PURDUE UNIVERSITY | Davidson School of Chemical Engineering
COLLEGE OF ENGINEERING

P²SAC
Purdue Process Safety & Assurance Center

Clearing the Air

Rethinking Dust Safety in Pharmaceutical Manufacturing

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Presentation Deliverables

Continuous Manufacturing Safety Dilemma

Creating a Probabilistic Model

Research Directions

Photo credit: flcyc.org

Dusts in the Workplace


Credit: Time Magazine


Credit: China Daily


Credit: Callidus Health and Safety

Credit: China Underground

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Credit: Time Magazine

Credit: China Daily

Credit: Chemical & Engineering News

Credit: Callidus Health and Safety

Credit: China Underground

Credit: Engineering News-Record

West Pharmaceuticals, 2003

6 killed, 38 injured

- **Clean Facility**
- **Unidentified Cause**
- **Operated "Safely" for Years**

credit: CSB

Dust Safety in Pharma

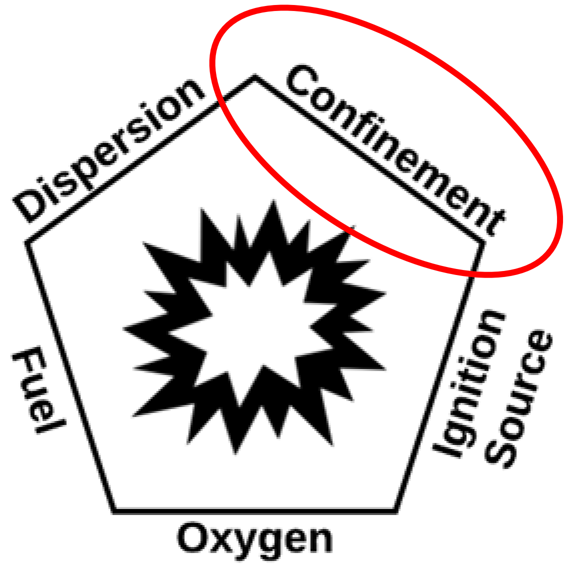
Is it safe?

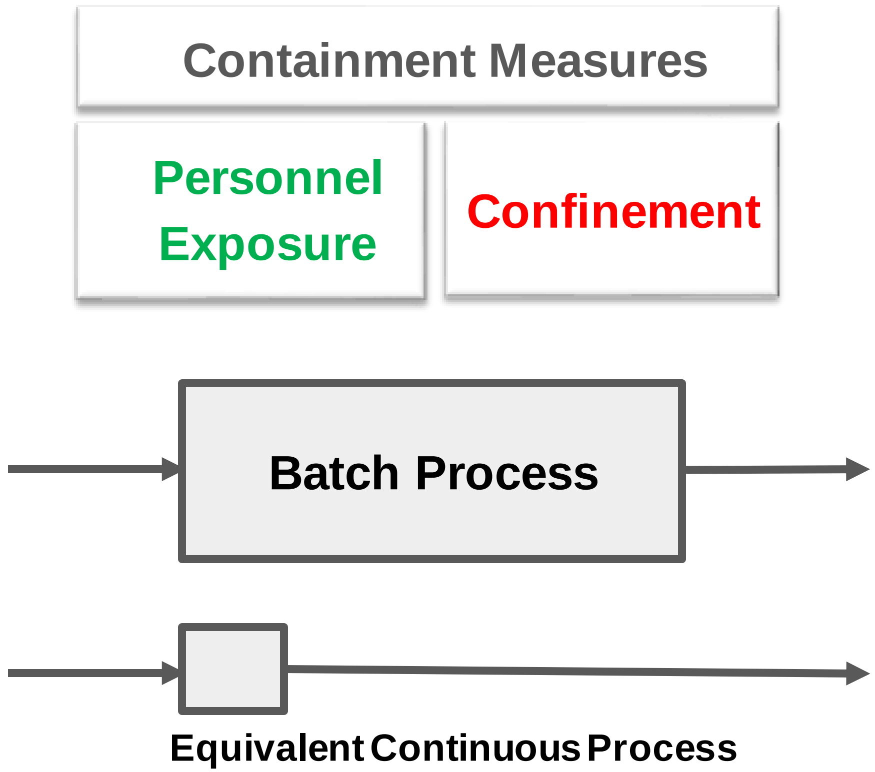
Bunny Suits and Enclosures:

Responding to personnel exposure risks

"Continuous processes are inherently safer"

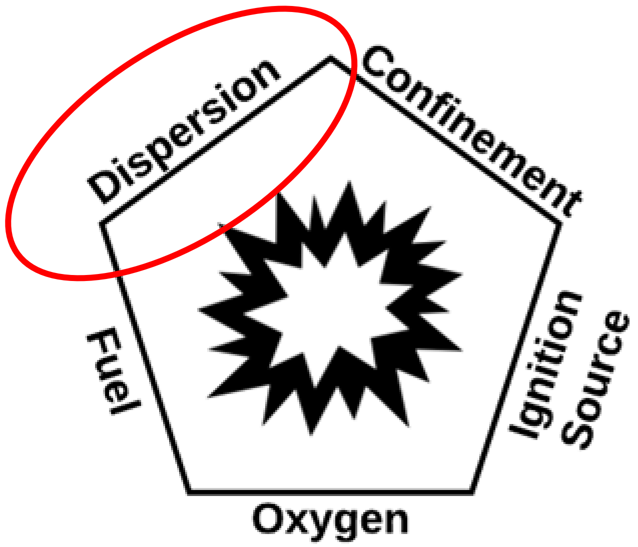
The Continuous Manufacturing Dilemma





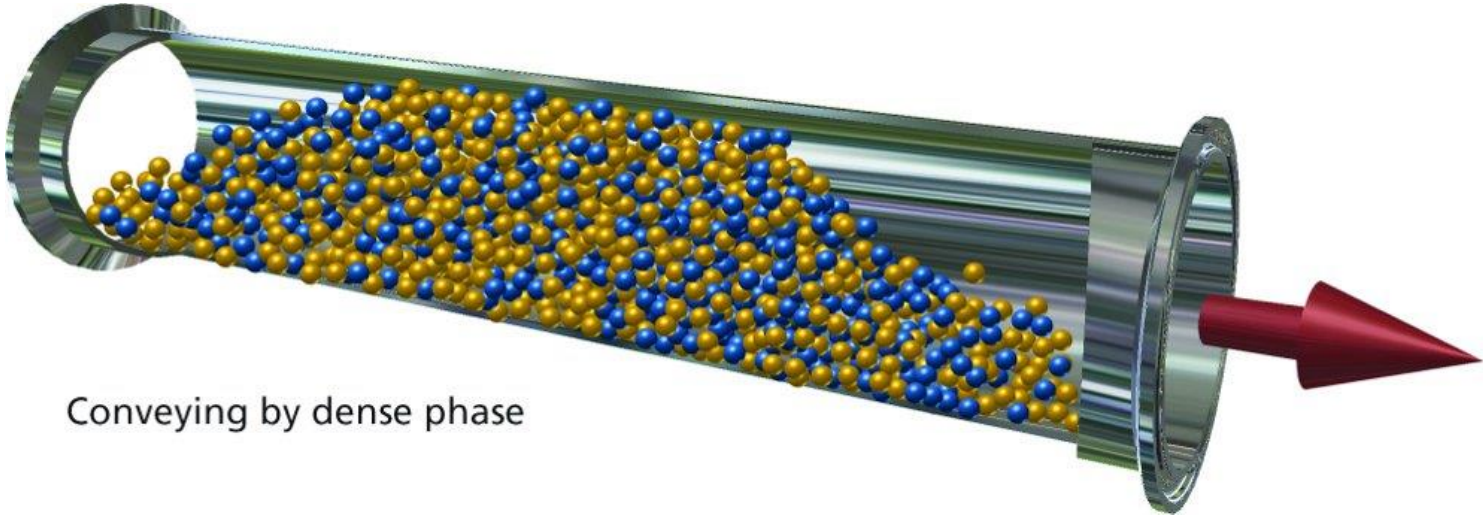
Isolation helps with personnel exposure, but worsens explosion hazards.

More Continuous Manufacturing Dilemma



Pneumatic Conveying

Personnel Exposure	Dispersion



credit: https://www.powderbulksolids.com/pneumatic-conveying/contained-powder-transfer-vacuum-based-pneumatic-conveying

Continuous manufacturing promotes dust dispersing methods like pneumatic conveying.

Even More Continuous Manufacturing Dilemma

Remote Operation	
Personnel Exposure	Hazard Impact

With minimal personnel supervision, fault detection becomes an even bigger issue.

Pharma manufacturing is **NOT** inherently safe

BUT

No high-profile incidents on combustible dusts

YET

Dust deflagration and explosion can still occur

Quantifying Risk

Making the best safety decision

Risk-based DHA

AIChE 2017, CCPS Guidelines for Combustible Dust Hazards Analysis

- Layer of Protection Analysis, Simplified Process Risk Assessment (CCPS 2001)
- Guidelines for Chemical Process Quantitative Risk Analysis, 2nd Edition (CCPS 1999)
- Guidelines for Developing Quantitative Safety Risk Criteria (CCPS 2009)
- Guidelines for Enabling Conditions and Conditional Modifiers in Layers of Protection Analysis (CCPS 2014)
- Guidelines in Initiating Events and Independent Protection Layers in Layer of Protection Analysis (CCPS 2015)

Risk = f(consequence, likelihood)

Equivalent Risks
0.1 Losses per Year

Losses/Event	Events/Year
1	1/10
10	1/100
100	1/1,000
3,000	1/30,000

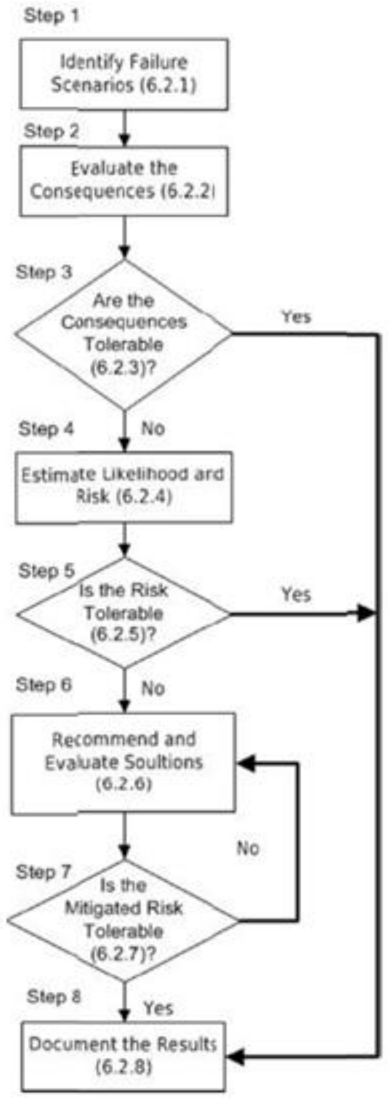


Figure 6.1 Technique for Selecting the Design Bases for Process Safety Systems (adapted from *Guidelines for Design Solutions for Process Equipment Failures* (CCPS 1998)).

Discipline on thought process, flexibility in application.

Risk Reduction (with PSV and SIF)

From the HAZOP risk matrix for this Process, with the Two safeguards :

1. Frequency of Initiating Event (IE) – (L=1)
2. Severity – (S=2)
3. Risk (with Two safeguards) = (Box 7) (Acceptable Risk level)

Likelihood →

Severity ↓	1	2	3	4	5	6
1	6	5	4	3	2	1
2	7	6	5	4	3	2
3	8	7	6	5	4	3
4	9	8	7	6	5	4
5	10	9	8	7	6	5

SIF

PSV (non-SIF IPL)

Likelihood	
1	Once in 10000 years
2	Once in 1000 years
3	Once in 100 years
4	Once in Ten Years
5	Once a year
6	Multiple times per year

Severity	
1	Multiple fatilities
2	Single Fatility
3	Serious injury
4	First Aid
5	First Aid

LOPA TMEL (Single Fatality) :

1E-05 per year

Credit: **Prasad Goteti**, Honeywell

Risk = f(severity, likelihood)

Likelihood → Frequency of events

Risk = Probability (event)

Dust Explosion Risk = Probability (explosion)

Dust Exposure Risk = Probability (exposure)

Risk-based DHA allows for the design of a completely safe facility.

But…

Unexpected things happen. Faults happen.

