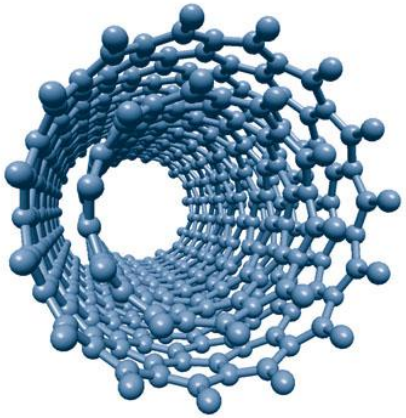
Nanotechnology Risk Assessment Models



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Center for High-rate Nanomanufacturing

QPL
Quality & Productivity Laboratory

Outline

- Overview & Motivation
  - High commercialization of nanotechnology
  - Health, economic, and regulatory uncertainties
- To-Date Nanotoxicology literature review
  - Huge concern, huge uncertainty
- Potential Modeling Approaches & Applications
  - Monte Carlo risk models
  - Multi-criteria models
  - Stochastic programming
  - Desirability functions
- Conclusions / Future Work

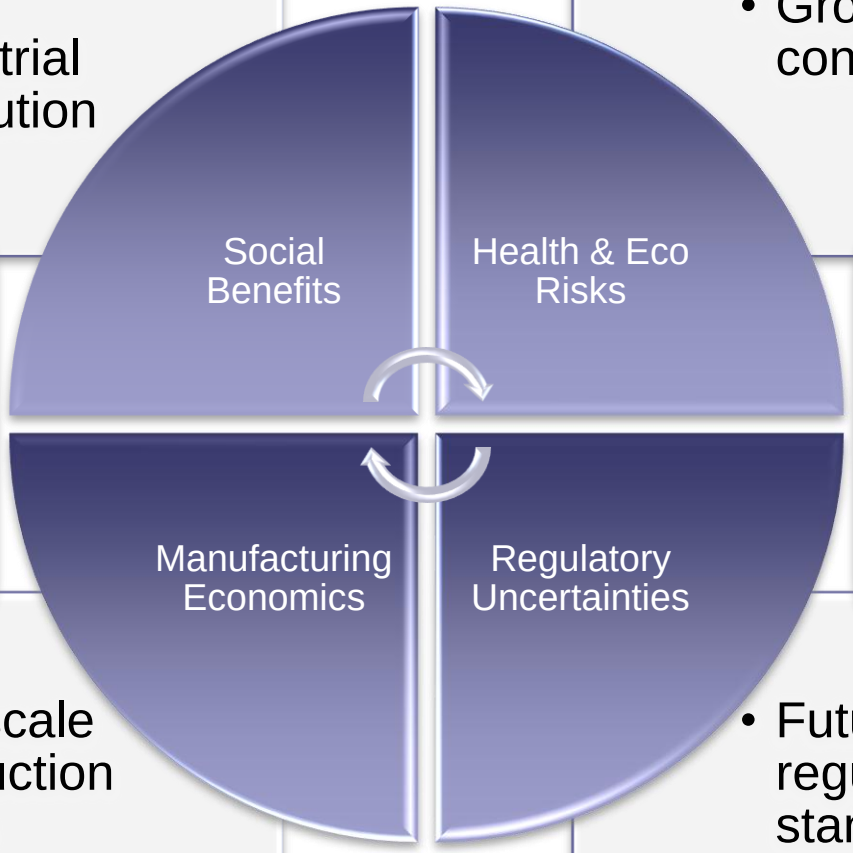
Nanomanufacturing Promise and Perils

- Next industrial revolution

- Growing concerns

Promise

- Over 800 commercial nanotech products on the market
- Main application areas:
  - Health & Fitness - 62%
  - Home & Garden - 11%
  - Food & Beverage - 10%
  - Electronics & Computers - 7%



Perils

- Possible negative attributes:
  - Penetrate dermal barriers
  - Cross cell membranes
  - Reach the gas exchange regions of the lung
  - Travel from the lung throughout the body
  - Interact at the molecular level

