Application-Motivated Combinations of Interval and Probabilistic Approaches, and their Use in Bioinformatics

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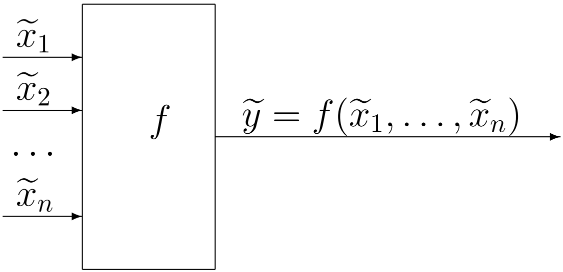
1. General Problem of Data Processing under Uncertainty

- *Indirect measurements:* way to measure y that are are difficult (or even impossible) to measure directly.
- *Idea:* $y = f(x_1, \ldots, x_n)$



- *Problem:* measurements are never 100% accurate: $\widetilde{x}_i \neq x_i$ ($\Delta x_i \neq 0$) hence

$$\widetilde{y} = f(\widetilde{x}_1, \ldots, \widetilde{x}_n) \neq y = f(x_1, \ldots, x_n).$$

What are bounds on $\Delta y \stackrel{\text{def}}{=} \widetilde{y} - y$?

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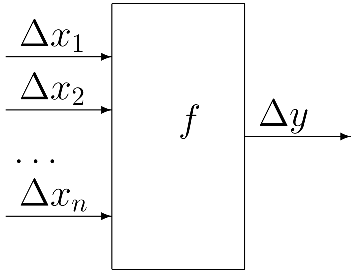
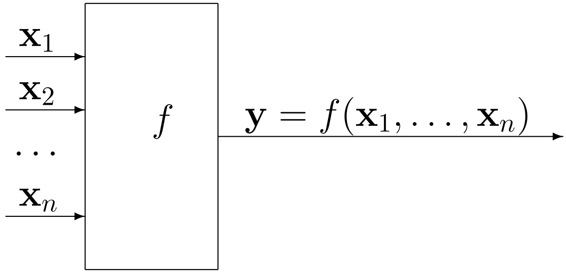
2. Probabilistic and Interval Uncertainty



- *Traditional approach:* we know probability distribution for Δx_i (usually Gaussian).
- *Where it comes from:* calibration using standard MI.
- *Problem:* calibration is not possible in:
  - fundamental science
  - manufacturing
- *Solution:* we know upper bounds Δ_i on $|\Delta x_i|$ hence

$$x_i \in [\widetilde{x}_i - \Delta_i, \widetilde{x}_i + \Delta_i].$$

3. Interval Computations: A Problem



- *Given:* an algorithm $y = f(x_1, \ldots, x_n)$ and n intervals $\mathbf{x}_i = [\underline{x}_i, \overline{x}_i]$.
- *Compute:* the corresponding range of y:

$$[\underline{y}, \overline{y}] = \{f(x_1, \ldots, x_n) \mid x_1 \in [\underline{x}_1, \overline{x}_1], \ldots, x_n \in [\underline{x}_n, \overline{x}_n]\}.$$

- *Fact:* NP-hard even for quadratic f.
- *Challenge:* when are feasible algorithm possible?
- *Challenge:* when computing $\mathbf{y} = [\underline{y}, \overline{y}]$ is not feasible, find a good approximation $\mathbf{Y} \supseteq \mathbf{y}$.

4. Interval Computations: A Brief History

- *Origins:* Archimedes (Ancient Greece)
- *Modern pioneers:* Warmus (Poland), Sunaga (Japan), Moore (USA), 1956–59
- *First boom:* early 1960s.
- *First challenge:* taking interval uncertainty into account when planning spaceflights to the Moon.
- *Current applications* (sample):
  - design of elementary particle colliders: Berz, Kyoko (USA)
  - will a comet hit the Earth: Berz, Moore (USA)
  - robotics: Jaulin (France), Neumaier (Austria)
  - chemical engineering: Stadtherr (USA)

5. Alternative Approach: Maximum Entropy

- *Situation:* in many practical applications, it is very difficult to come up with the probabilities.
- *Traditional engineering approach:* use probabilistic techniques.
- *Problem:* many different probability distributions are consistent with the same observations.
- *Solution:* select one of these distributions – e.g., the one with the largest entropy.
- *Example – single variable:* if all we know is that $x \in [\underline{x}, \overline{x}]$, then MaxEnt leads to a uniform distribution.
- *Example – multiple variables:* different variables are independently distributed.