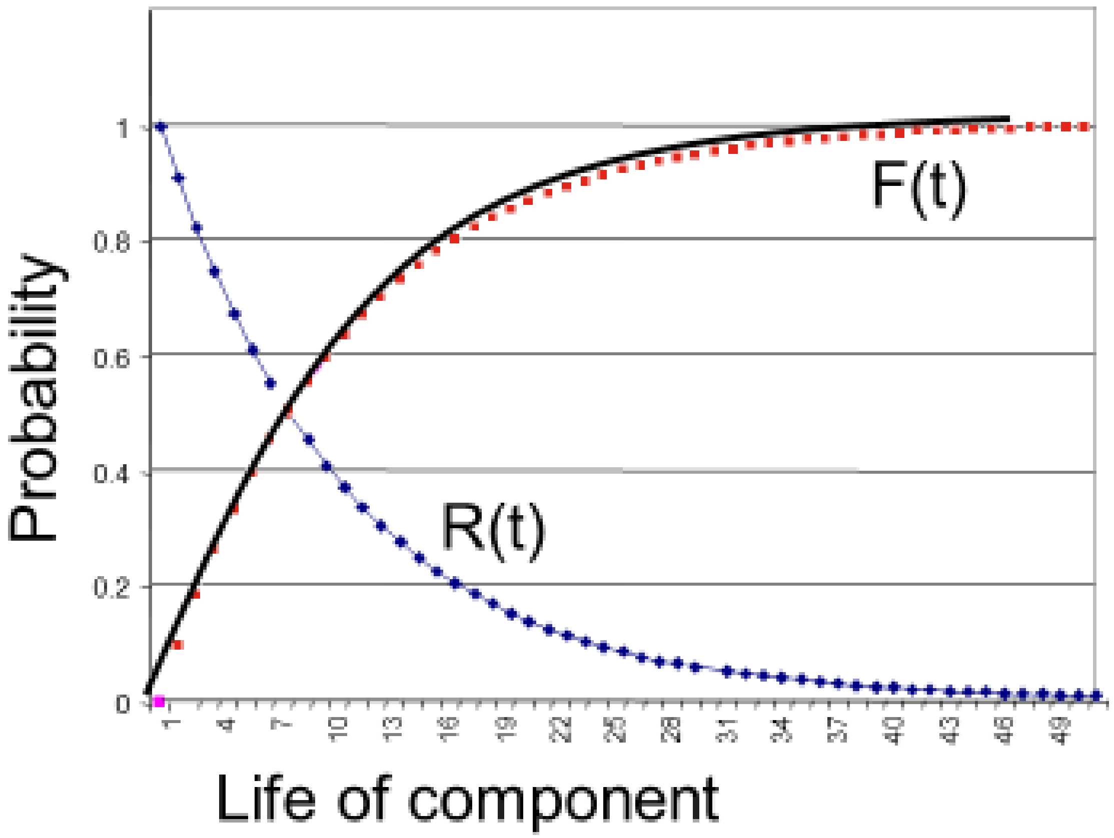
Equipment parts break down. Systems fail.

How do you manage these abnormal events?

Component Reliability

$$R(t) = e^{-\lambda t}$$

$$F(t) = 1 - e^{-\lambda t}$$



Finally component will fail !

Credit: **Prasad Goteti**, Honeywell

Summary so far…

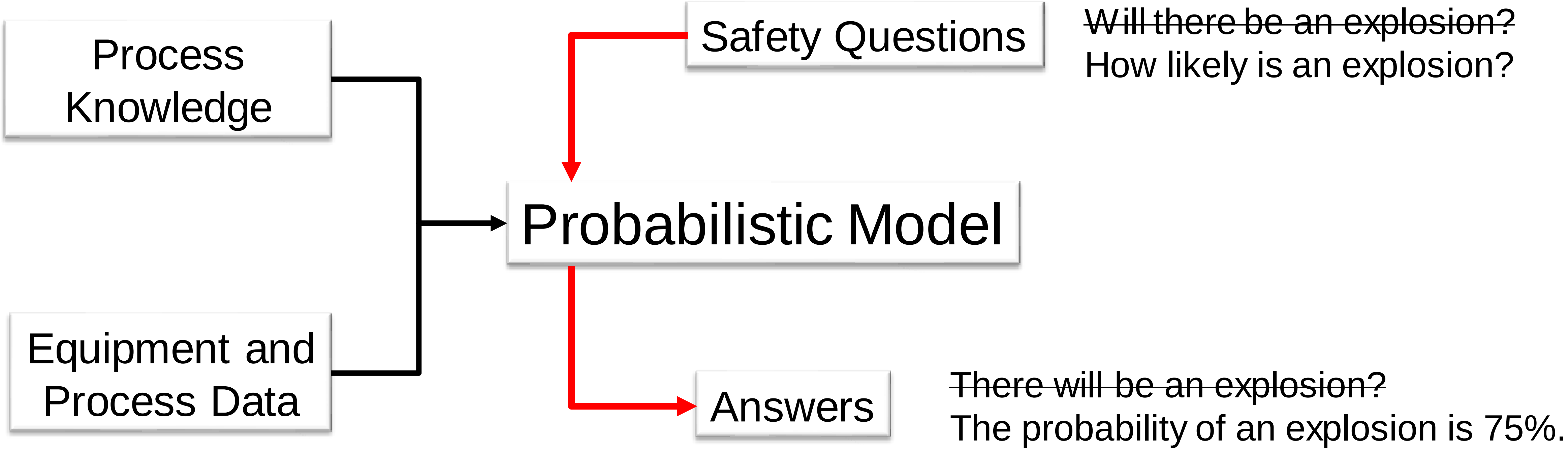
Continuous manufacturing dilemma
Personnel exposure vs dust explosion

Quantify risk
Bayesian probability

Real-time failure detection is critical
Plan for parts to fail

Probabilistic Model
Condition Monitoring

Probabilistic Condition Monitoring



Modeling Using Factor Graphs

A Probabilistic Graphical Model (PGM)

PGM: A Representation of Knowledge

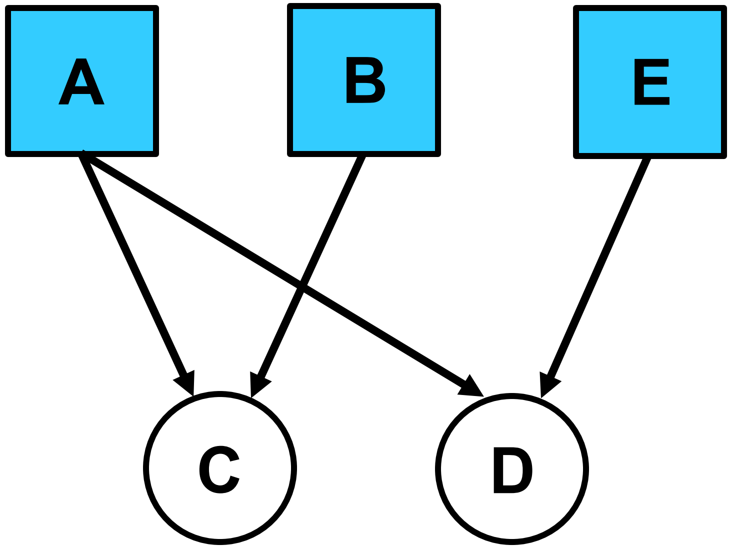
A = Process is Faulty

B = Sensor 1 is Faulty

C = Sensor 1 Readings

D = Sensor 2 Readings

E = Sensor 2 is Faulty



Inference

P(B|C)

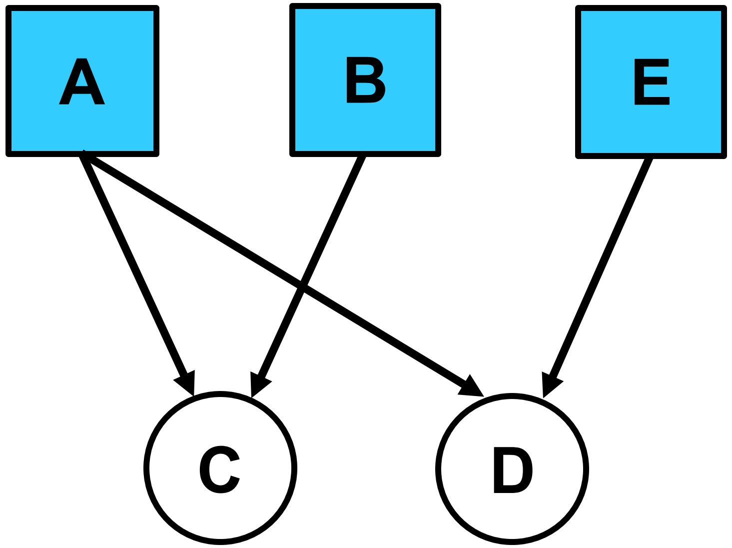
Given observations via sensor measurements, what is the probability that the sensor is faulty?

P(A|C,D)

Given the observations from two sensors, what is the probability that the process is faulty?

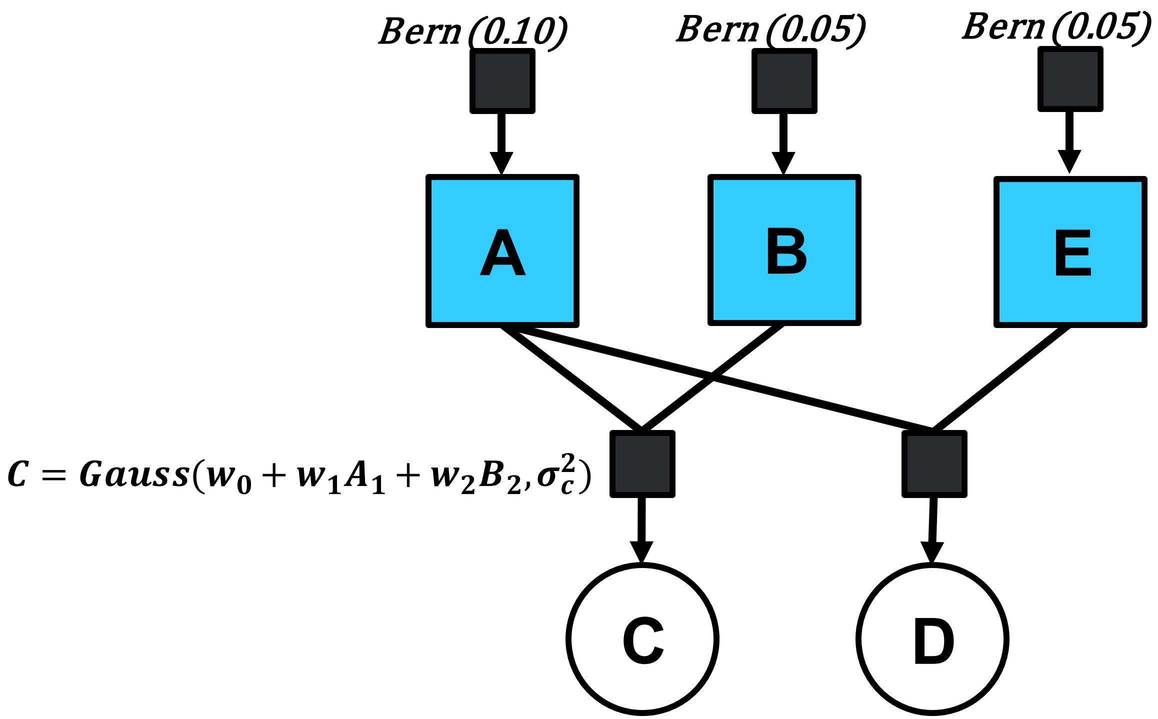
Types of Probabilistic Graphical Models (PGM)