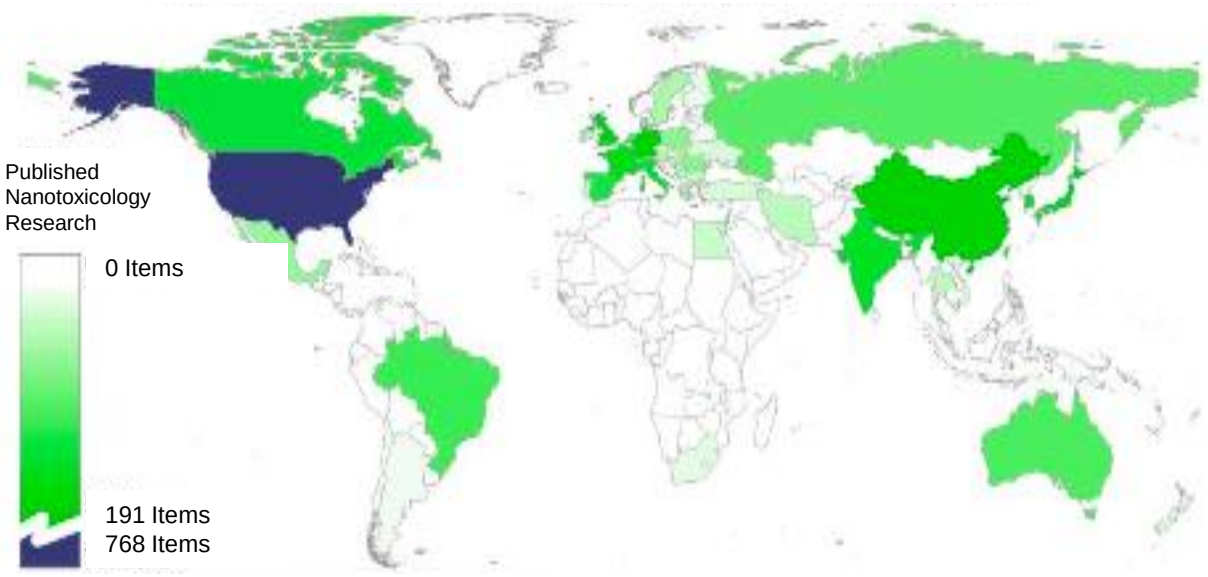
- Full-scale production costs

- Future regulatory standards

Global Distribution of Nanotoxicology Literature

- 1,935 items of peer-reviewed literature on nanotoxicology
  - Period of year 2000 to year 2007
  - English journals, letters, and reviews

Global Distribution of Nanotoxicology Scientific Literature

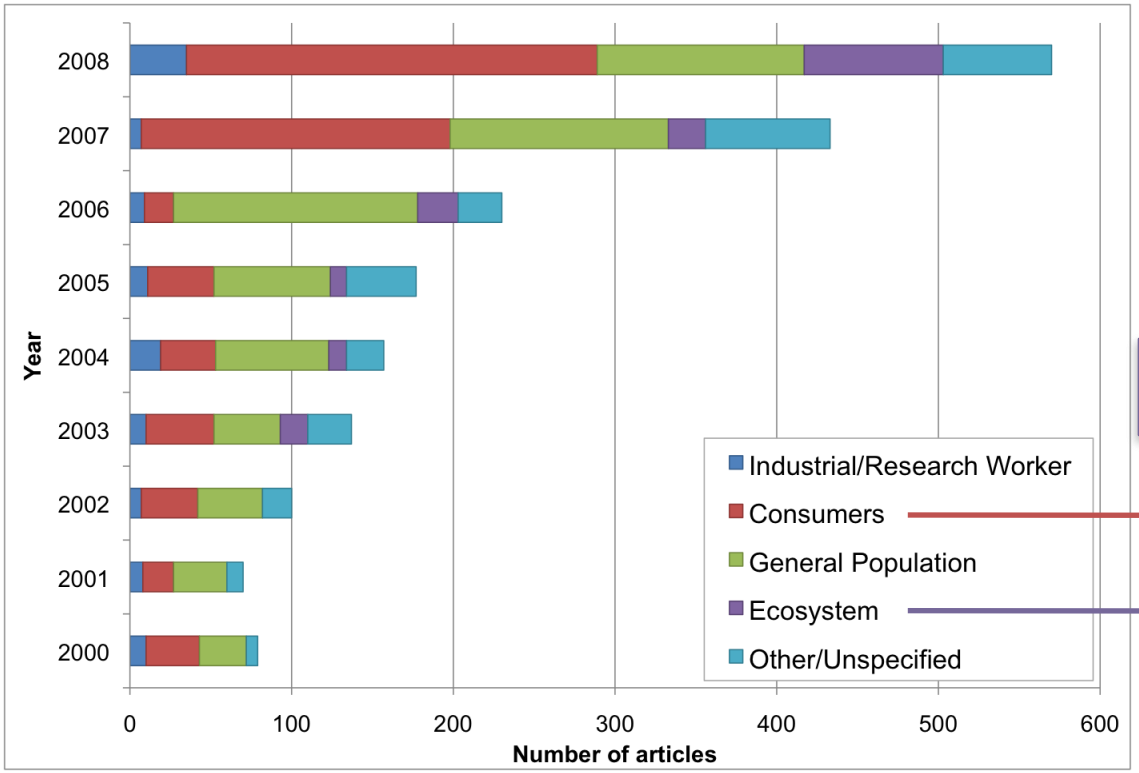


Number of Publications	
Unites States	768
China	191
Germany	116
United Kingdom	103
Japan	101
France	80
India	74
Italy	56
South Korea	56
Canada	42
Spain	34
Taiwan	34
Switzerland	30
Brazil	21
Netherlands	21
Australia	20
Russia	17
Singapore	15
Belgium	12
Israel	11
Denmark	11
Poland	10
Romania	10