6. Limitations of Maximum Entropy Approach

- *Example:* simplest algorithm $y = x_1 + \ldots + x_n$.
- *Measurement errors:* $\Delta x_i \in [-\Delta, \Delta]$.
- *Analysis:* $\Delta y = \Delta x_1 + \ldots + \Delta x_n$.
- *Worst case situation:* $\Delta y = n \cdot \Delta$.
- *Maximum Entropy approach:* due to Central Limit Theorem, Δy is $\approx$ normal, with $\sigma = \Delta \cdot \dfrac{\sqrt{n}}{\sqrt{3}}$.
- *Why this may be inadequate:* we get $\Delta \sim \sqrt{n}$, but due to correlation, it is possible that $\Delta = n \cdot \Delta \sim n \gg \sqrt{n}$.
- *Conclusion:* using a single distribution can be very misleading, especially if we want guaranteed results.
- Examples: high-risk application areas such as space exploration or nuclear engineering.

7. Interval Arithmetic: Foundations of Interval Techniques

- *Problem:* compute the range

  $$[\underline{y}, \overline{y}] = \{f(x_1, \ldots, x_n) \,|\, x_1 \in [\underline{x}_1, \overline{x}_1], \ldots, x_n \in [\underline{x}_n, \overline{x}_n]\}.$$

- *Interval arithmetic:* for arithmetic operations $f(x_1, x_2)$ (and for elementary functions), we have explicit formulas for the range.

- *Examples:* when $x_1 \in \mathbf{x}_1 = [\underline{x}_1, \overline{x}_1]$ and $x_2 \in \mathbf{x}_2 = [\underline{x}_2, \overline{x}_2]$, then:
  - The range $\mathbf{x}_1 + \mathbf{x}_2$ for $x_1 + x_2$ is $[\underline{x}_1 + \underline{x}_2, \overline{x}_1 + \overline{x}_2]$.
  - The range $\mathbf{x}_1 - \mathbf{x}_2$ for $x_1 - x_2$ is $[\underline{x}_1 - \overline{x}_2, \overline{x}_1 - \underline{x}_2]$.
  - The range $\mathbf{x}_1 \cdot \mathbf{x}_2$ for $x_1 \cdot x_2$ is $[\underline{y}, \overline{y}]$, where

    $$\underline{y} = \min(\underline{x}_1 \cdot \underline{x}_2, \underline{x}_1 \cdot \overline{x}_2, \overline{x}_1 \cdot \underline{x}_2, \overline{x}_1 \cdot \overline{x}_2);$$

    $$\overline{y} = \max(\underline{x}_1 \cdot \underline{x}_2, \underline{x}_1 \cdot \overline{x}_2, \overline{x}_1 \cdot \underline{x}_2, \overline{x}_1 \cdot \overline{x}_2).$$

- The range $1/\mathbf{x}_1$ for $1/x_1$ is $[1/\overline{x}_1, 1/\underline{x}_1]$ (if $0 \notin \mathbf{x}_1$).

8. Straightforward Interval Computations: Example

- *Example:* $f(x) = (x-2)\cdot(x+2)$, $x \in [1,2]$.
- How will the computer compute it?
  - $r_1 := x - 2$;
  - $r_2 := x + 2$;
  - $r_3 := r_1 \cdot r_2$.
- *Main idea:* perform the same operations, but with *intervals* instead of *numbers*:
  - $\mathbf{r}_1 := [1,2] - [2,2] = [-1,0]$;
  - $\mathbf{r}_2 := [1,2] + [2,2] = [3,4]$;
  - $\mathbf{r}_3 := [-1,0] \cdot [3,4] = [-4,0]$.
- *Actual range:* $f(\mathbf{x}) = [-3,0]$.
- *Comment:* this is just a toy example, there are more efficient ways of computing an enclosure $\mathbf{Y} \supseteq \mathbf{y}$.

9. First Idea: Use of Monotonicity

- *Reminder:* for arithmetic, we had exact ranges.
- *Reason:* $+$, $-$, $\cdot$ are monotonic in each variable.
- *How monotonicity helps:* if $f(x_1, \ldots, x_n)$ is (non-strictly) increasing ($f \uparrow$) in each x_i, then

$$f(\mathbf{x}_1, \ldots, \mathbf{x}_n) = [f(\underline{x}_1, \ldots, \underline{x}_n), f(\overline{x}_1, \ldots, \overline{x}_n)].$$

- *Similarly:* if $f \uparrow$ for some x_i and $f \downarrow$ for other x_j $(-)$.
- *Fact:* $f \uparrow$ in x_i if $\dfrac{\partial f}{\partial x_i} \geq 0$.
- *Checking monotonicity:* check that the range $[\underline{r}_i, \overline{r}_i]$ of $\dfrac{\partial f}{\partial x_i}$ on $\mathbf{x}_i$ has $\underline{r}_i \geq 0$.
- *Differentiation:* by Automatic Differentiation (AD) tools.
- *Estimating ranges of* $\dfrac{\partial f}{\partial x_i}$*:* straightforward interval comp.