Bayes Network



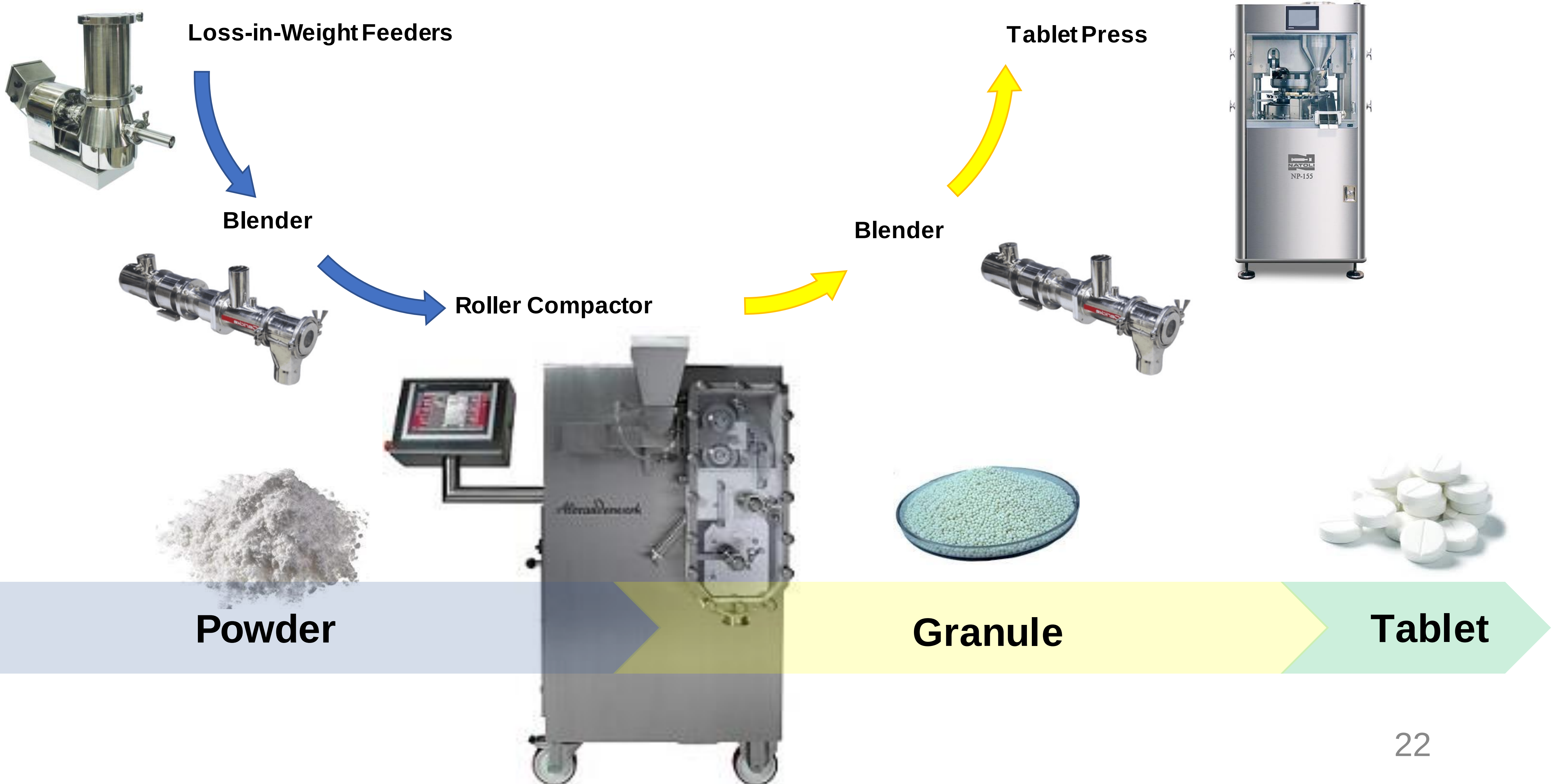
- X Hidden, Discrete Variables
- Y Hidden, Continuous Variables
- Z Observed, Continuous Variables

Factor Graph

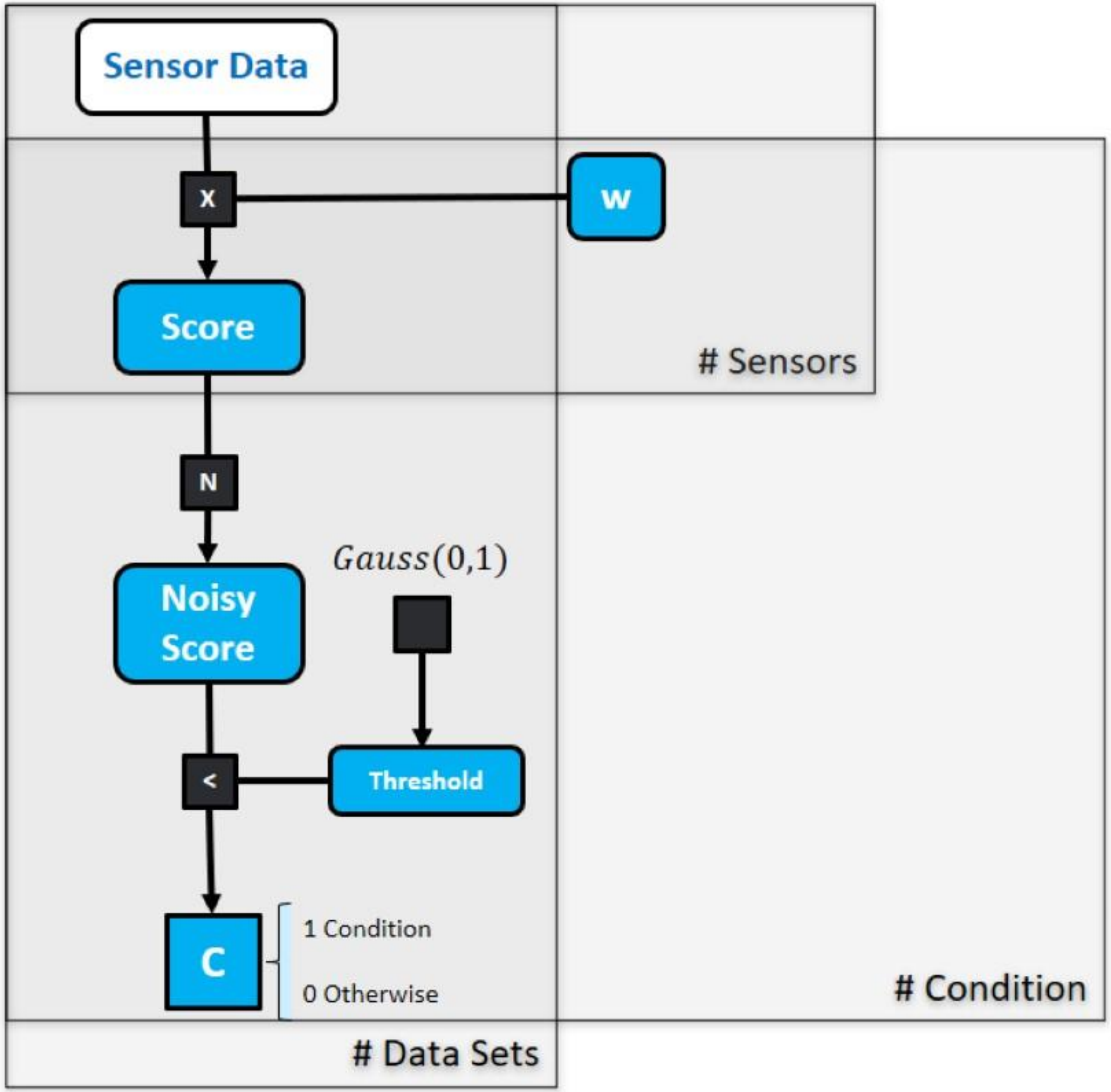


Factors
Functions/Tables that mathematically represent priors, relationships

Purdue University Continuous Tablet (OSD Form) Manufacturing Pilot Plant



Condensed Representation



Bayes Point Machine

Herbrich, R., Graepel, T., & Campbell, C. (2001). Bayes point machines. *Journal of Machine Learning Research*, *1*(Aug), 245-279.

T. Minka, J. Winn, J. Guiver, Y. Zaykov, D. Fabian, and J. Bronskill Infer.NET 0.3, Microsoft Research Cambridge, 2018. http://dotnet.github.io/infer

Condition:

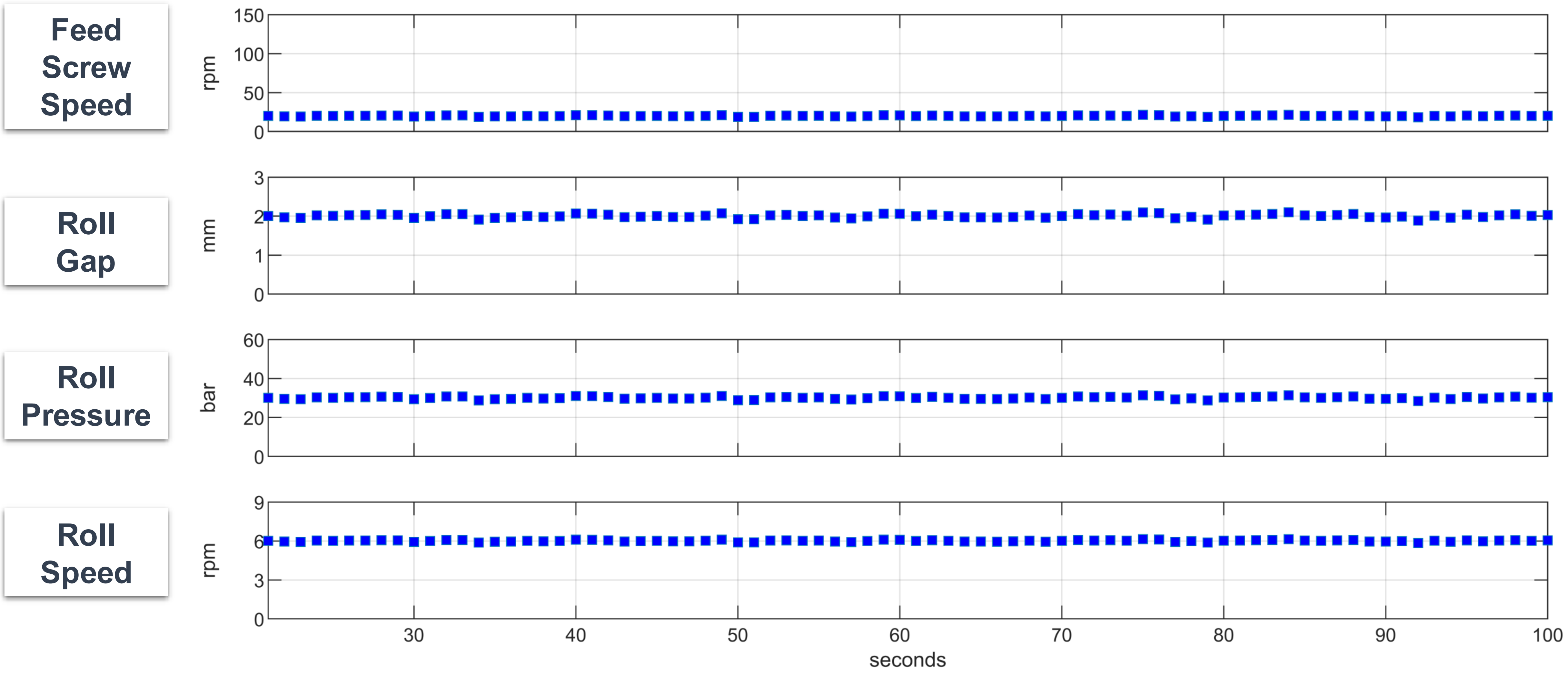
Normal
Fault1
Fault2

Implementing the Model

T. Minka, J. Winn, J. Guiver, Y. Zaykov, D. Fabian, and J. Bronskill
Infer.NET 0.3, Microsoft Research Cambridge, 2018.
http://dotnet.github.io/infer