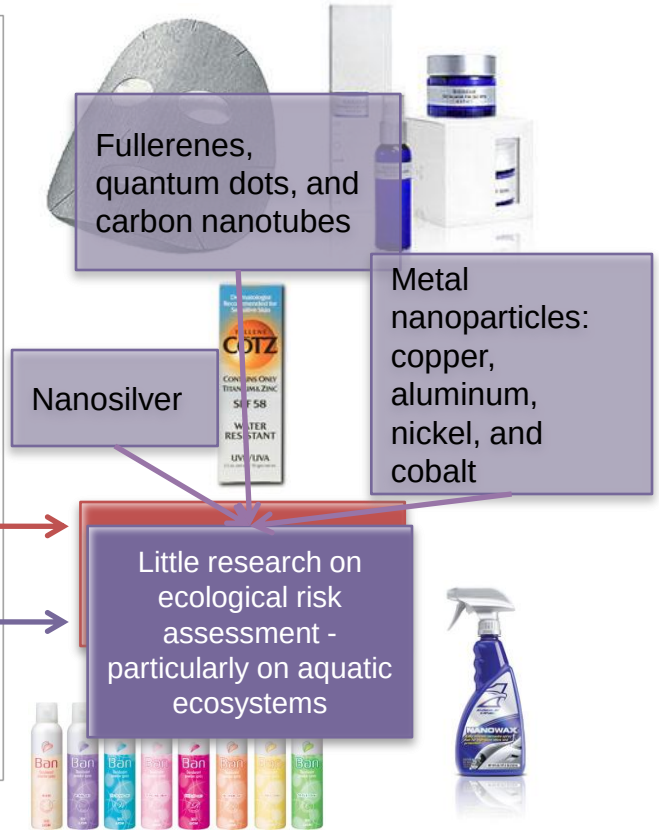
Source: A. Ostrowski, T. Martin, J. Conti, I. Hurt, and B. H. Harthorn, "Nanotoxicology: characterizing the scientific literature, 2000-2007," *Journal of Nanoparticle Research, vol. 11, pp. 251-257, 2009.*

Growing Nano-EHS Concerns…

- 600% increase in total number of studies since 2000
  - Growing concerns for consumer risk group
  - Little research on ecological risk assessment

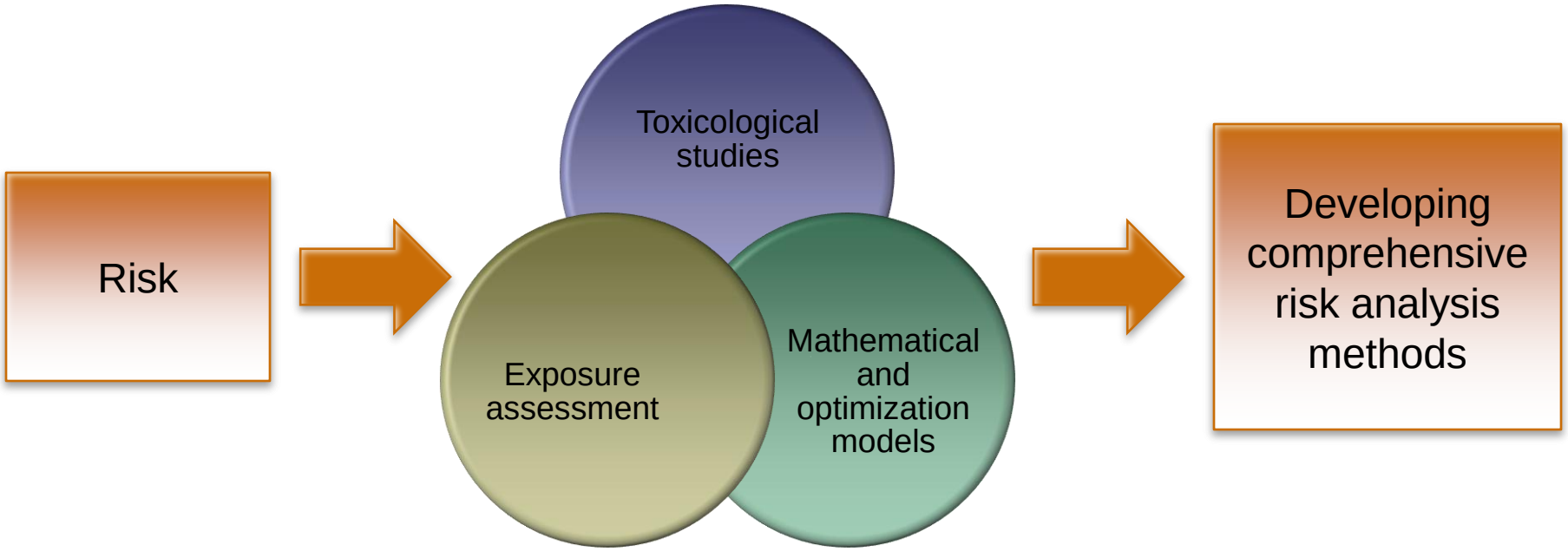


Data input from ICON



Making Informed Decisions

- Numerous nanotoxicity and ecotoxicity questions
  - Example: Carbon nanotubes are among the most studied nanomaterials, the differences in behavior of single versus multi-carbon nanotubes remain unclear.
- Uncertainty in dose-response relationships and long-term accumulation affects
- Lack of data limits the utility of methods such as life cycle assessment