10. Monotonicity: Example

- *Idea:* if the range $[\underline{r}_i, \overline{r}_i]$ of each $\dfrac{\partial f}{\partial x_i}$ on $\mathbf{x}_i$ has $\underline{r}_i \geq 0$, then

$$f(\mathbf{x}_1, \ldots, \mathbf{x}_n) = [f(\underline{x}_1, \ldots, \underline{x}_n), f(\overline{x}_1, \ldots, \overline{x}_n)].$$

- *Example:* $f(x) = (x-2) \cdot (x+2)$, $\mathbf{x} = [1, 2]$.
- *Case $n = 1$:* if the range $[\underline{r}, \overline{r}]$ of $\dfrac{df}{dx}$ on $\mathbf{x}$ has $\underline{r} \geq 0$, then

$$f(\mathbf{x}) = [f(\underline{x}), f(\overline{x})].$$

- *AD:* $\dfrac{df}{dx} = 1 \cdot (x+2) + (x-2) \cdot 1 = 2x$.
- *Checking:* $[\underline{r}, \overline{r}] = [2, 4]$, with $2 \geq 0$.
- *Result:* $f([1, 2]) = [f(1), f(2)] = [-3, 0]$.
- *Comparison:* this is the exact range.

11. Non-Monotonic Example

- *Example:* $f(x) = x \cdot (1 - x)$, $x \in [0, 1]$.
- How will the computer compute it?
    - $r_1 := 1 - x$;
    - $r_2 := x \cdot r_1$.
- *Straightforward interval computations:*
    - $\mathbf{r}_1 := [1, 1] - [0, 1] = [0, 1]$;
    - $\mathbf{r}_2 := [0, 1] \cdot [0, 1] = [0, 1]$.
- *Actual range:* min, max of f at $\underline{x}$, $\overline{x}$, or when $\dfrac{df}{dx} = 0$.
- Here, $\dfrac{df}{dx} = 1 - 2x = 0$ for $x = 0.5$, so
    - compute $f(0) = 0$, $f(0.5) = 0.25$, and $f(1) = 0$.
    - $\underline{y} = \min(0, 0.25, 0) = 0$, $\overline{y} = \max(0, 0.25, 0) = 0.25$.
- *Resulting range:* $f(\mathbf{x}) = [0, 0.25]$.

12. Second Idea: Centered Form

- *Main idea:* Intermediate Value Theorem

$$f(x_1, \ldots, x_n) = f(\widetilde{x}_1, \ldots, \widetilde{x}_n) + \sum_{i=1}^{n} \frac{\partial f}{\partial x_i}(\chi) \cdot (x_i - \widetilde{x}_i)$$

  for some $\chi_i \in \mathbf{x}_i$.

- *Corollary:* $f(x_1, \ldots, x_n) \in \mathbf{Y}$, where

$$\mathbf{Y} = \widetilde{y} + \sum_{i=1}^{n} \frac{\partial f}{\partial x_i}(\mathbf{x}_1, \ldots, \mathbf{x}_n) \cdot [-\Delta_i, \Delta_i].$$

- *Differentiation:* by Automatic Differentiation (AD) tools.
- *Estimating the ranges of derivatives:*
  - if appropriate, by monotonicity, or
  - by straightforward interval computations, or
  - by centered form (more time but more accurate).

13. Centered Form: Example

- *General formula:*

$$\mathbf{Y} = f(\widetilde{x}_1, \ldots, \widetilde{x}_n) + \sum_{i=1}^{n} \frac{\partial f}{\partial x_i}(\mathbf{x}_1, \ldots, \mathbf{x}_n) \cdot [-\Delta_i, \Delta_i].$$

- *Example:* $f(x) = x \cdot (1 - x)$, $\mathbf{x} = [0, 1]$.
- Here, $\mathbf{x} = [\widetilde{x} - \Delta, \widetilde{x} + \Delta]$, with $\widetilde{x} = 0.5$ and $\Delta = 0.5$.
- *Case $n = 1$:* $\mathbf{Y} = f(\widetilde{x}) + \dfrac{df}{dx}(\mathbf{x}) \cdot [-\Delta, \Delta]$.
- *AD:* $\dfrac{df}{dx} = 1 \cdot (1 - x) + x \cdot (-1) = 1 - 2x$.
- *Estimation:* we have $\dfrac{df}{dx}(\mathbf{x}) = 1 - 2 \cdot [0, 1] = [-1, 1]$.
- *Result:* $\mathbf{Y} = 0.5 \cdot (1 - 0.5) + [-1, 1] \cdot [-0.5, 0.5] = 0.25 + [-0.5, 0.5] = [-0.25, 0.75]$.
- *Comparison:* actual range $[0, 0.25]$, straightforward $[0, 1]$.