infer.net

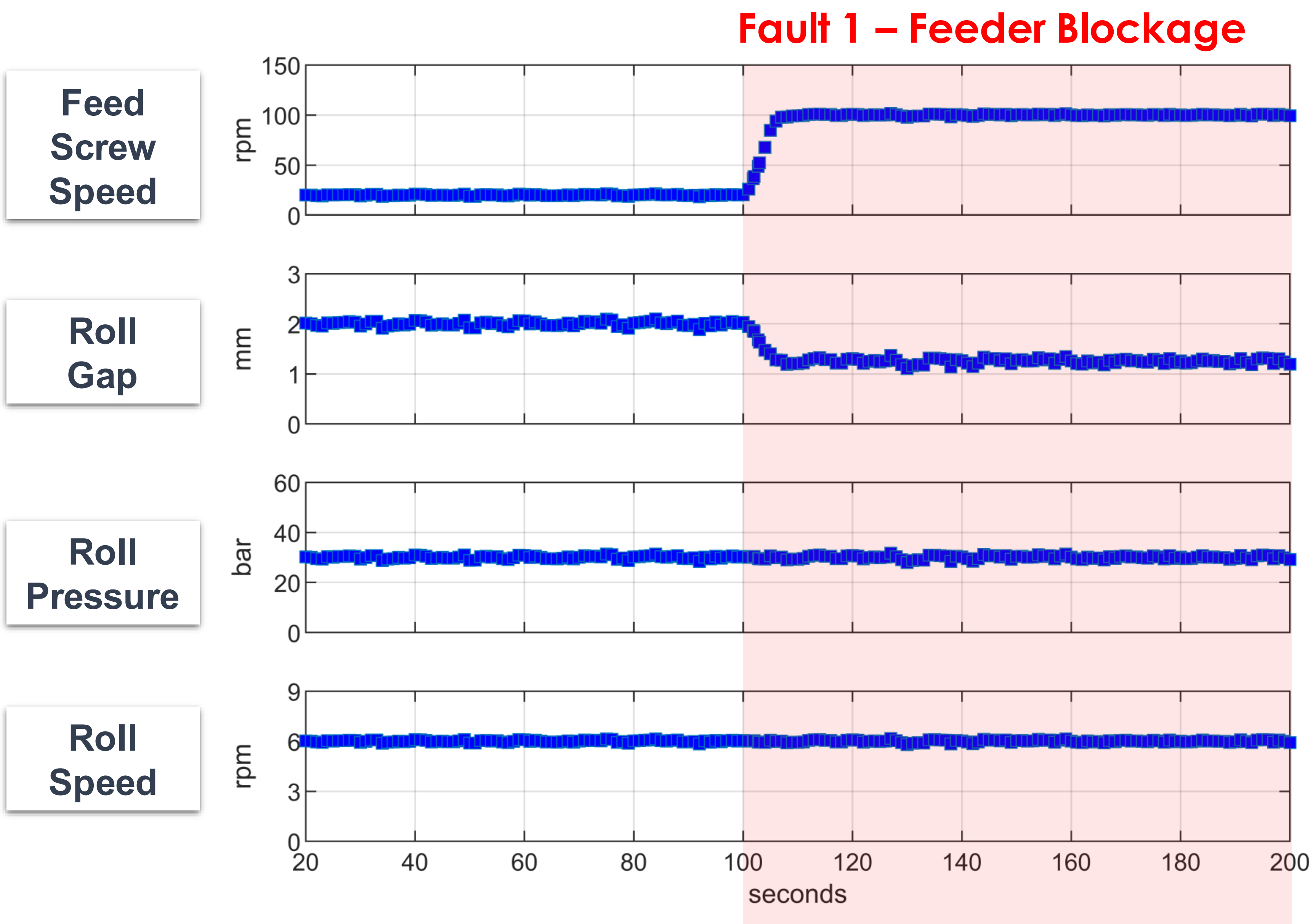
Training Data – Normal Condition



Simulated Data based on Previous Study:

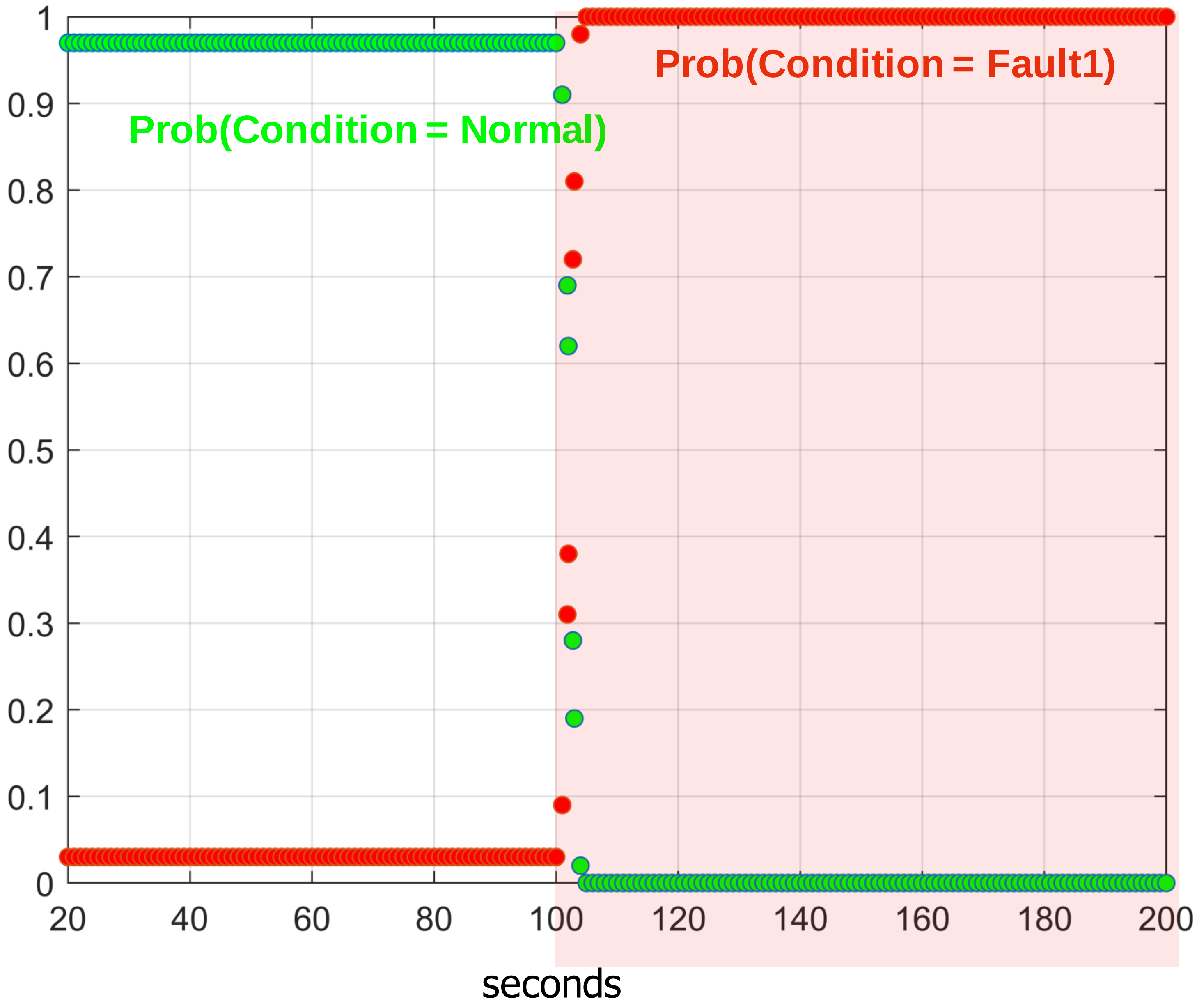
Gupta, A., Giridhar, A., Venkatasubramanian, V., & Reklaitis, G. V. (2013). Intelligent alarm management applied to continuous pharmaceutical tablet manufacturing: an integrated approach. *Industrial & Engineering Chemistry Research*, *52*(35), 12357-12368.

Training Data: Fault 1 Induced at 100s



Can the system detect fault 1?

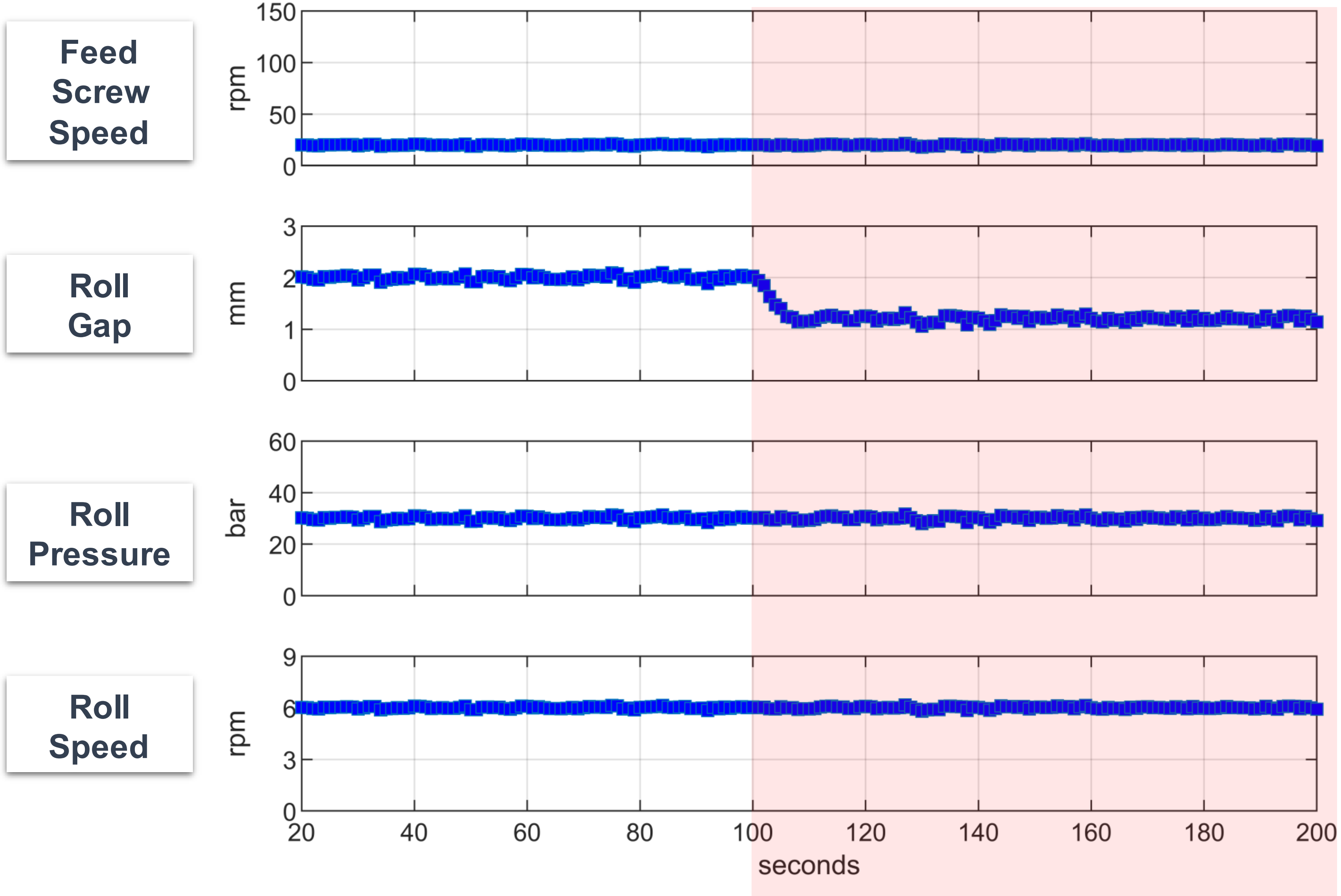
Yes it can!



Fault 1 Induced at t = 100s

Unknown Fault? Fault 2 Induced at 100s

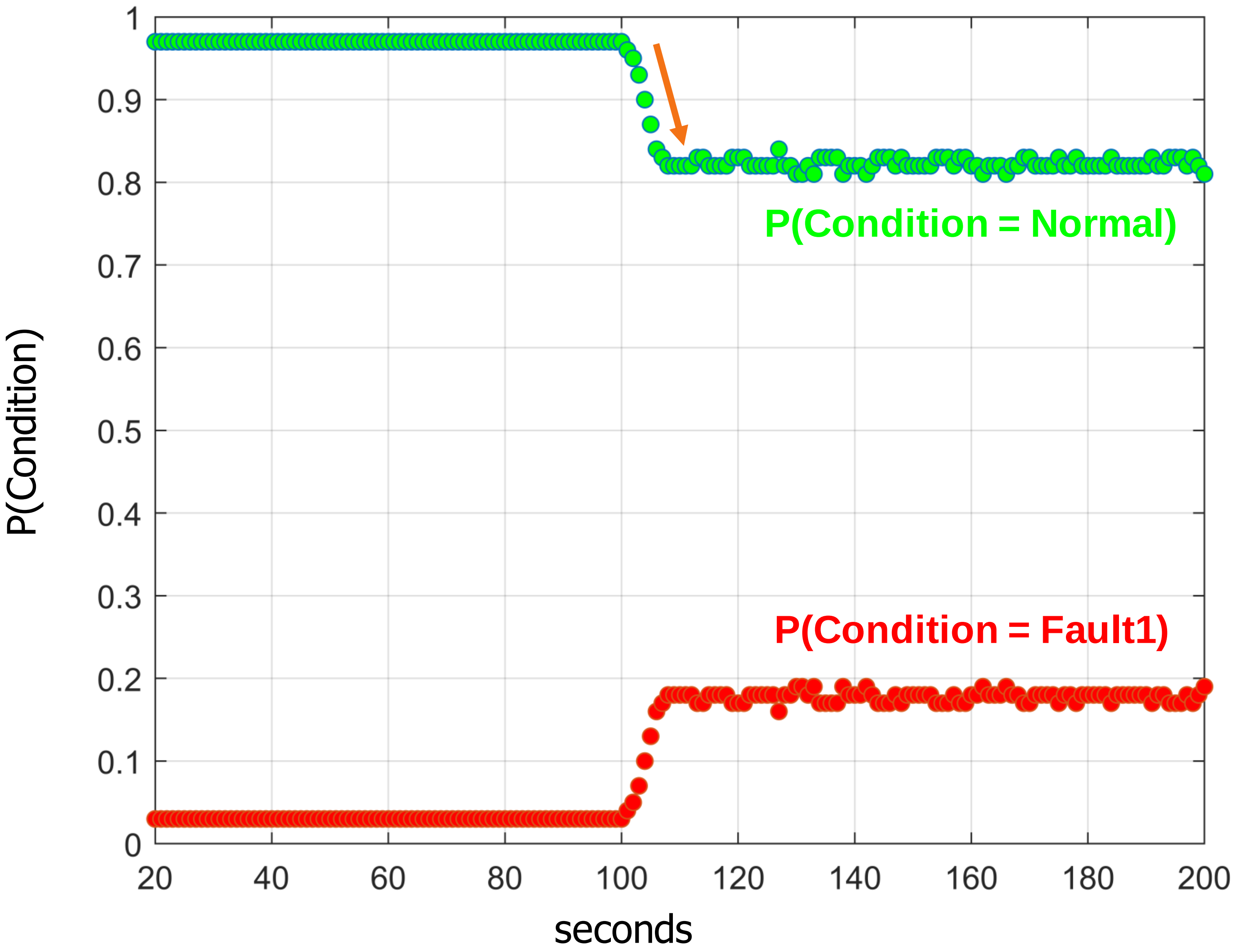
Model untrained for the fault 2 – Controller Malfunction



Can the system differentiate this from Normal Condition and Fault 1?