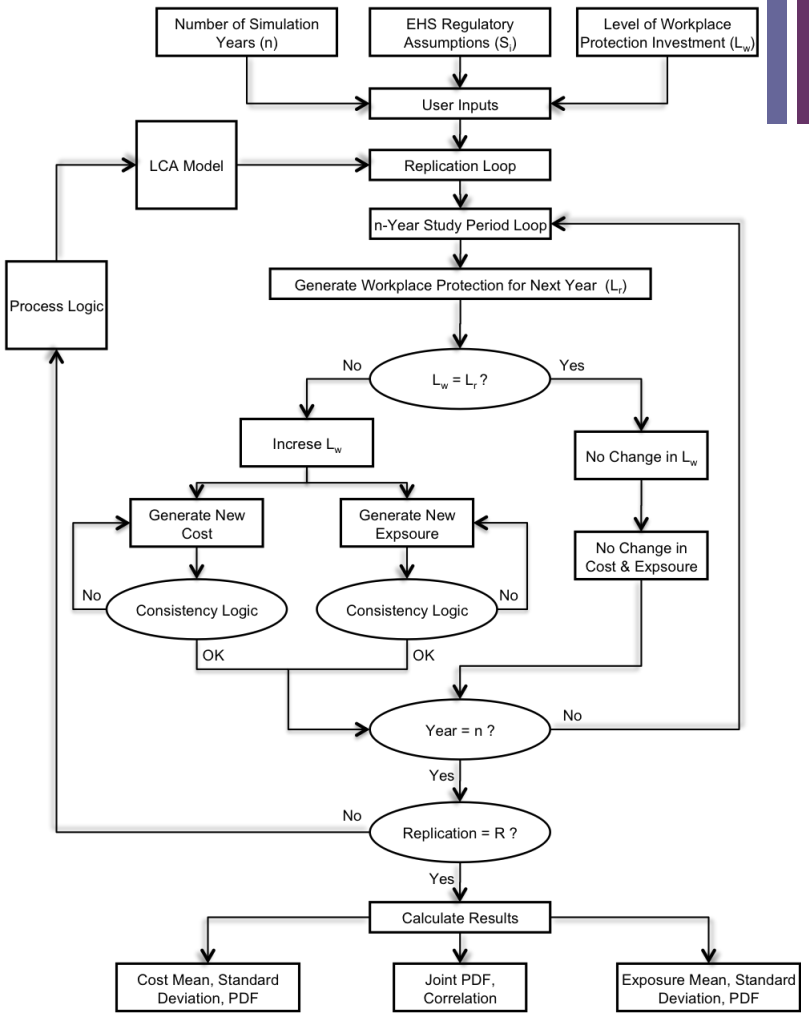
Risk Assessment Models

- Potential nanomanufacturing risk assessment modeling approaches
- Differ in the manner by which they handle uncertainty, multiple criteria, and risk-benefit trade-offs

Method	*Advantages & Disadvantages*	*Contexts*
Monte Carlo simulation	+ Allows modeling uncertainty – No tradeoff framework	Random sampling for output distribution
Multi-criteria decision making	+ Tradeoff frontiers – Deterministic	Tradeoff or compromise solutions
Stochastic programming	+ Allows stochastic parameters – Computational time	Probabilistic constraints or objectives
Desirability functions	+ Can compare discrete alternatives, robust – Abstract approach, arbitrary weights	Balance weighted total multi-criteria

Monte Carlo Model

- Cost-exposure trade-off analyses for HiPco single wall carbon nanotube manufacturing
- Uncertainties – costs, occupational health risks, and EHS standards – modeled as probabilistic events
  - ✓ Largely unknown
  - ✓ Difficult to estimate
- Similar analyses for
  - Best worker protection
  - Cost effective plant design
  - Optimum technology investments