14. Third Idea: Bisection

- *Known:* accuracy $O(\Delta_i^2)$ of first order formula

$$f(x_1,\ldots,x_n)=f(\widetilde{x}_1,\ldots,\widetilde{x}_n)+\sum_{i=1}^n \frac{\partial f}{\partial x_i}(\chi)\cdot(x_i-\widetilde{x}_i).$$

- *Idea:* if the intervals are too wide, we:
  - split one of them in half ($\Delta_i^2 \to \Delta_i^2/4$); and
  - take the union of the resulting ranges.
- *Example:* $f(x)=x\cdot(1-x)$, where $x\in \mathbf{x}=[0,1]$.
- *Split:* take $\mathbf{x}'=[0,0.5]$ and $\mathbf{x}''=[0.5,1]$.
- *1st range:* $1-2\cdot\mathbf{x}=1-2\cdot[0,0.5]=[0,1]$, so $f\uparrow$ and $f(\mathbf{x}')=[f(0),f(0.5)]=[0,0.25]$.
- *2nd range:* $1-2\cdot\mathbf{x}=1-2\cdot[0.5,1]=[-1,0]$, so $f\downarrow$ and $f(\mathbf{x}'')=[f(1),f(0.5)]=[0,0.25]$.
- *Result:* $f(\mathbf{x}')\cup f(\mathbf{x}'')=[0,0.25]$ – exact.

15. Alternative Approach: Affine Arithmetic

- *So far:* we compute the range of $x \cdot (1 - x)$ by multiplying ranges of x and $1 - x$.
- *We ignore:* that both factors depend on x and are, thus, dependent.
- *Idea:* for each intermediate result a, keep an explicit dependence on $\Delta x_i = \widetilde{x}_i - x_i$ (at least its linear terms).
- *Implementation:*

$$a = a_0 + \sum_{i=1}^{n} a_i \cdot \Delta x_i + [\underline{a}, \overline{a}].$$

- *We start:* with $x_i = \widetilde{x}_i - \Delta x_i$, i.e.,

$$\widetilde{x}_i + 0 \cdot \Delta x_1 + \ldots + 0 \cdot \Delta x_{i-1} + (-1) \cdot \Delta x_i + 0 \cdot \Delta x_{i+1} + \ldots + 0 \cdot \Delta x_n + [0, 0].$$

- *Description:* $a_0 = \widetilde{x}_i$, $a_i = -1$, $a_j = 0$ for $j \neq i$, and $[\underline{a}, \overline{a}] = [0, 0]$.

16. Affine Arithmetic: Operations

- *Representation:* $a = a_0 + \sum_{i=1}^{n} a_i \cdot \Delta x_i + [\underline{a}, \overline{a}]$.
- *Input:* $a = a_0 + \sum_{i=1}^{n} a_i \cdot \Delta x_i + \mathbf{a}$ and $b = b_0 + \sum_{i=1}^{n} b_i \cdot \Delta x_i + \mathbf{b}$.
- *Operations:* $c = a \otimes b$.
- *Addition:* $c_0 = a_0 + b_0$, $c_i = a_i + b_i$, $\mathbf{c} = \mathbf{a} + \mathbf{b}$.
- *Subtraction:* $c_0 = a_0 - b_0$, $c_i = a_i - b_i$, $\mathbf{c} = \mathbf{a} - \mathbf{b}$.
- *Multiplication:* $c_0 = a_0 \cdot b_0$, $c_i = a_0 \cdot b_i + b_0 \cdot a_i$,

$$\mathbf{c} = a_0 \cdot \mathbf{b} + b_0 \cdot \mathbf{a} + \sum_{i \neq j} a_i \cdot b_j \cdot [-\Delta_i, \Delta_i] \cdot [-\Delta_j, \Delta_j] +$$

$$\sum_i a_i \cdot b_i \cdot [-\Delta_i, \Delta_i]^2 +$$

$$\left(\sum_i a_i \cdot [-\Delta_i, \Delta_i]\right) \cdot \mathbf{b} + \left(\sum_i b_i \cdot [-\Delta_i, \Delta_i]\right) \cdot \mathbf{a} + \mathbf{a} \cdot \mathbf{b}.$$