It can detect novel faults!

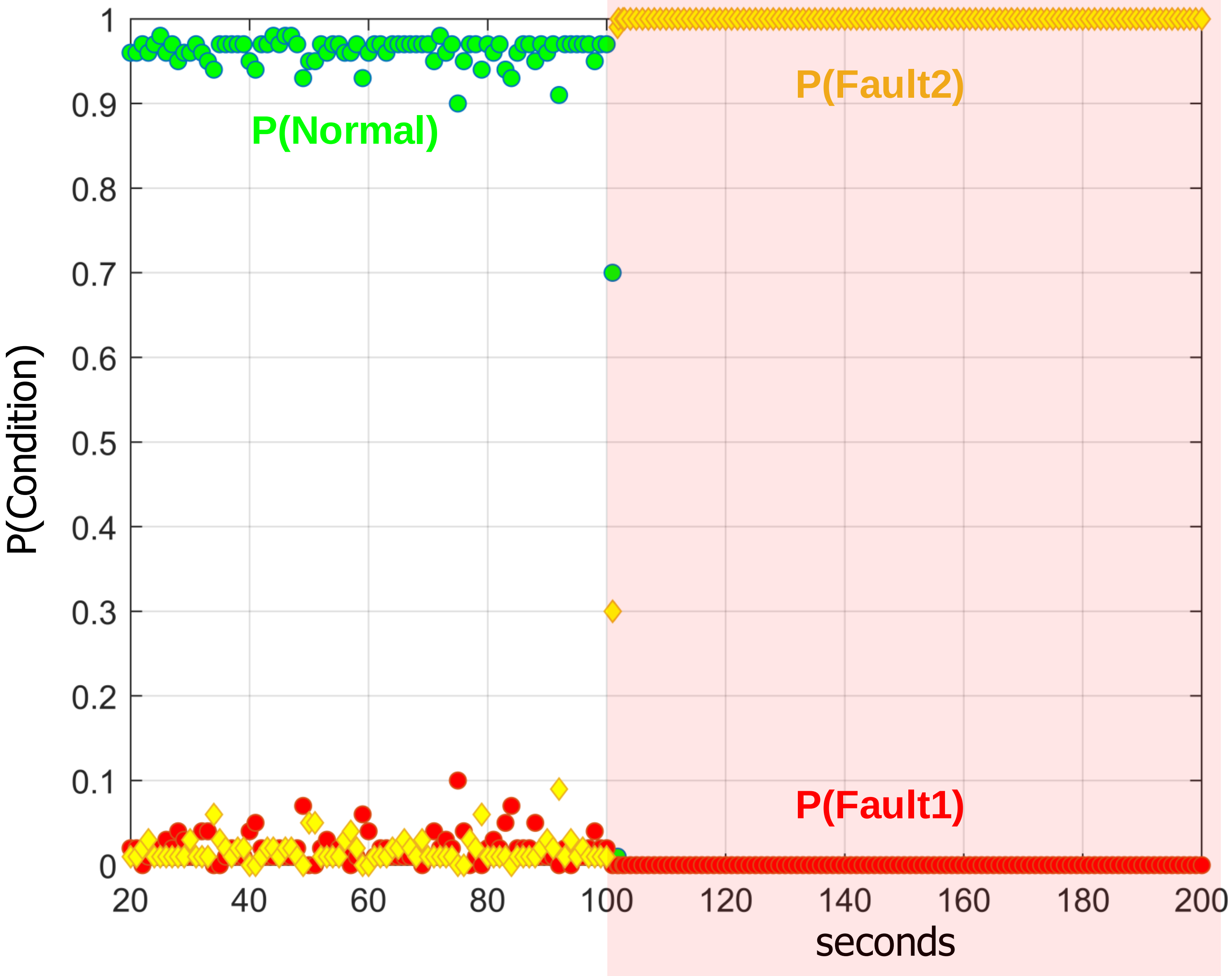
System is "less certain" of its prediction



Detect new faults or conditions based on certainty of prediction.

Training Model with Fault2: Fault 2 Induced at 100s

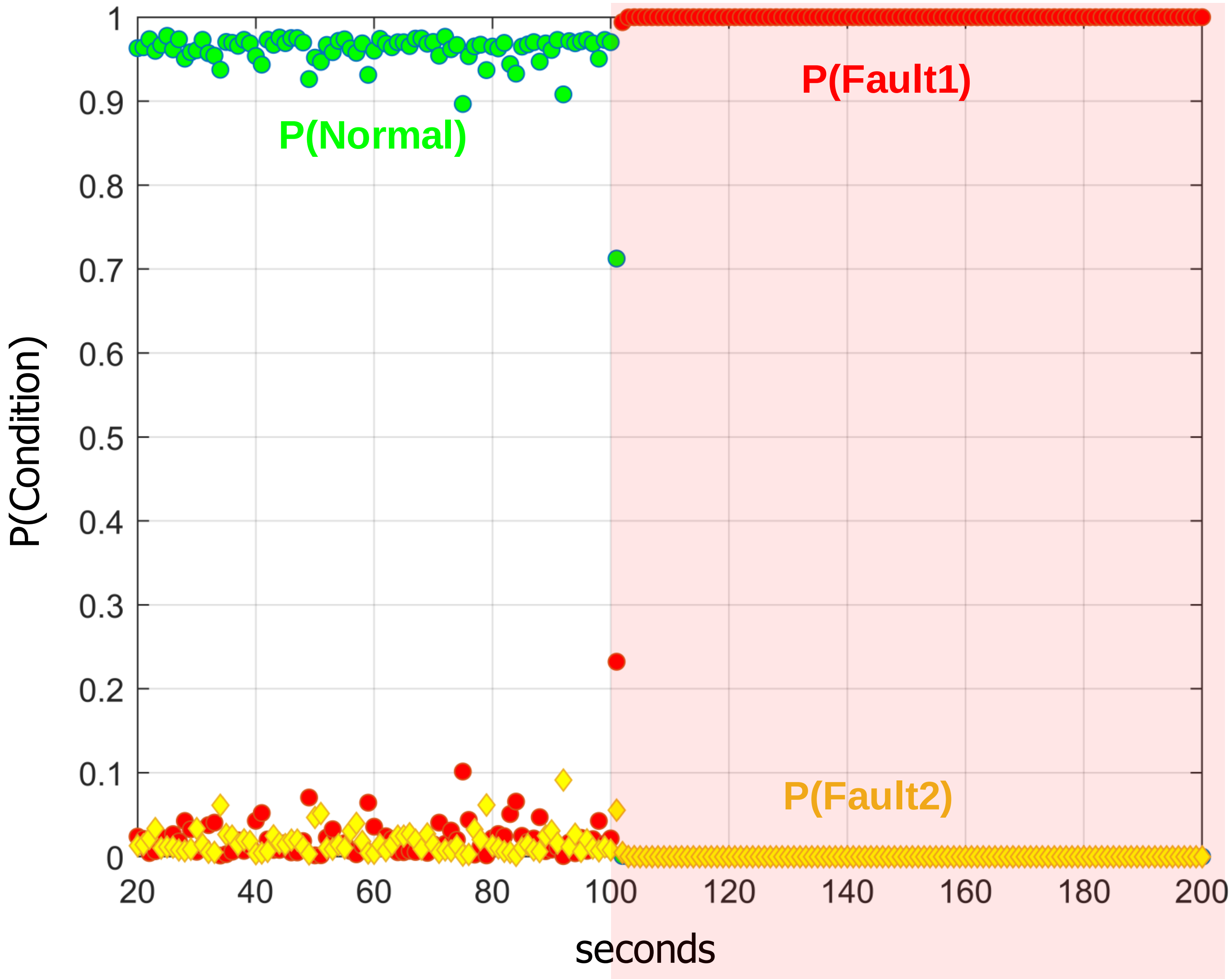
Increased Certainty about Predictions of Condition



Added Fault 2 as variable to the model.

Training Model with Fault2: Fault 1 Induced at 100s

Fault 1 was still properly assessed



Added Fault 2 as variable to the model.

Capabilities:

Fault Management

Detect and Diagnose Known Faults
Detect Novel Faults
Store New Faults

Fault Repository

Developing a Probabilistic Model for Dust Safety

For Condition Monitoring

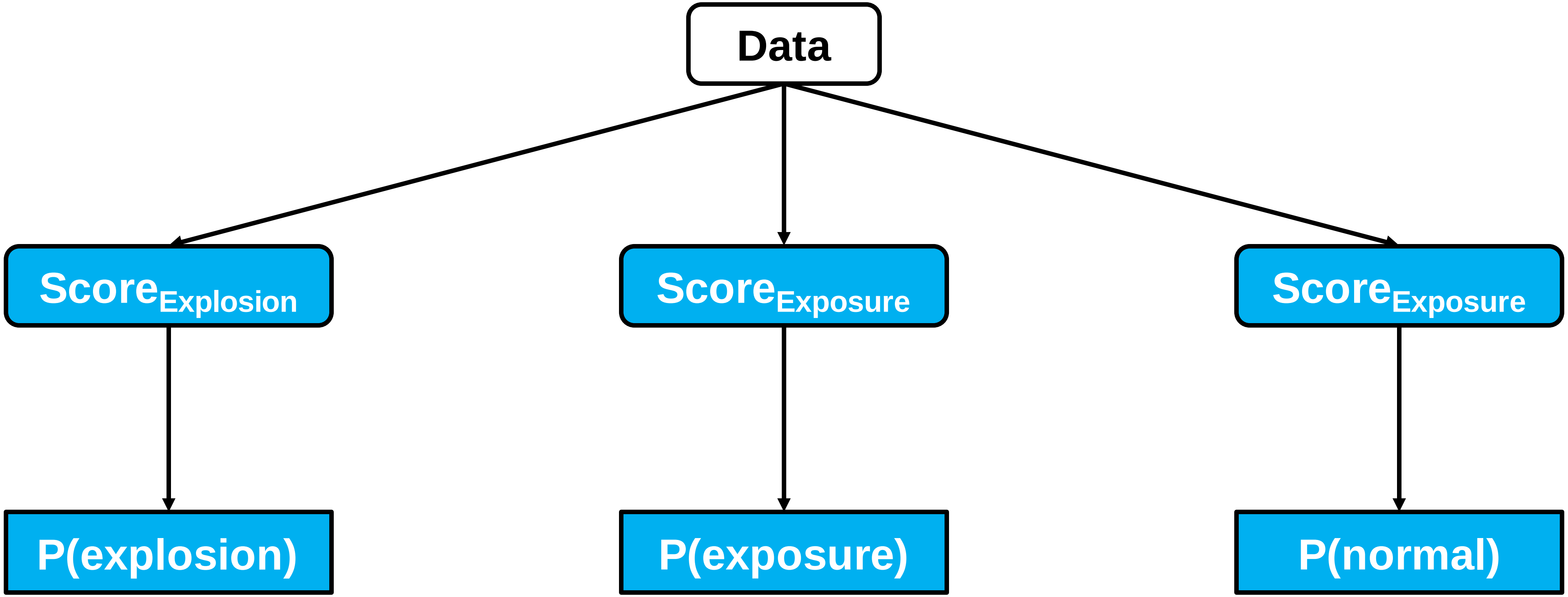
Assign Random Variables: Safety Questions

