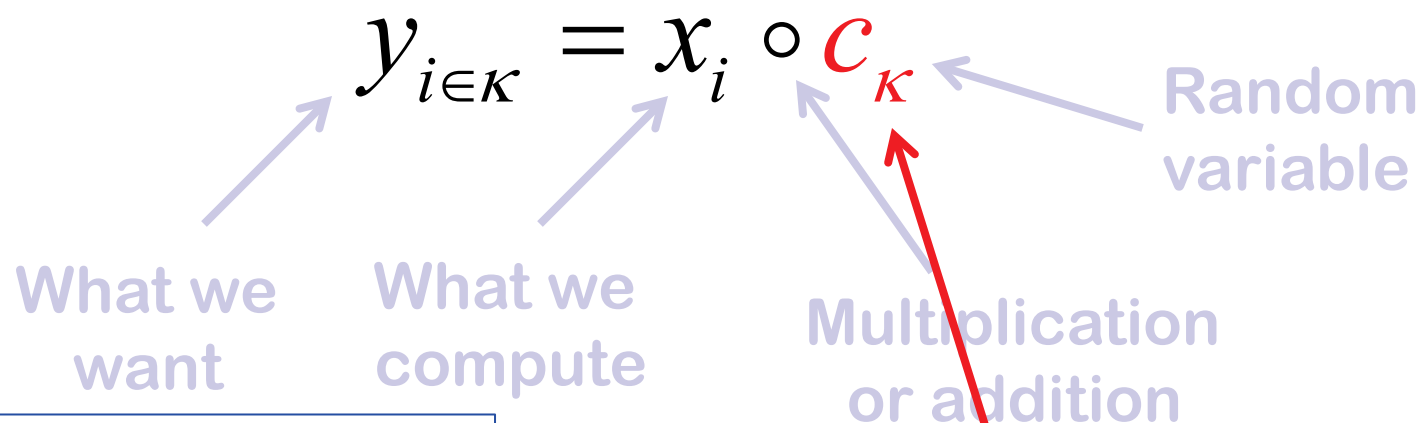
$i$  = molecule  
 $\kappa$  = class of molecules  
 $y$  = true value of property  
 $x$  = model prediction  
 $c$  = correction for bias

# Magnitude of Correction is a Random Variable



$i$  = molecule  
 $\kappa$  = class of molecules  
 $y$  = true value of property  
 $x$  = model prediction  
 $c$  = correction for bias

# Most Uncertainty is from the Correction for Bias



$i$  = molecule  
 $\kappa$  = class of molecules  
 $y$  = true value of property  
 $x$  = model prediction  
 $c$  = correction for bias

Inferred from comparisons  
with experimental benchmarks  
for  $j \in \kappa$





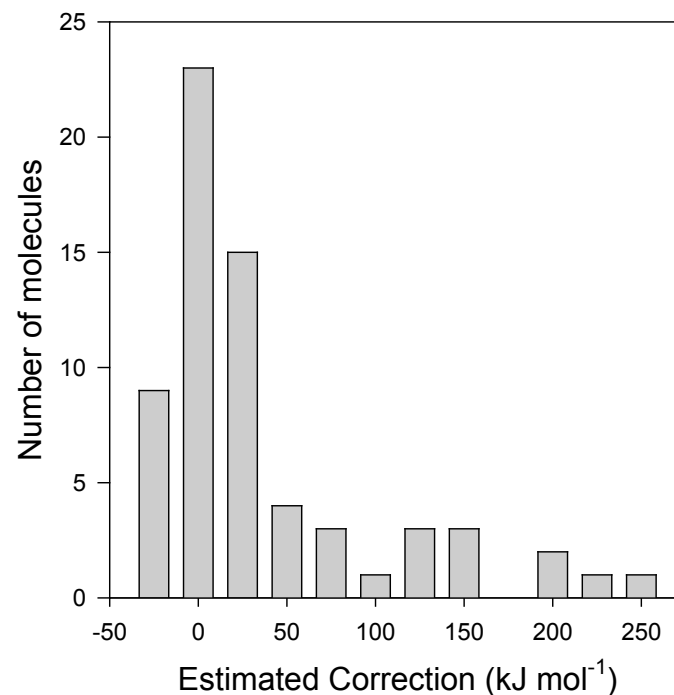
# Modeling Bias as a Random Variable?