17. Affine Arithmetic: Example

- *Example:* $f(x) = x \cdot (1 - x)$, $x \in [0, 1]$.
- Here, $n = 1$, $\widetilde{x} = 0.5$, and $\Delta = 0.5$.
- How will the computer compute it?
  - $r_1 := 1 - x$;
  - $r_2 := x \cdot r_1$.
- *Affine arithmetic:* we start with $x = 0.5 - \Delta x + [0, 0]$;
  - $\mathbf{r}_1 := 1 - (0.5 - \Delta) = 0.5 + \Delta x$;
  - $\mathbf{r}_2 := (0.5 - \Delta x) \cdot (0.5 + \Delta x)$, i.e.,

$$\mathbf{r}_2 = 0.25 + 0 \cdot \Delta x - [-\Delta, \Delta]^2 = 0.25 + [-\Delta^2, 0].$$

- *Resulting range:* $\mathbf{y} = 0.25 + [-0.25, 0] = [0, 0.25]$.
- *Comparison:* this is the exact range.

18. Affine Arithmetic: Towards More Accurate Estimates

- *In our simple example:* we got the exact range.
- *In general:* range estimation is NP-hard.
- *Meaning:* a feasible (polynomial-time) algorithm will sometimes lead to excess width: $\mathbf{Y} \supset \mathbf{y}$.
- *Conclusion:* affine arithmetic may lead to excess width.
- *Question:* how to get more accurate estimates?
- *First idea:* bisection.
- *Second idea* (Taylor arithmetic):
  - *affine arithmetic:* $a = a_0 + \sum a_i \cdot \Delta x_i + \mathbf{a}$;
  - *meaning:* we keep linear terms in Δx_i;
  - *idea:* keep, e.g., quadratic terms

$$a = a_0 + \sum a_i \cdot \Delta x_i + \sum a_{ij} \cdot \Delta x_i \cdot \Delta x_j + \mathbf{a}.$$

19. Interval Computations vs. Affine Arithmetic: Comparative Analysis

- *Objective:* we want a method that computes a reasonable estimate for the range in reasonable time.
- *Conclusion – how to compare different methods:*
  - how accurate are the estimates, and
  - how fast we can compute them.
- *Accuracy:* affine arithmetic leads to more accurate ranges.
- *Computation time:*
  - *Interval arithmetic:* for each intermediate result a, we compute two values: endpoints $\underline{a}$ and $\overline{a}$ of $[\underline{a}, \overline{a}]$.
  - *Affine arithmetic:* for each a, we compute $n+3$ values:
    $$a_0 \quad a_1, \ldots, a_n \quad \underline{a}, \overline{a}.$$
- *Conclusion:* affine arithmetic is $\sim n$ times slower.

20. Solving Systems of Equations: Extending Known Algorithms to Situations with Interval Uncertainty

- *We have:* a system of equations $g_i(y_1, \ldots, y_n) = a_i$ with unknowns y_i;
- *We know:* a_i with interval uncertainty: $a_i \in [\underline{a}_i, \overline{a}_i]$;
- *We want:* to find the corresponding ranges of y_j.
- *First case:* for exactly known a_i, we have an algorithm $y_j = f_j(a_1, \ldots, a_n)$ for solving the system.
- *Example:* system of linear equations.
- *Solution:* apply interval computations techniques to find the range $f_j([\underline{a}_1, \overline{a}_1], \ldots, [\underline{a}_n, \overline{a}_n])$.
- *Better solution:* for specific equations, we often already know which ideas work best.
- *Example:* linear equations $Ay = b$; y is monotonic in b.

21. Solving Systems of Equations When No Algorithm Is Known

- *Idea:*
  - parse each equation into elementary constraints, and
  - use interval computations to improve original ranges until we get a narrow range (= solution).
- *First example:* $x - x^2 = 0.5$, $x \in [0, 1]$ (no solution).
- *Parsing:* $r_1 = x^2$, $0.5\ (= r_2)\ = x - r_1$.
- *Rules:* from $r_1 = x^2$, we extract two rules:

$$(1)\ x \to r_1 = x^2; \quad (2)\ r_1 \to x = \sqrt{r_1};$$

from $0.5 = x - r_1$, we extract two more rules:

$$(3)\ x \to r_1 = x - 0.5; \quad (4)\ r_1 \to x = r_1 + 0.5.$$

22. Solving Systems of Equations When No Algorithm Is Known: Example

- (1) $r = x^2$; (2) $x = \sqrt{r}$; (3) $r = x - 0.5$; (4) $x = r + 0.5$.
- *We start with:* $\mathbf{x} = [0, 1]$, $\mathbf{r} = (-\infty, \infty)$.