P(explosion)
- **1 facility will explode**
- **0 otherwise**

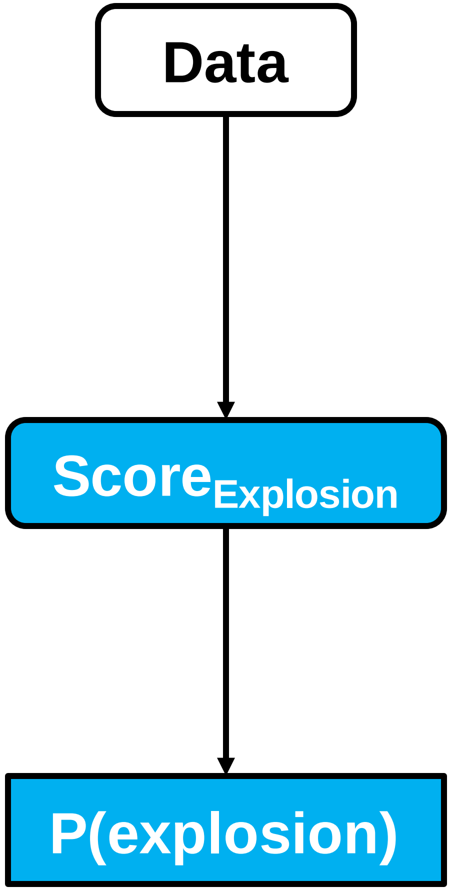
P(exposure)
- **1 dangerous exposure if person is present in facility**
- **0 otherwise**

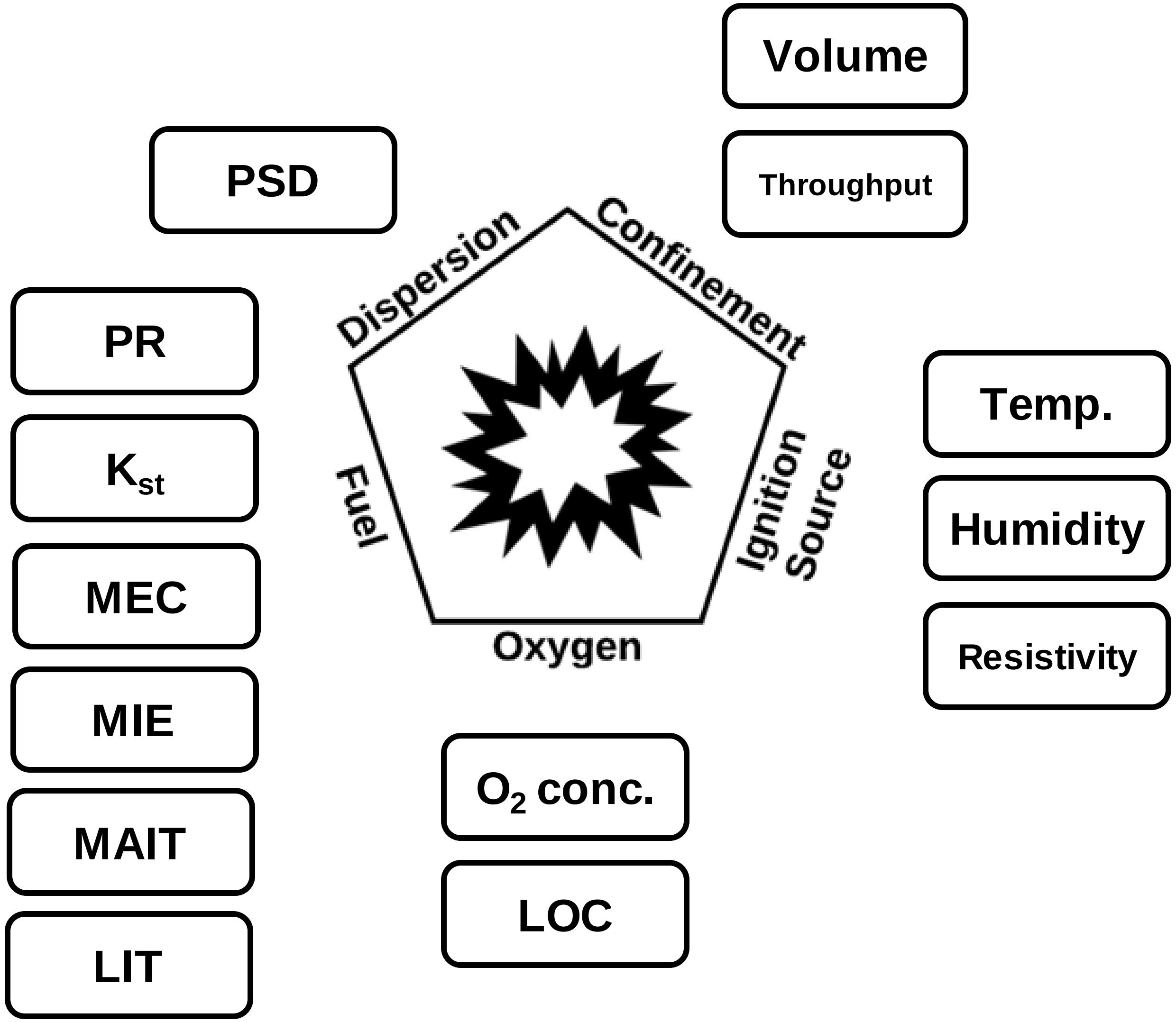
P(normal)
- **1 normal/safe**
- **0 otherwise**