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- Bias is the error in a prediction
- It is not random!
  - Fully determined, highly repeatable
- But we don't understand why it takes its particular value
  - It looks random because we're sufficiently bewildered
  - Classification partitions the bewilderment

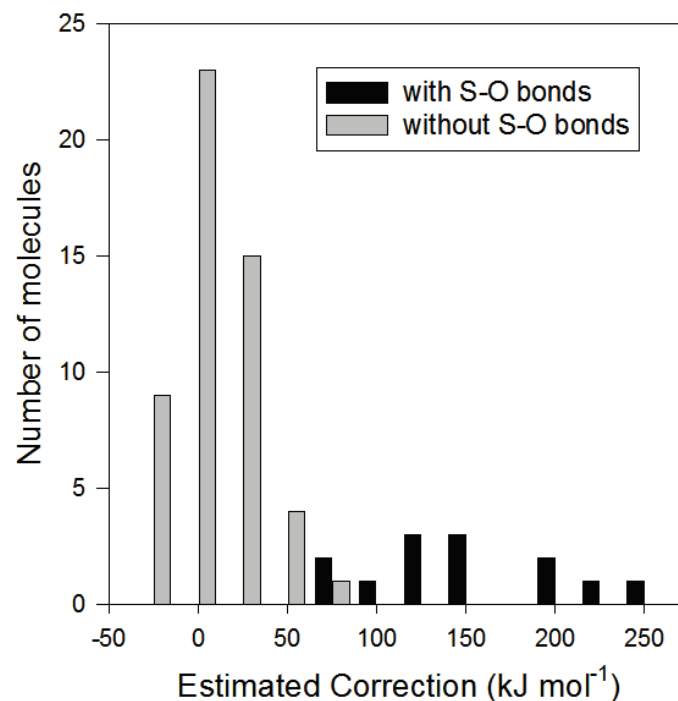
# Classification Example

- Stability of sulfur-containing compounds
  - “Correction” is inverse of bias/error
  - Additive here
  - Ugly distribution



# Better Classification

- Finer distinction helps
  - Distributions more symmetrical
  - Easier to describe
  - Narrower intervals
- Connect to *GUM*



IJK, "Uncertainty Associated with [Virtual Measurements](#) from Computational Quantum Chemistry Models," *Metrologia* **41**, 369 (2004)