(1) $\mathbf{r} = [0, 1]^2 = [0, 1]$, so $\mathbf{r}_{\text{new}} = (-\infty, \infty) \cap [0, 1] = [0, 1]$.

(2) $\mathbf{x}_{\text{new}} = \sqrt{[0, 1]} \cap [0, 1] = [0, 1]$ – no change.

(3) $\mathbf{r}_{\text{new}} = ([0, 1] - 0.5) \cap [0, 1] = [-0.5, 0.5] \cap [0, 1] = [0, 0.5]$.

(4) $\mathbf{x}_{\text{new}} = ([0, 0.5] + 0.5) \cap [0, 1] = [0.5, 1] \cap [0, 1] = [0.5, 1]$.

(1) $\mathbf{r}_{\text{new}} = [0.5, 1]^2 \cap [0, 0.5] = [0.25, 0.5]$.

(2) $\mathbf{x}_{\text{new}} = \sqrt{[0.25, 0.5]} \cap [0.5, 1] = [0.5, 0.71]$;
round $\underline{a}$ down $\downarrow$ and $\overline{a}$ up $\uparrow$, to guarantee enclosure.

(3) $\mathbf{r}_{\text{new}} = ([0.5, 0.71] - 0.5) \cap [0.25, 5] = [0.0.21] \cap [0.25, 0.5]$,
i.e., $\mathbf{r}_{\text{new}} = \emptyset$.

- *Conclusion:* the original equation has no solutions.

23. Solving Systems of Equations: Second Example

- *Example:* $x - x^2 = 0$, $x \in [0, 1]$.
- *Parsing:* $r_1 = x^2$, $0 \ (= r_2) \ = x - r_1$.
- *Rules:* (1) $r = x^2$; (2) $x = \sqrt{r}$; (3) $r = x$; (4) $x = r$.
- *We start with:* $\mathbf{x} = [0, 1]$, $\mathbf{r} = (-\infty, \infty)$.
- *Problem:* after Rule 1, we're stuck with $\mathbf{x} = \mathbf{r} = [0, 1]$.
- *Solution:* bisect $\mathbf{x} = [0, 1]$ into $[0, 0.5]$ and $[0.5, 1]$.
- *For 1st subinterval:*
  - Rule 1 leads to $\mathbf{r}_{\text{new}} = [0, 0.5]^2 \cap [0, 0.5] = [0, 0.25]$;
  - Rule 4 leads to $\mathbf{x}_{\text{new}} = [0, 0.25]$;
  - Rule 1 leads to $\mathbf{r}_{\text{new}} = [0, 0.25]^2 = [0, 0.0625]$;
  - Rule 4 leads to $\mathbf{x}_{\text{new}} = [0, 0.0625]$; etc.
  - we converge to $x = 0$.
- *For 2nd subinterval:* we converge to $x = 1$.

24. Optimization: Extending Known Algorithms to Situations with Interval Uncertainty

- *Problem:* find $y_1, \ldots, y_m$ for which

$$g(y_1, \ldots, y_m, a_1, \ldots, a_m) \to \max .$$

- *We know:* a_i with interval uncertainty: $a_i \in [\underline{a}_i, \overline{a}_i]$;
- *We want:* to find the corresponding ranges of y_j.
- *First case:* for exactly known a_i, we have an algorithm $y_j = f_j(a_1, \ldots, a_n)$ for solving the optimization problem.
- *Example:* quadratic objective function g.
- *Solution:* apply interval computations techniques to find the range $f_j([\underline{a}_1, \overline{a}_1], \ldots, [\underline{a}_n, \overline{a}_n])$.
- *Better solution:* for specific f, we often already know which ideas work best.

25. Optimization When No Algorithm Is Known

- *Idea:* divide the original box $\mathbf{x}$ into subboxes $\mathbf{b}$.
- If $\max\limits_{x\in\mathbf{b}} g(x) < g(x')$ for a known x', dismiss $\mathbf{b}$.
- *Example:* $g(x) = x \cdot (1 - x)$, $\mathbf{x} = [0, 1]$.
- Divide into 10 (?) subboxes $\mathbf{b} = [0, 0.1], [0.1, 0.2], \ldots$
- Find $g(\widetilde{b})$ for each $\mathbf{b}$; the largest is $0.45 \cdot 0.55 = 0.2475$.
- Compute $G(\mathbf{b}) = g(\widetilde{b}) + (1 - 2 \cdot \mathbf{b}) \cdot [-\Delta, \Delta]$.
- Dismiss subboxes for which $\overline{Y} < 0.2475$.
- *Example:* for $[0.2, 0.3]$, we have