Assign Random Variables: Using Data to Answer Safety Questions

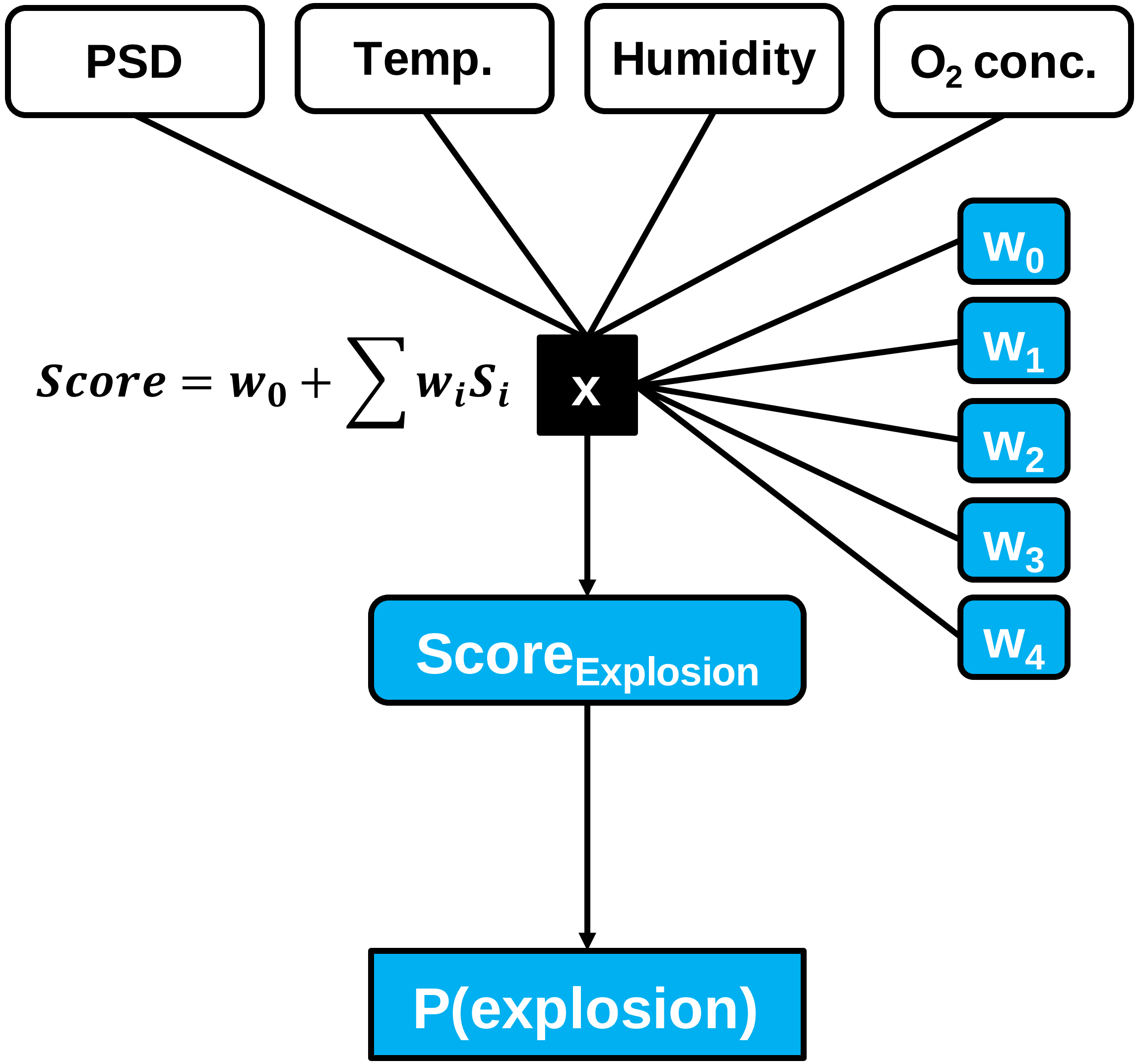


Adding Factor Nodes: Dust Explosion Data

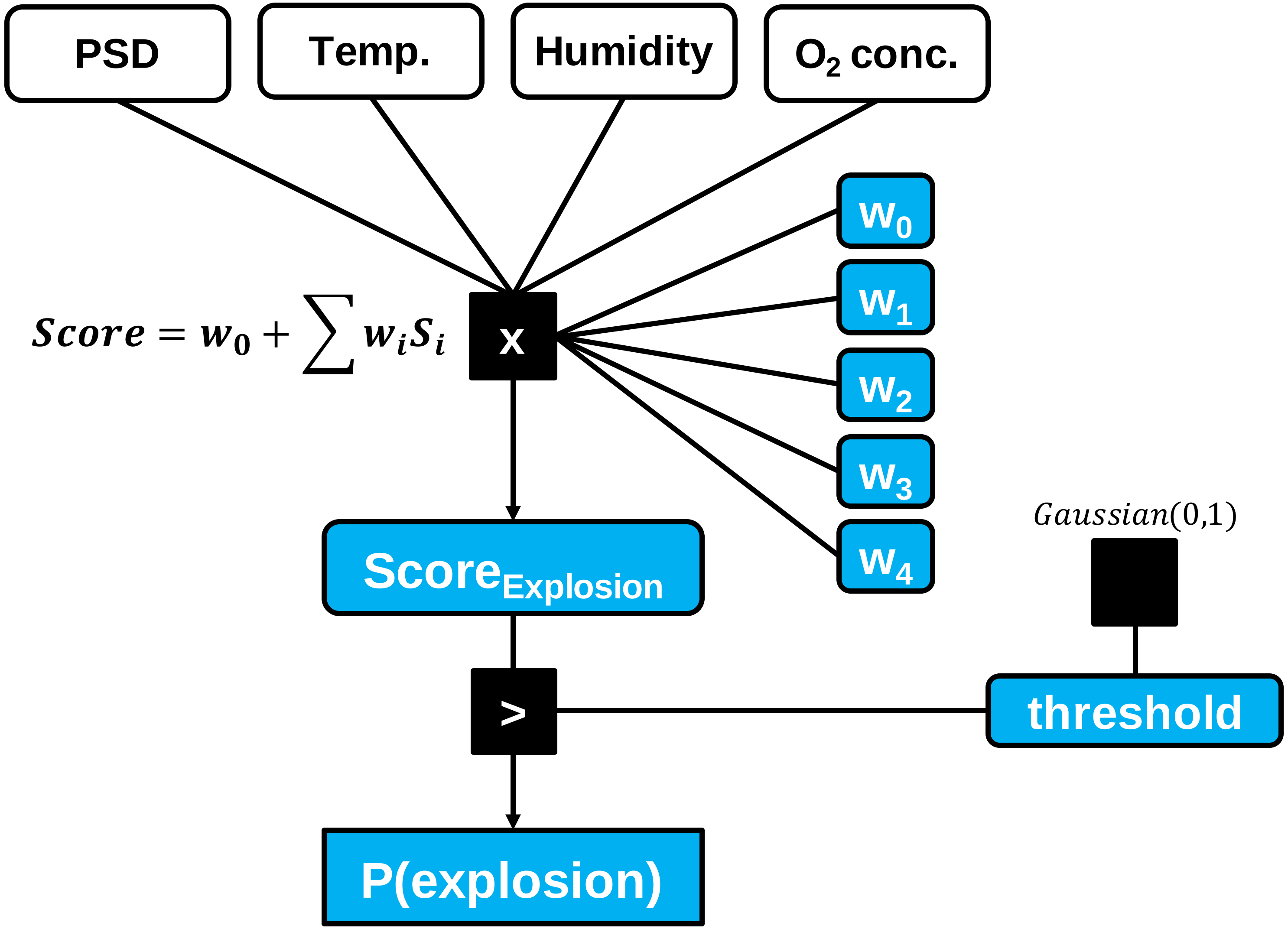




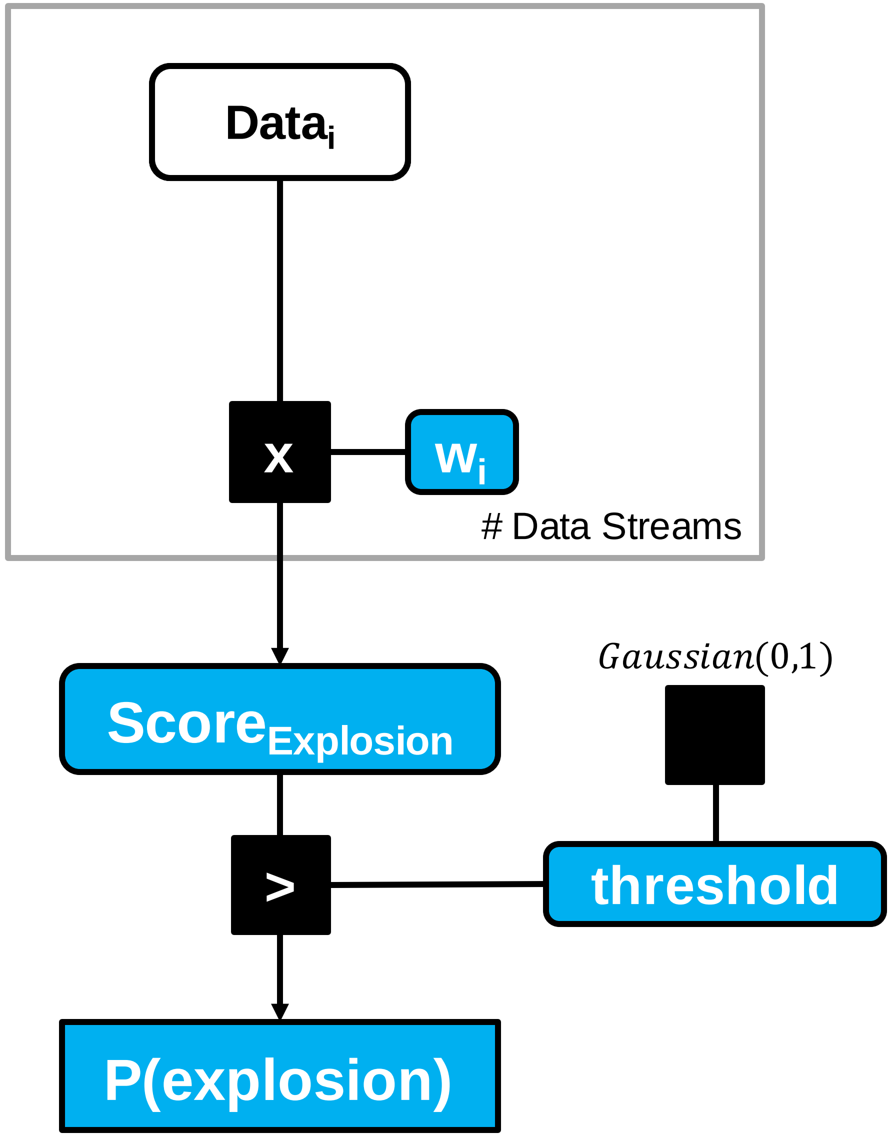
Adding Factor Nodes: Dust Explosion Score Parameters



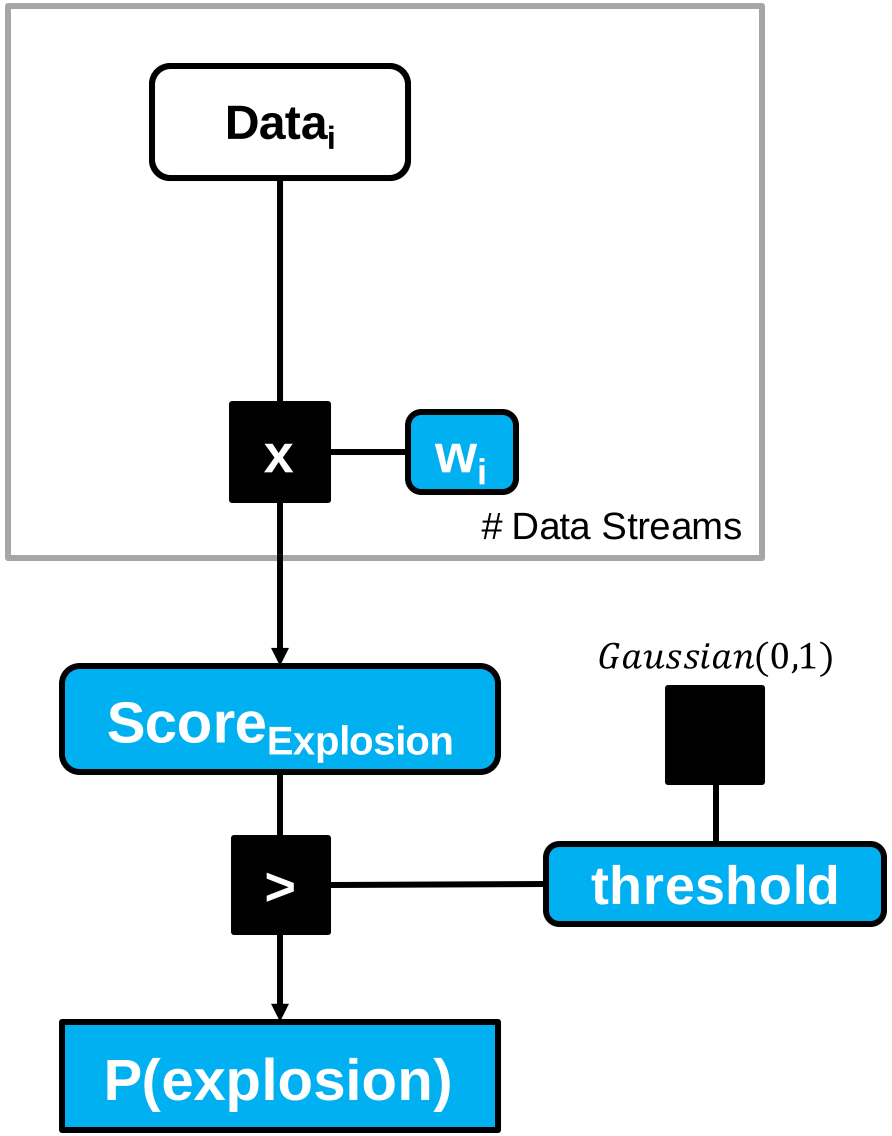
Adding Factor Nodes: Continuous to Discrete Variable