# Example with a Pitfall

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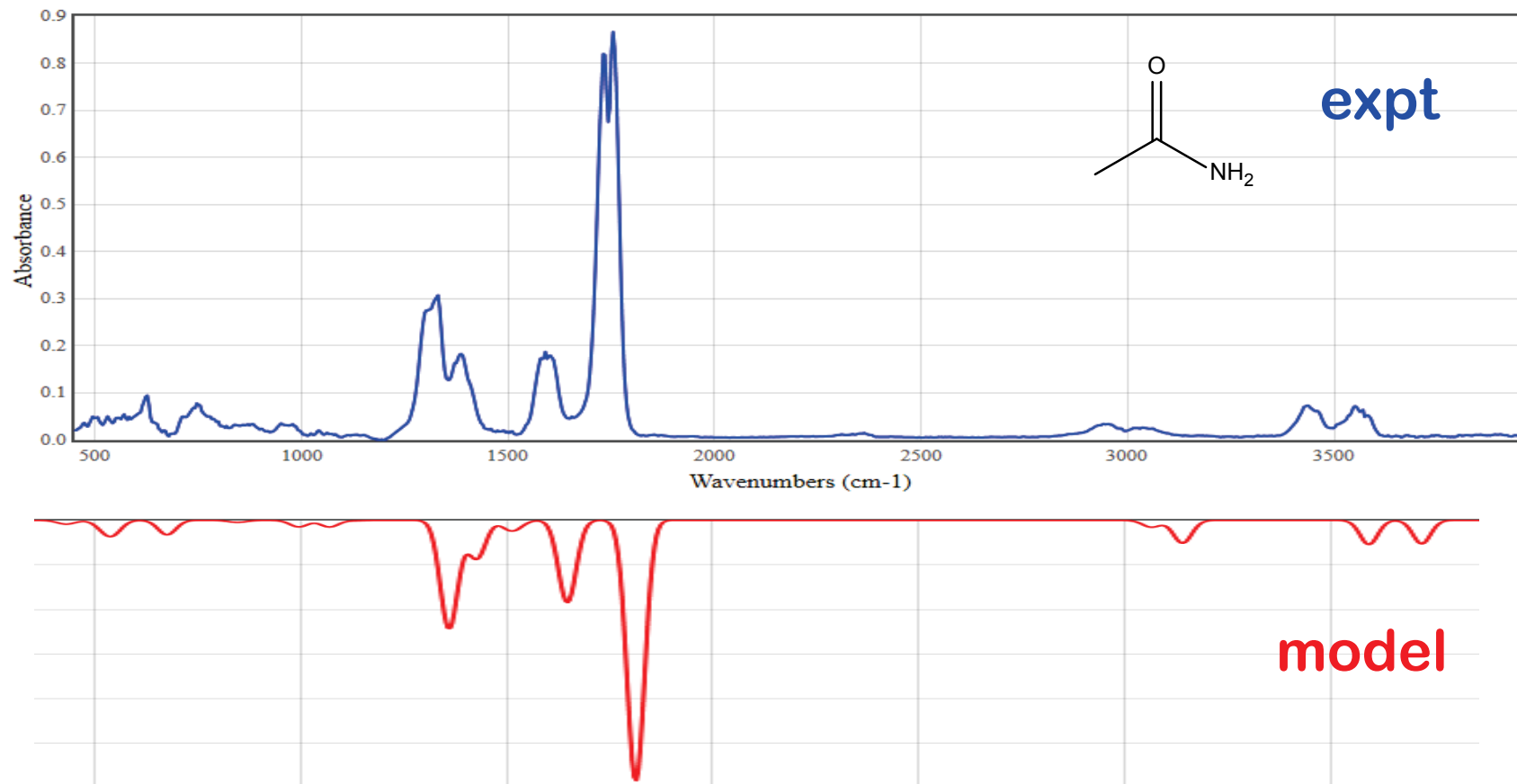
- Molecular vibrational frequencies
  - Basis for infrared (IR) and Raman spectroscopies
- Quantum chemistry results
  - Usually multiplied by empirical scaling factor
    - Corrects for bias
    - Standard practice

IJK, “Uncertainties in Scaling Factors for ab Initio Vibrational Frequencies,” *J. Phys. Chem. A* **109**, 8430 (2005)