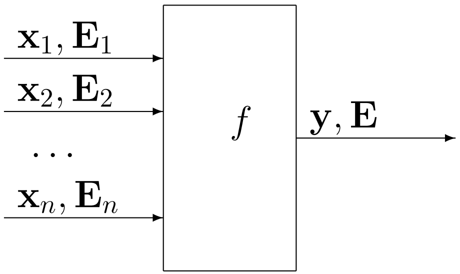
  $$0.25 \cdot (1 - 0.25) + (1 - 2 \cdot [0.2, 0.3]) \cdot [-0.05, 0.05].$$
- Here $\overline{Y} = 0.2175 < 0.2475$, so we dismiss $[0.2, 0.3]$.
- *Result:* keep only boxes $\subseteq [0.3, 0.7]$.
- *Further subdivision:* get us closer and closer to $x = 0.5$.

26. Combining Interval and Probabilistic Uncertainty: General Case

- *Problem:* there are many ways to represent a probability distribution.
- *Idea:* look for an objective.
- *Objective:* make decisions $E_x[u(x,a)] \to \max_a$.
- *Case 1:* smooth $u(x)$.
- *Analysis:* we have $u(x) = u(x_0) + (x - x_0) \cdot u'(x_0) + \ldots$
- *Conclusion:* we must know moments to estimate $E[u]$.
- *Case of uncertainty:* interval bounds on moments.
- *Case 2:* threshold-type $u(x)$.
- *Conclusion:* we need cdf $F(x) = \text{Prob}(\xi \le x)$.
- *Case of uncertainty:* p-box $[\underline{F}(x), \overline{F}(x)]$.

27. Extension of Interval Arithmetic to Probabilistic Case: Successes

- *General solution:* parse to elementary operations $+$, $-$, $\cdot$, $1/x$, max, min.
- Explicit formulas for arithmetic operations known for intervals, for p-boxes $\mathbf{F}(x) = [\underline{F}(x), \overline{F}(x)]$, for intervals + 1st moments $E_i \stackrel{\text{def}}{=} E[x_i]$:



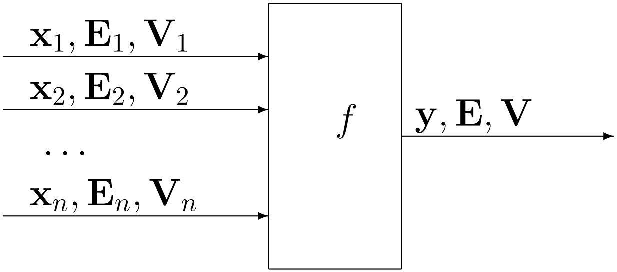
28. Successes (cont-d)

- *Easy cases:* $+$, $-$, product of independent x_i.
- *Example of a non-trivial case:* multiplication $y = x_1 \cdot x_2$, when we have no information about the correlation:
  - $\underline{E} = \max(p_1+p_2-1, 0)\cdot\overline{x}_1\cdot\overline{x}_2+\min(p_1, 1-p_2)\cdot\overline{x}_1\cdot\underline{x}_2+\min(1-p_1, p_2)\cdot\underline{x}_1\cdot\overline{x}_2+\max(1-p_1-p_2, 0)\cdot\underline{x}_1\cdot\underline{x}_2$;
  - $\overline{E} = \min(p_1, p_2)\cdot\overline{x}_1\cdot\overline{x}_2+\max(p_1-p_2, 0)\cdot\overline{x}_1\cdot\underline{x}_2+\max(p_2-p_1, 0)\cdot\underline{x}_1\cdot\overline{x}_2+\min(1-p_1, 1-p_2)\cdot\underline{x}_1\cdot\underline{x}_2$,

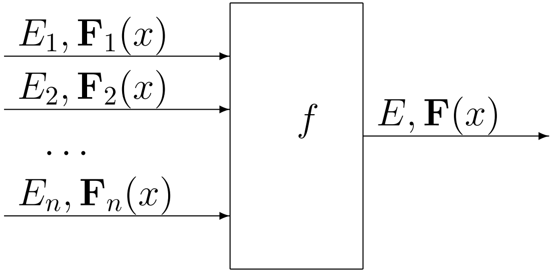
  where $p_i \stackrel{\text{def}}{=} (E_i - \underline{x}_i)/(\overline{x}_i - \underline{x}_i)$.

29. Challenges

- intervals + 2nd moments:



- moments + p-boxes; e.g.:



30. Case Study: Bioinformatics

- *Practical problem:* find genetic difference between cancer cells and healthy cells.
- *Ideal case:* we directly measure concentration c of the gene in cancer cells and h in healthy cells.
- *In reality:* difficult to separate.
- *Solution:* we measure $y_i \approx x_i \cdot c + (1 - x_i) \cdot h$, where x_i is the percentage of cancer cells in i-th sample.
- *Equivalent form:* $a \cdot x_i + h \approx y_i$, where $a \stackrel{\text{def}}{=} c - h$.