Given Current Uncertainty…

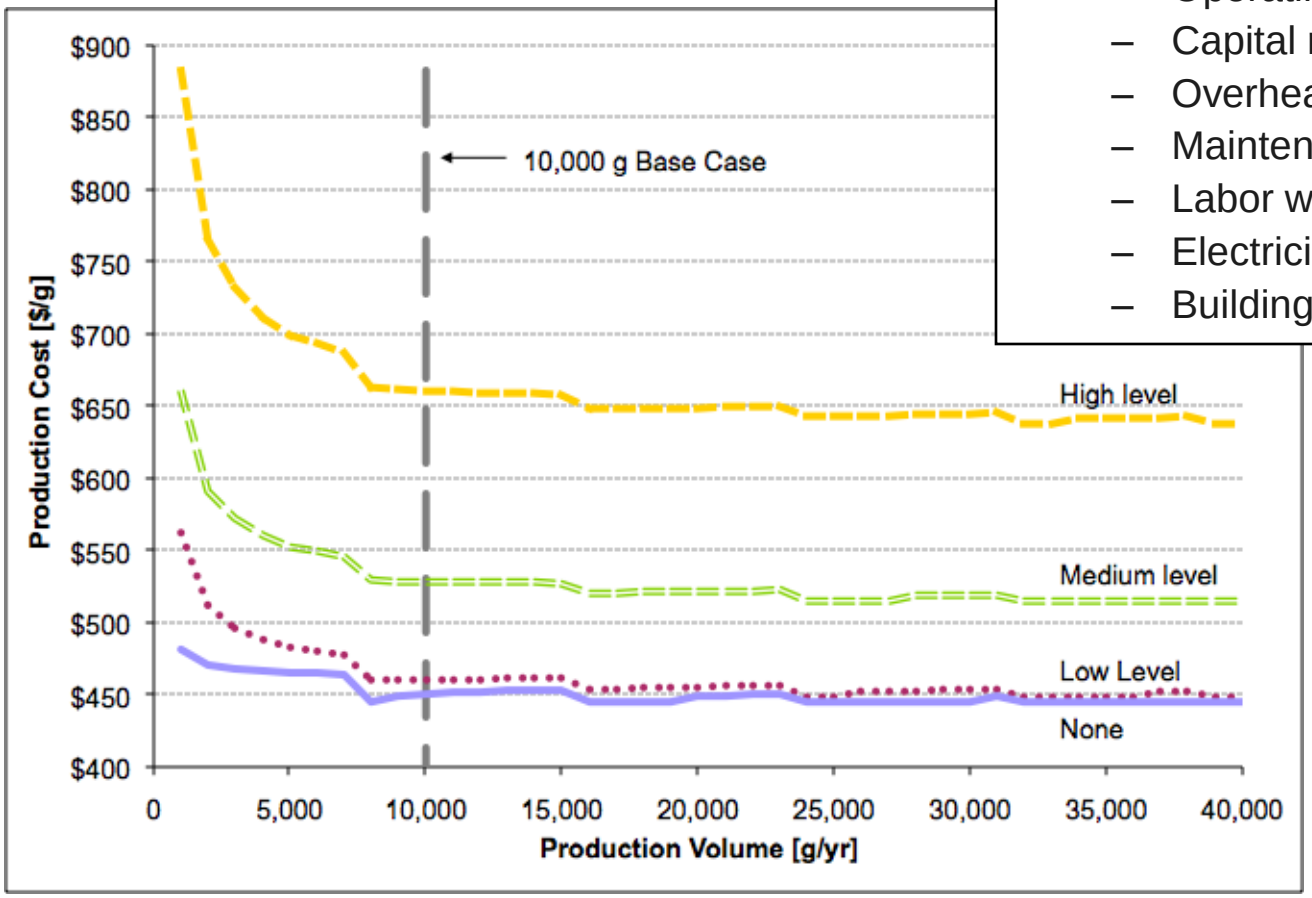
		Level of EHS Standards			
		None	Low	Medium	High
Engineering Controls					
General Exhaust - Ventilation			24 hours, 1,000 cfm ventilation rate, $10,000 capital cost, $3,000/year operating cost	24 hours, 1,000 cfm ventilation rate, $10,000 capital cost, $3,000/year operating cost	24 hours, 1,000 cfm ventilation rate, $10,000 capital cost, $3,000/year operating cost
Fume hoods				$4,000 capital cost for 6.25 ft^2 equipment and $9,500 for 25 ft^2 equipment	$4,000 capital cost for 6.25 ft^2 equipment and $9,500 for 25 ft^2 equipment
Enclosure of processes					50% decrease in labor productivity, 50% extra equipment cost
Administrative Controls					
Annual worker training			8 hours of training, $560/year instructor cost	8 hours of training, $560/year instructor cost	8 hours of training, $560/year instructor cost
Air monitoring			Monthly monitoring, $20k/equipment capital cost	Weekly monitoring, $20k/equipment capital cost	Biweekly monitoring, $20k/equipment capital cost
Medical monitoring					$950/worker/year
Personal Protective Equipment					
Gloves	Latex		5 pairs/shift, $0.06/pair		
	Nitrile			5 pairs/shift, $0.09/pair	5 pairs/shift, $0.09/pair
Respirators	Disposable		1/shift, $0.70	1/shift, $0.70	
	HEPA filters				1 pair/ 30 hrs, $10/pair
Tyvek suits					1/shift, $4

Four general levels of environmental, health, and safety (EHS) standards defined…

HiPco Production Costs Determined

Base case assumptions

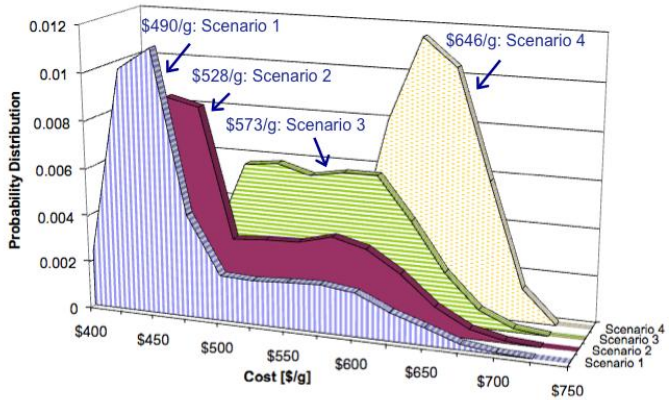
- Production volume: 10,000 g/yr
- Operating hours: 2000 hr/yr
- Capital recovery rate: 10%
- Overhead cost: 40% of direct labor
- Maintenance cost: 5% equip. cost
- Labor wage: $20/hr
- Electricity cost: $0.10/kW*hr
- Building cost: $13/ft^2*yr