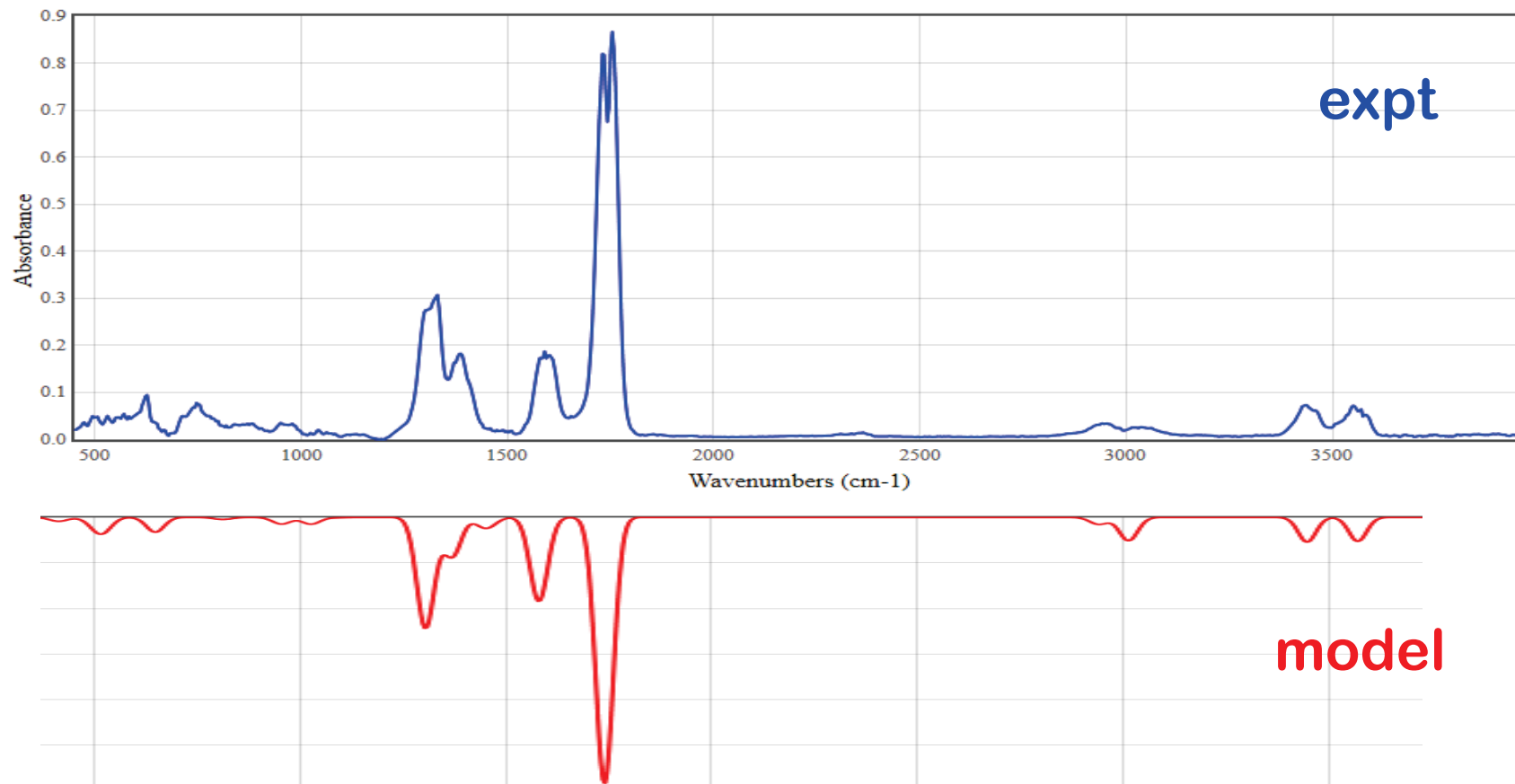
Highly Cited Paper

# Vibrational Spectrum Example: Acetamide, $\text{CH}_3\text{CONH}_2$



without empirical scaling

# With Empirical Frequency Scaling



with empirical scaling

# Scaling Factors from Least-Squares

*J. Phys. Chem., Vol. 100, No. 41, 1996* 16505

TABLE 1: Frequency Scaling Factors Suitable for Fundamental Vibrations and  $\text{rms}_{\text{ov}}$  ( $\text{cm}^{-1}$ ) Derived from a Least-Squares Fit of Frequencies<sup>a</sup>

method	scale factor <sup>b</sup>	$\text{rms}_{\text{ov}}$ <sup>c</sup>
AM1	0.9532	126
PM3	0.9761	159
HF/3-21G	0.9085	87
HF/6-31G(d)	0.8953	50
HF/6-31+G(d)	0.8970	49
HF/6-31G(d,p)	0.8992	53
HF/6-311G(d,p)	0.9051	54
HF/6-311G(df,p)	0.9054	56
MP2-fu/6-31G(d)	0.9427	61
MP2-fc/6-31G(d)	0.9434	63
MP2-fc/6-31G(d,p)	0.9370	61
MP2-fc/6-311G(d,p)	0.9496	60
QCISD-fc/6-31G(d)	0.9537	37
B-LYP/6-31G(d)	0.9945	45
B-LYP/6-311G(df,p)	0.9986	42
B-P86/6-31G(d)	0.9914	41
B3-LYP/6-31G(d)	0.9614	34
B3-P86/6-31G(d)	0.9558	38
B3-PW91/6-31G(d)	0.9573	34