31. Case Study: Bioinformatics (cont-d)

- *If we know x_i exactly:* Least Squares Method $\sum_{i=1}^{n}(a \cdot x_i + h - y_i)^2 \to \min_{a,h}$, hence $a = \dfrac{C(x,y)}{V(x)}$ and $h = E(y) - a \cdot E(x)$, where $E(x) = \dfrac{1}{n} \cdot \sum_{i=1}^{n} x_i$,

$$V(x) = \frac{1}{n-1} \cdot \sum_{i=1}^{n} (x_i - E(x))^2,$$

$$C(x,y) = \frac{1}{n-1} \cdot \sum_{i=1}^{n} (x_i - E(x)) \cdot (y_i - E(y)).$$

- *Interval uncertainty:* experts manually count x_i, and only provide interval bounds $\mathbf{x}_i$, e.g., $x_i \in [0.7, 0.8]$.
- *Problem:* find the range of a and h corresponding to all possible values $x_i \in [\underline{x}_i, \overline{x}_i]$.

32. General Problem

- *General problem:*
  - we know intervals $\mathbf{x}_1 = [\underline{x}_1, \overline{x}_1]$, ..., $\mathbf{x}_n = [\underline{x}_n, \overline{x}_n]$,
  - compute the range of $E(x) = \frac{1}{n}\sum_{i=1}^{n} x_i$, population variance $V = \frac{1}{n}\sum_{i=1}^{n}(x_i - E(x))^2$, etc.
- *Difficulty:* NP-hard even for variance.
- *Known:*
  - efficient algorithms for $\underline{V}$,
  - efficient algorithms for $\overline{V}$ and $C(x, y)$ for reasonable situations.
- *Bioinformatics case:* find intervals for $C(x, y)$ and for $V(x)$ and divide.

33. Case Study: Detecting Outliers

- In many application areas, it is important to detect *outliers*, i.e., unusual, abnormal values.
- In *medicine*, unusual values may indicate disease.
- In *geophysics*, abnormal values may indicate a mineral deposit (or an erroneous measurement result).
- In *structural integrity* testing, abnormal values may indicate faults in a structure.
- *Traditional engineering approach:* a new measurement result x is classified as an outlier if $x \notin [L, U]$, where

$$L \stackrel{\text{def}}{=} E - k_0 \cdot \sigma, \quad U \stackrel{\text{def}}{=} E + k_0 \cdot \sigma,$$

  and $k_0 > 1$ is pre-selected.
- *Comment:* most frequently, $k_0 = 2$, 3, or 6.

34. Outlier Detection Under Interval Uncertainty: A Problem

- In some practical situations, we only have intervals $\mathbf{x}_i = [\underline{x}_i, \overline{x}_i]$.
- Different $x_i \in \mathbf{x}_i$ lead to different intervals $[L, U]$.
- A *possible* outlier: outside *some* k_0-sigma interval.
- *Example:* structural integrity – not to miss a fault.
- A *guaranteed* outlier: outside *all* k_0-sigma intervals.
- *Example:* before a surgery, we want to make sure that there is a micro-calcification.
- A value x is a possible outlier if $x \notin [\overline{L}, \underline{U}]$.
- A value x is a guaranteed outlier if $x \notin [\underline{L}, \overline{U}]$.
- *Conclusion:* to detect outliers, we must know the ranges of $L = E - k_0 \cdot \sigma$ and $U = E + k_0 \cdot \sigma$.

35. Outlier Detection Under Interval Uncertainty: A Solution

- *We need:* to detect outliers, we must compute the ranges of $L = E - k_0 \cdot \sigma$ and $U = E + k_0 \cdot \sigma$.
- *We know:* how to compute the ranges $\mathbf{E}$ and $[\underline{\sigma}, \overline{\sigma}]$ for E and σ.
- *Possibility:* use interval computations to conclude that $L \in \mathbf{E} - k_0 \cdot [\underline{\sigma}, \overline{\sigma}]$ and $L \in \mathbf{E} + k_0 \cdot [\underline{\sigma}, \overline{\sigma}]$.
- *Problem:* the resulting intervals for L and U are *wider* than the actual ranges.
- *Reason:* E and σ use the same inputs $x_1, \ldots, x_n$ and are hence not independent from each other.
- *Practical consequence:* we miss some outliers.
- *Desirable:* compute *exact* ranges for L and U.
- *Application:* detecting outliers in gravity measurements.

36. Acknowledgments

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