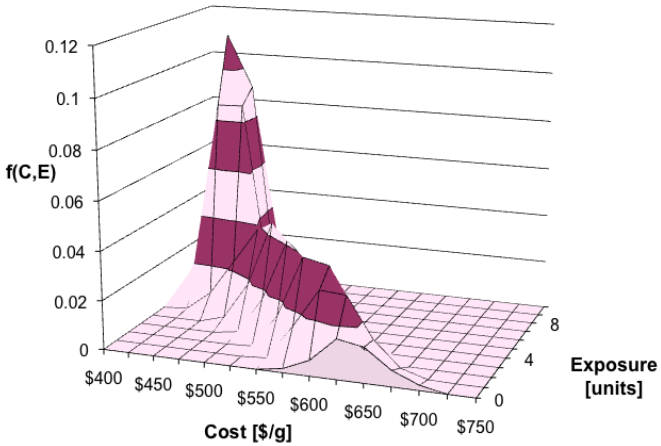
Scenario Analysis Results

- Expected costs alone are insufficient for informed decision making
- Difficulty in decision making due to overlapping cost and exposure distributions

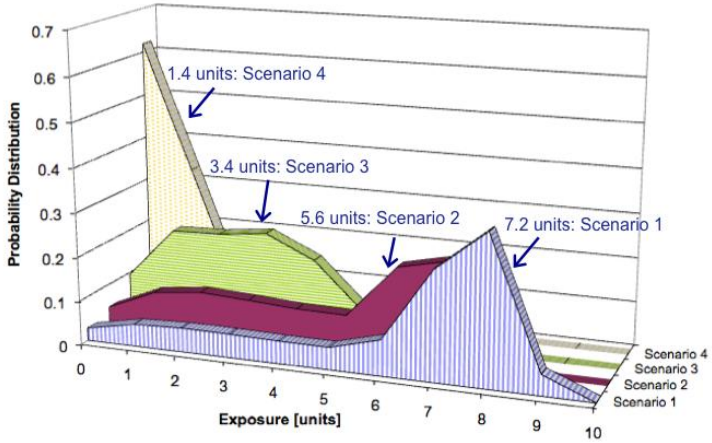
Potential 10-year Cost



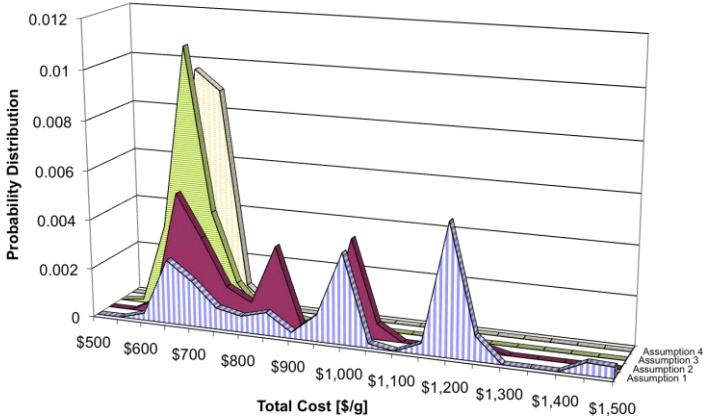
Joint Cost-Exposure Density



Potential 10-year Exposure



Total Manufacturing + Exposure Cost



Multi-criteria Models

- Many multi-criteria methods available that are applicable to a wide range of nanomanufacturing applications

- Goal Programming Example:
  - Balance reliability, production rate, and workplace exposure in a nanomanufacturing process
  - Decision variables: pH (x1), conductivity (x2), temperature (x3)
  - Objective: To identify values of decision variables that minimize a weighted total deviation from set goals for the three criteria

Priority	Factor	Goal	Penalty Weights
First-priority	Reliability rate	≥90%	M
Second-priority	Production rate	≥10 gr/hr	5
	Exposure level	≤5 units	3

Problem formulation

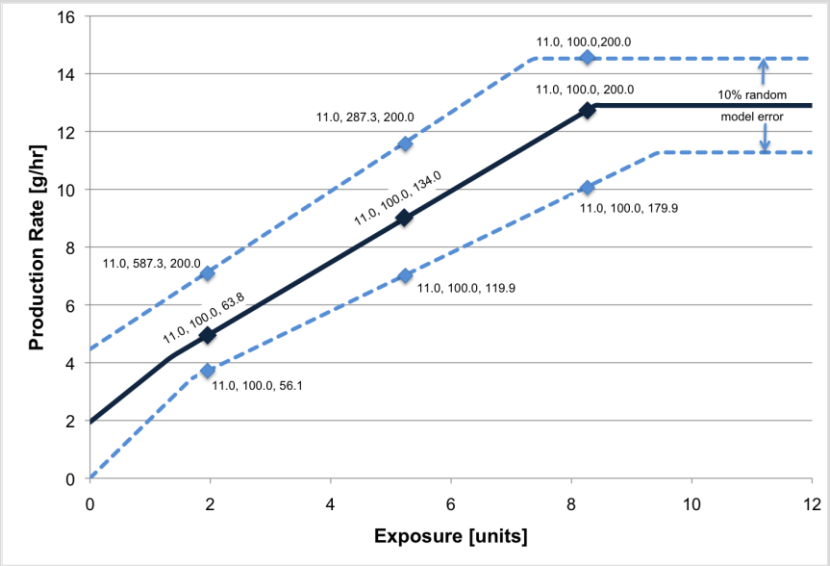
$lex\min\{d_1^-, d_2^-, d_3^+\}$ is equivalent to