<sup>a</sup> Using F1 set of 1066 frequencies. <sup>b</sup> As defined by eq 10. <sup>c</sup> Overall root-mean-square error, as defined by eq 13.

- There have been many studies; this one is the most cited by far
- This table is typical
- Note reported precision and similarity of values

Scott and Radom, "Harmonic vibrational frequencies: An evaluation of Hartree-Fock, Moller-Plesset, quadratic configuration interaction, density functional theory, and semiempirical scale factors," *J. Phys. Chem.* **100**, 16502 (1996). **5129 citations**



# Uncertainties for Scaling Factors?

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- Not discussed!
- Scaling *ad hoc* despite large literature
  - Adjust as desired to fit experiment
  - Qualitative
- Can it be made a quantitative virtual measurement?



# Vibrational Scaling to Predict Unknown Vibrational Frequency #0

$$y_0 = x_0 c_0$$

$y = \text{truth}; x = \text{model};$   
 $c = \text{correction}$

$$u_r^2(y_0) \approx u_r^2(x_0) + u_r^2(c_0)$$

linearized propagation

$$u_r^2(x_0) \approx 0$$

repeatability

$$c_i = x_i / z_i \text{ for } i \in \text{calibration set}$$

$z = \text{experimental value}$

$$c_0 = \sum_{i>0} x_i z_i / \sum_{i>0} x_i^2$$

usual least-squares est. for  $c_0$

$$u^2(c_0) \approx \sum_{i>0} x_i^2 (c_i - c_0)^2 / \sum_{i>0} x_i^2$$

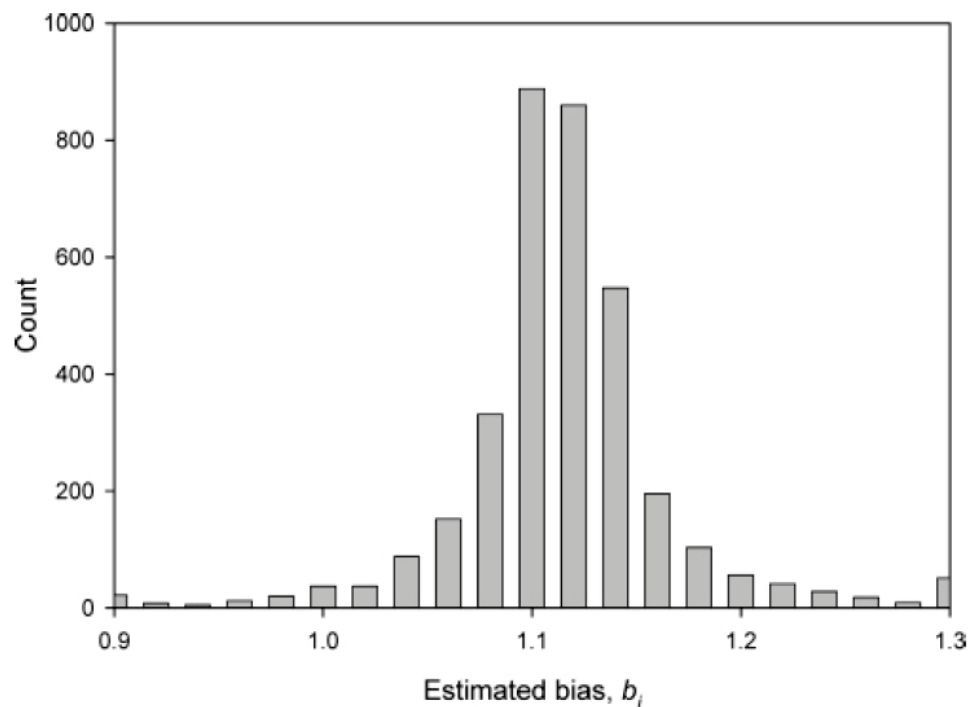
conclusion for scaling factor

$$u(y_0) \approx x_0 u(c_0)$$

conclusion for vib. freq.