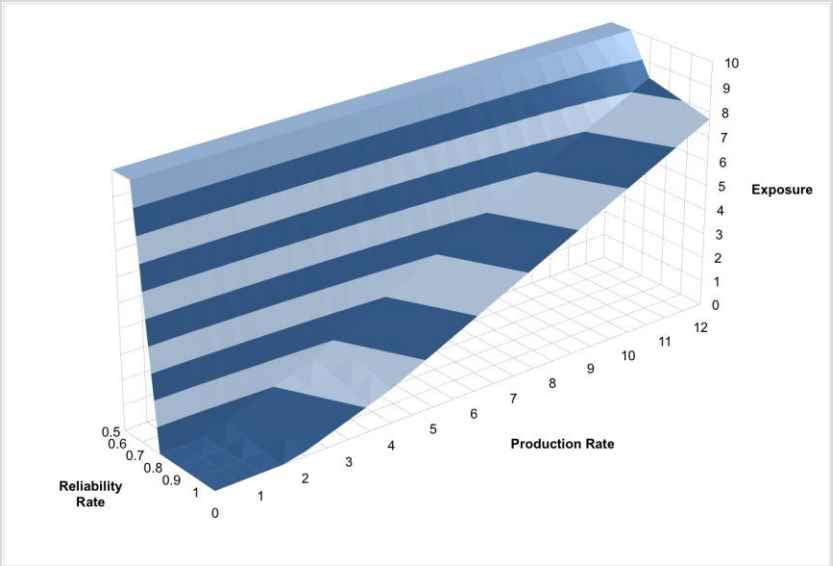
$$\min \quad Md_1^- + 5d_2^- + 3d_3^+$$

$$\begin{aligned} s.t. \quad & 0.098x_1 + 0.00014x_2 - 0.0004x_3 + d_1^- \geq 90\% \\ & 0.27x_1 - 0.0167x_2 + 0.058x_3 + d_2^- \geq 10 \\ & -0.01x_2 + 0.047x_3 - d_3^+ \leq 5 \\ & 7 \leq x_1 \leq 11,\ 100 \leq x_2 \leq 1000,\ 50 \leq x_3 \leq 200 \\ & \text{all } d_i \geq 0 \end{aligned}$$

Probabilistic Bounds & Trade-off Frontiers

- Sensitivity to weights and constraints – experimental errors
- Optimal trade-off frontiers/surfaces – mapping all optimal solutions of the multiple criteria



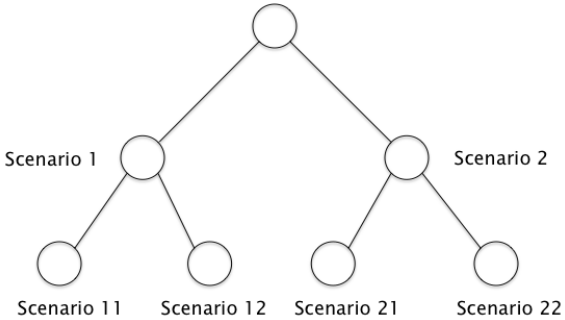


Stochastic Programming

- Treating secondary objectives as chance constraints – Chance-constrained models
  - Example: To ensure low probability that exposure exceeds some limit

$$
\begin{aligned}
\text{Minimize} \quad & f(x_1, x_2, x_3, x_4) \\
\text{subject to} \quad & \Pr(c^1 x \geq g_1) \geq \alpha_1 \\
& \Pr(c^2 x \geq g_2) \geq \alpha_2 \\
& \Pr(c^3 x \leq g_3) \geq \alpha_3 \\
& x \geq 0 \\
\text{where} \quad & 0 < \alpha < 1
\end{aligned}
$$

- Using probabilistic objective functions
  - Example: To minimize expected exposure or the probability that cost exceeds some amount
- Developing sequential multi-period contingency decision schedules
  - Example: To produce a schedule of present and future workplace safeguard decisions to minimize expected total societal costs



Chance-constrained Model Example

- As new technologies developed, probability thresholds might be relaxed to reduce cost but still meet a target with some lesser probability.

- Decision variables: pH (x_1), conductivity (x_2), temperature (x_3), occupational health protection level (x_4)
- Objective: To identify values of decision variables that minimize cost while satisfying reliability, production rate, and workplace exposure constraints with some specified probability

Problem formulation

$$
\begin{aligned}
\text{Minimize} \quad & \$6.5x_1 + \$0.7x_2 + \$3.25x_3 + \$10x_4 \\
\text{subject to} \quad & P(0.137x_1 + 0.007x_2 - 0.0023x_3 + 0.033x_4 \geq 60\%) \geq 0.95 && \text{Yield rate} \\
& P(1.82x_1 - 2.34x_2 + 7.1x_3 - 1x_4 \geq 10) \geq 0.90 && \text{Production rate} \\
& P(0.94x_1 - 0.0043x_2 + 0.13x_3 - 10x_4 \leq 2) \geq 0.95 && \text{Cumulative exposure} \\
& 7 \leq x_1 \leq 11, 100 \leq x_2 \leq 1000, 50 \leq x_3 \leq 200, 1 \leq x_4 \leq 4 \\
& x_1, x_2, x_3, x_4 \geq 0, \text{ and } x_4 \text{ integer}
\end{aligned}
$$

- Optimal solution:
  x1 (pH) = 11, x2 (conductivity) = 292.5, x3 (temperature) = 97.9, x4 (occupational health protection level) = 3, and Cost = $624.57