# Example Distribution of Bias

8434 *J. Phys. Chem. A*, Vol. 109, No. 37, 2005



$$b_i = c_i^{-1} = z_i/x_i$$

**Figure 1.** Distribution of estimated biases,  $b_i$ , for HF/6-31G(d) calculations of 3508 vibrational frequencies of 312 molecules.

# Recommended Uncertainties

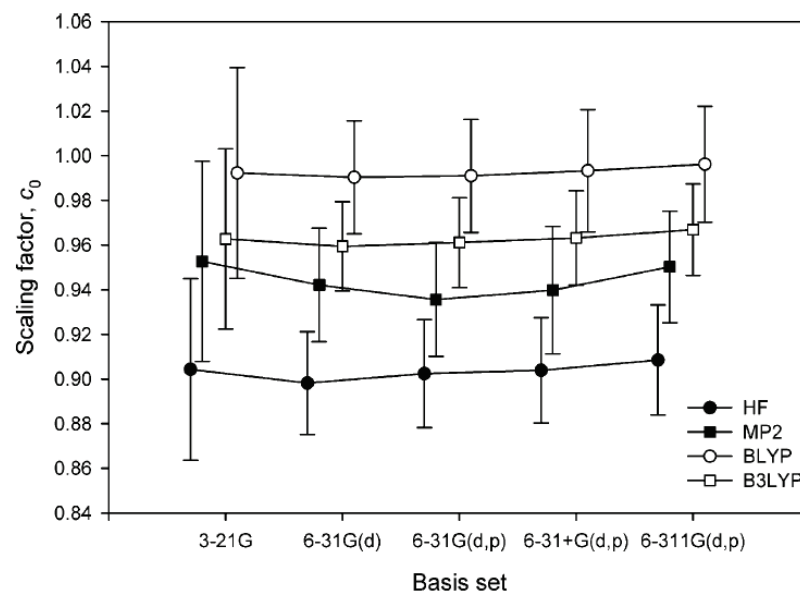
Ab Initio Calculations of Vibrational Frequencies

*J. Phys. Chem. A*, Vol. 109, No. 37, 2005 8435

TABLE 1: Scaling Factors,  $c_0$ , and Their Associated Standard Uncertainties,  $u(c_0)$ , Expressed as  $c_0 \pm u(c_0)$ , for the Prediction of Vibrational Fundamentals, Arranged by Theoretical Method and Basis Set<sup>a</sup>

	3-21G	6-31G(d)	6-31G(d,p)	6-31+G(d,p)	6-311G(d,p)
HF	$0.9043 \pm 0.0407$ [3295] (0.89, <sup>c</sup> 0.9085 <sup>a</sup> )	$0.8982 \pm 0.0230$ [3508] (0.8929, <sup>c</sup> 0.8881, <sup>f</sup> 0.8953 <sup>e</sup> )	$0.9024 \pm 0.0241$ [3419] (0.8992 <sup>d</sup> )	$0.9039 \pm 0.0236$ [3360]	$0.9085 \pm 0.0246$ [3478] (0.9051 <sup>d</sup> )
MP2	$0.9527 \pm 0.0448^b$ [3316]	$0.9411 \pm 0.0245$ [3360]; $0.9421 \pm 0.0254^b$	$0.9356 \pm 0.0255^b$ [3407] (0.9370 <sup>b,d</sup> )	$0.9398 \pm 0.0285^b$ [3399]	$0.9502 \pm 0.0250^b$ [3416] (0.9496 <sup>b,d</sup> )

- Only two significant digits
- Few differences among models are significant
- Basis set with (d) or more






# You Fell in a Pit!

- Linear propagation understates uncertainty for low frequencies and overstates for high frequencies
- RMS residual is a better estimate for uncertainty of predicted frequencies
- Our analysis stands for  $u(c_0)$  per se

P. Pernot and F. Cailliez, “Comment on...,” *J. Chem. Phys.* **134**, 1 (2011).

Full paper: “Semi-empirical correction of ab initio harmonic properties by scaling factors: a validated uncertainty model for calibration and prediction,” <http://arxiv.org/abs/1010.5669>



# Why Are Uncertainties Neglected in Quantum Chemistry?

- What experts seek:
  - Better high-end models
  - Faster algorithms for existing models
  - Fame & funding
- Popular, common models are boring & ignored
- Scope (i.e., classification) is ignored
  - Not glamorous
  - Difficult
- Russ's "Sicklist"

Sprague and Irikura, "Quantitative estimation of uncertainties from wavefunction diagnostics," *Theor. Chim. Acc.* **133**, 1544 (2014)



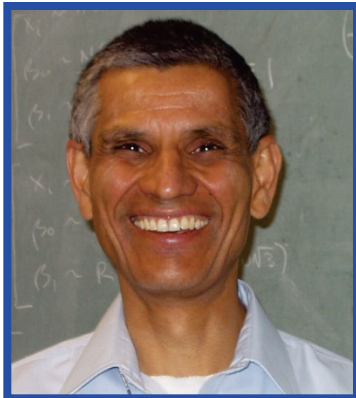
# NIST Publications on This Topic

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- P. Hassanzadeh and K. K. Irikura, Nearly Ab Initio Thermochemistry: The Use of Reaction Schemes. Application to IO and HOI, *J. Phys. Chem. A* **101**, 1580 (1997).
- K. K. Irikura, Systematic Errors in Ab Initio Bond Dissociation Energies, *J. Phys. Chem. A* **102**, 9031 (1998).
- K. K. Irikura, New Empirical Procedures for Improving Ab Initio Energetics, *J. Phys. Chem. A* **106**, 9910 (2002).
- K. K. Irikura, R. D. Johnson, III, and R. N. Kacker, Uncertainty Associated with Virtual Measurements from Computational Quantum Chemistry Models, *Metrologia* **41**, 369 (2004).
- K. K. Irikura, R. D. Johnson, III, and R. N. Kacker, Uncertainties in Scaling Factors for Ab Initio Vibrational Frequencies, *J. Phys. Chem. A* **109**, 8430 (2005).
- K. K. Irikura, Experimental Vibrational Zero-Point Energies: Diatomic Molecules, *J. Phys. Chem. Ref. Data* **36**, 389 (2007).
- K. K. Irikura, R. D. Johnson, III, R. N. Kacker, and R. Kessel, Uncertainties in Scaling Factors for Ab Initio Vibrational Zero-Point Energies, *J. Chem. Phys.* **130**, 1, 114102 (2009).
- R. D. Johnson, III, K. K. Irikura, R. N. Kacker, and R. Kessel, Scaling Factors and Uncertainties for Ab Initio Anharmonic Vibrational Frequencies, *J. Chem. Theor. Comput.* **6**, 2822 (2010).
- R. L. Jacobsen, R. D. Johnson, III, K. K. Irikura, and R. N. Kacker, Anharmonic Vibrational Frequency Calculations Are Not Worthwhile for Small Basis Sets, *J. Chem. Theor. Comput.* **9**, 951 (2013).
- M. K. Sprague and K. K. Irikura, Quantitative Estimation of Uncertainties from Wavefunction Diagnostics, *Theor. Chem. Acc.* **133**, 1544 (2014).

# Acknowledgments

- Russ Johnson
  - [CCCBDB.nist.gov](http://CCCBDB.nist.gov)



- Raghu Kacker