Desirability Functions

Framework for
- Choosing between finite number of alternatives
- Identify optimal process variable settings

- Each criteria Y_i transformed to a dimensionless value d_i
- d_i increases as the desirability of Y_i increases
  - $0 \le d_i \le 1$
  - $d_i = 0.00$ completely unacceptable (undesirable)
  - $d_i = 1.00$ completely acceptable (desirable or ideal)
- Individual d_i values combined into an overall desirability value, D

Larger-is-better transformation

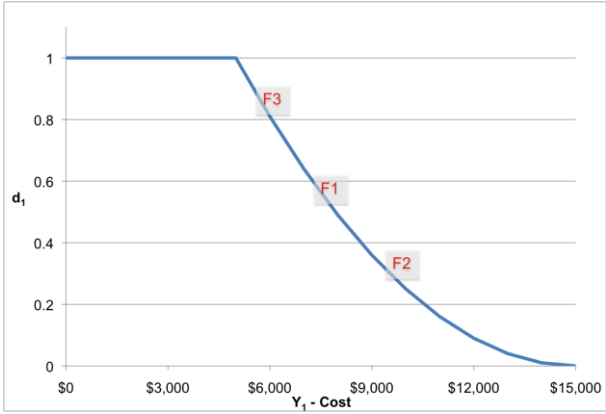
$$d_i = \begin{cases} 0 & Y_i \le Y_{i-\min} \\ \left[\dfrac{(Y_i - Y_{i-\min})}{(Y_{i-\max} - Y_{i-\min})}\right]^R & Y_{i-\min} \le Y_i \le Y_{i-\max} \\ 1 & Y_i \ge Y_{i-\max} \end{cases}$$

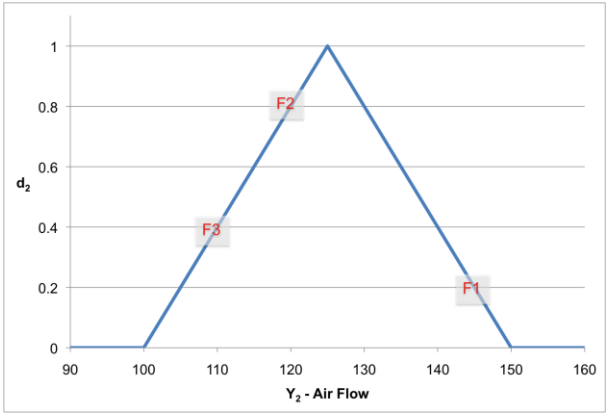
Nominal-is-better transformation

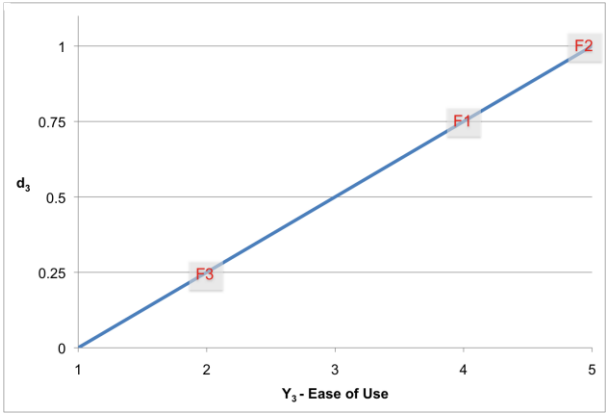
$$d_i = \begin{cases} \left[\dfrac{(Y_i - Y_{i-\min})}{(\tau_i - Y_{i-\min})}\right]^S & Y_{i-\min} \le Y_i \le \tau_i \\ \left[\dfrac{(Y_i - Y_{i-\max})}{(\tau_i - Y_{i-\max})}\right]^T & \tau_i \le Y_i \le Y_{i-\max} \\ 0 & Y_i < Y_{i-\min} \text{ or } Y_i > Y_{i-\max} \end{cases}$$

Fume Hood Selection Example

- Criteria: cost (Y_1), air flow (Y_2), and ease of use (Y_3)







Candidate Fume Hood	Individual Criteria and Desirabilities (d_i)						Overall Desirability D (w_1, w_2, w_3)		
	Cost	d_1	Air Flow	d_2	Ease of Use	d_3	(2, 4, 1)	(3, 1, 1)	(4, 1, 3)
F1	$7,500	0.56	145	0.2	4	0.75	0.32	0.48	**0.55**
F2	$9,500	0.30	120	0.8	5	1	**0.62**	0.46	0.53
F3	$6,000	0.81	110	0.4	2	0.25	0.46	**0.56**	0.48

Best selection in balancing the three properties against each other

Conclusions

- Challenges with nanotechnology risk assessment
- Inherent tradeoffs and enormous uncertainty exist for nanomanufacturing economics and workplace exposure
- Probabilistic, optimization, and multi-criteria models allow a characterization of a range of possible consequences
  - Examples shown for application of several modeling approaches
  - Focus expansion of desirability functions modeling on tradeoffs for safe handling of engineered nanomaterials with safe fume hoods
- Until sufficient toxicology and other studies progresses, these type of risk assessment models can help private & regulatory decision-makers to protect workers, consumers, and the environment

Acknowledgements

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Nanotechnology & Society Research Group

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