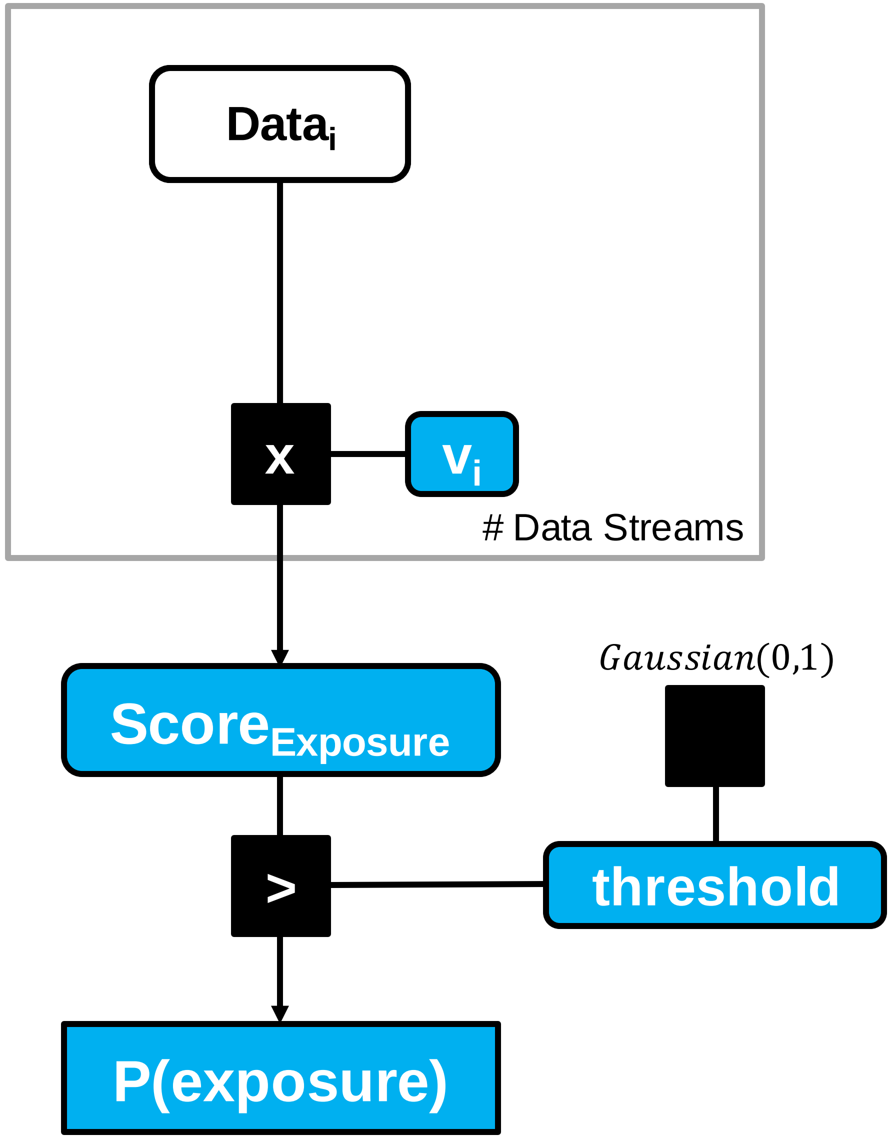


Condensed Representation

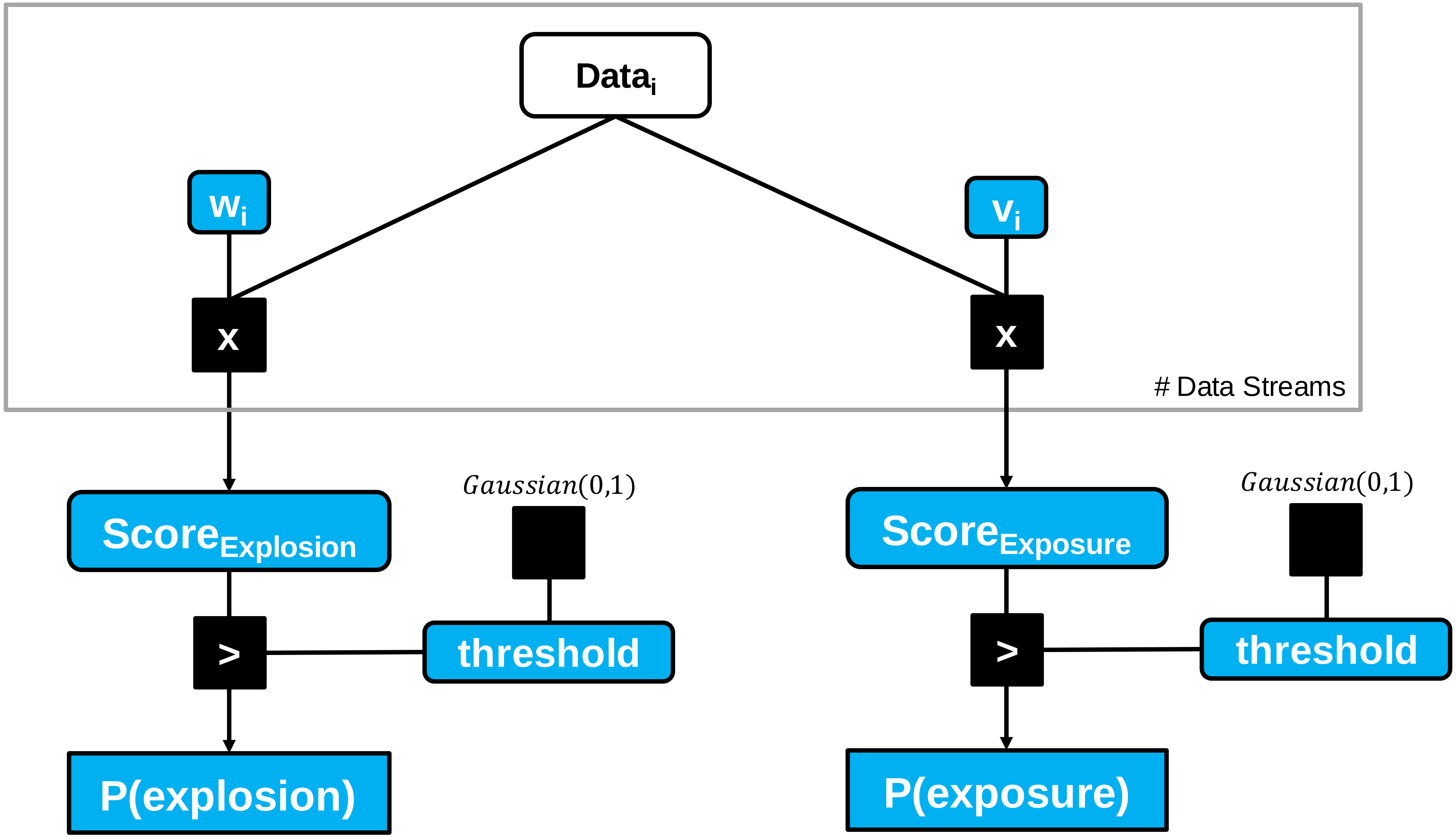


Repeating Structure for Other Events

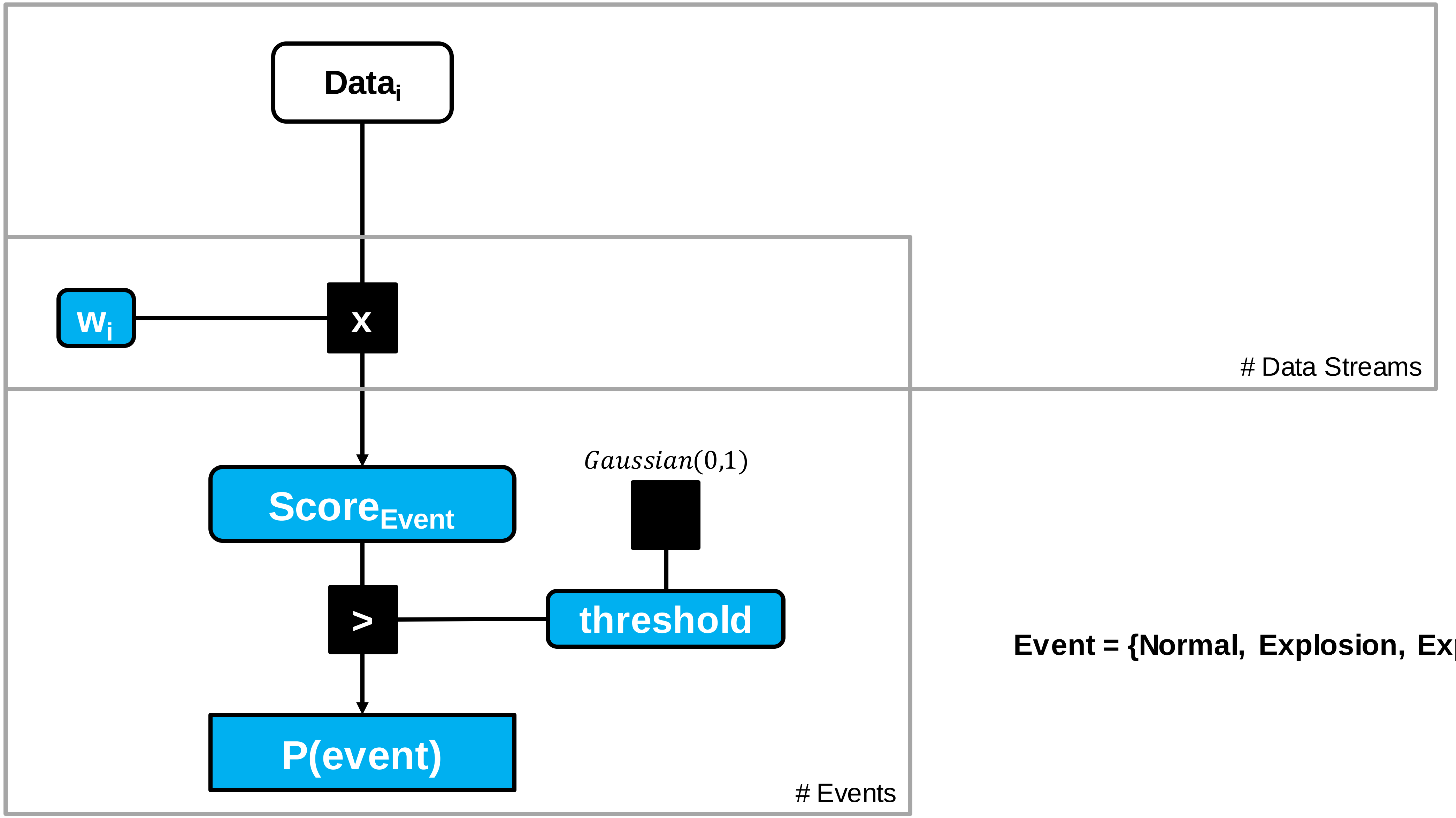




Even More Condensed Structure



Even More Condensed Structure



Event = {Normal, Explosion, Exposure}

Next Steps: Dispersion-related Data

Volume

PSD

Throughput

PR

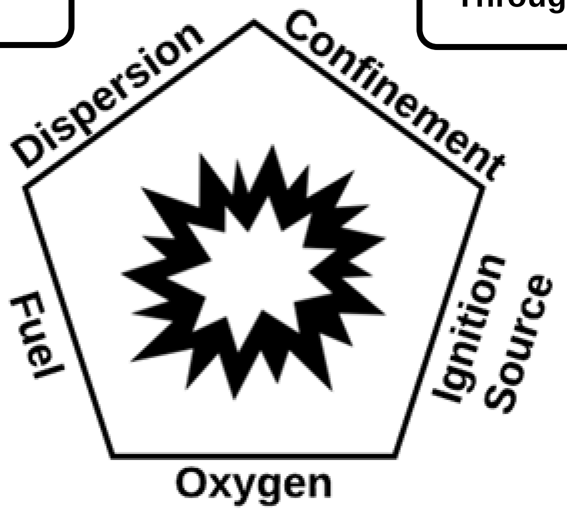
K_{st}

MEC

MIE

MAIT

LIT



Temp.

Humidity

Resistivity

O_2 conc.

LOC

Opportunities for Research

Novel Sensors for Monitoring Dispersion

Measure particle size distribution.

https://www.innopharmatechnology.com/products/eyecon2tm

Eyecon2

Particle Size Analyzer:

D10, D25, D50, D75, D90 in real time

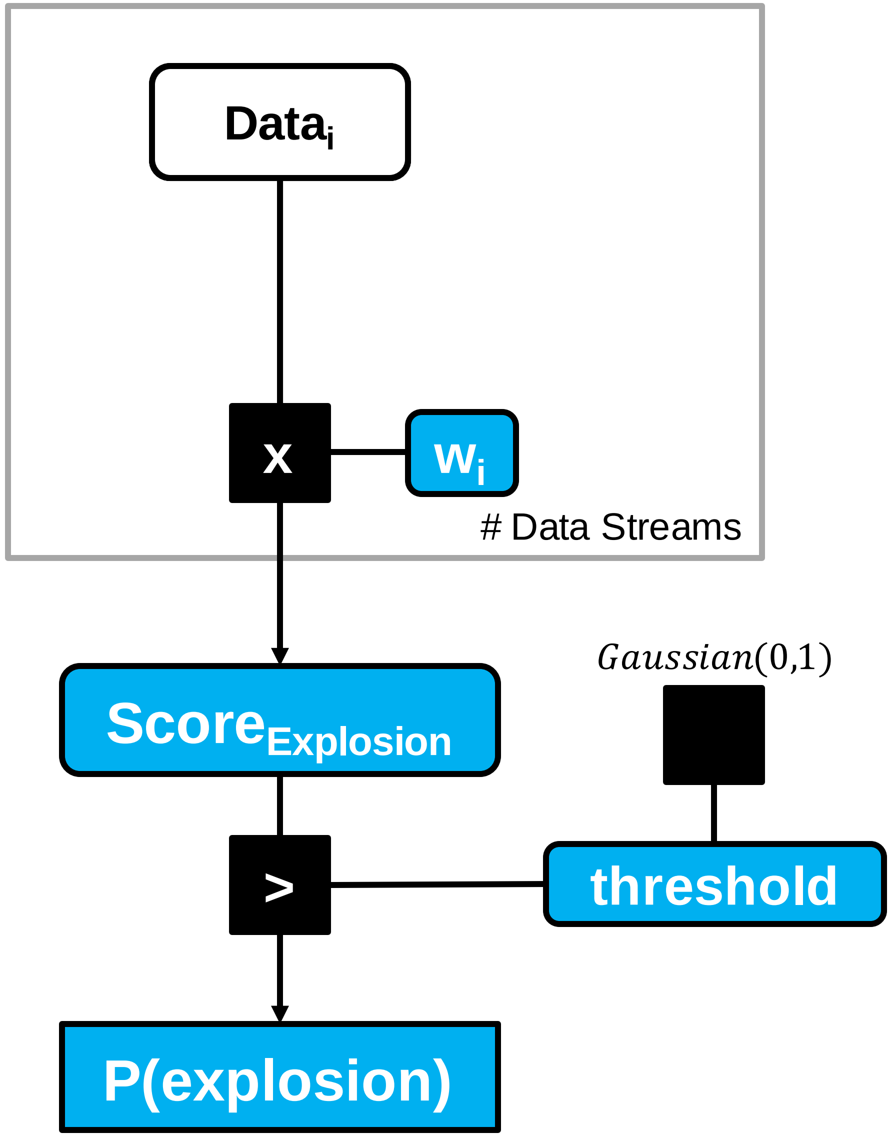
Measure dust concentration in the air.

Collaboration with Professor Ambrose.

Smartphone into regular camera.

Integrate into fault detection system.

Next Steps: Training the Model



Impractical to induce deflagrations

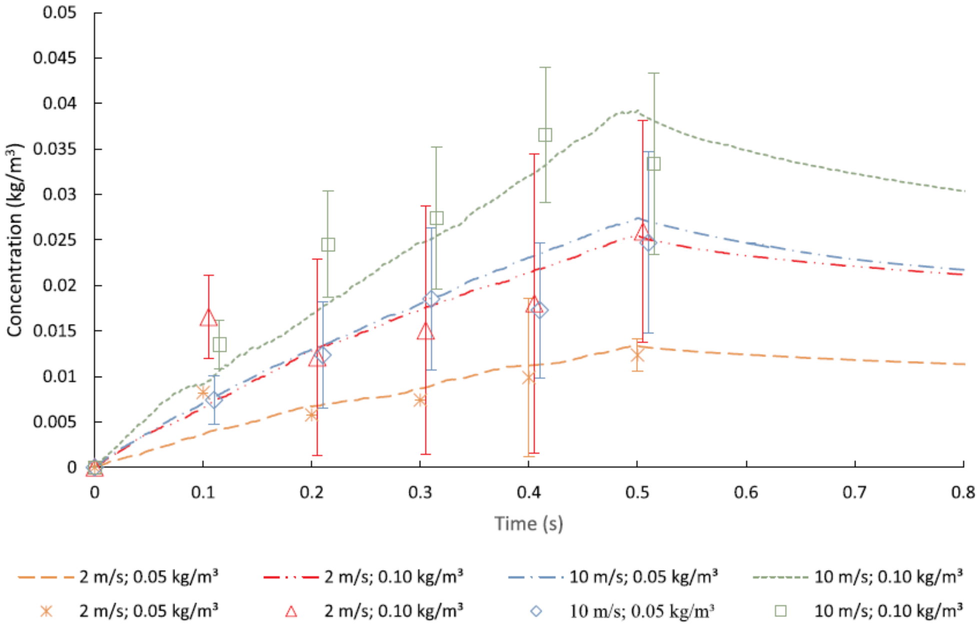
CFD Simulations are necessary

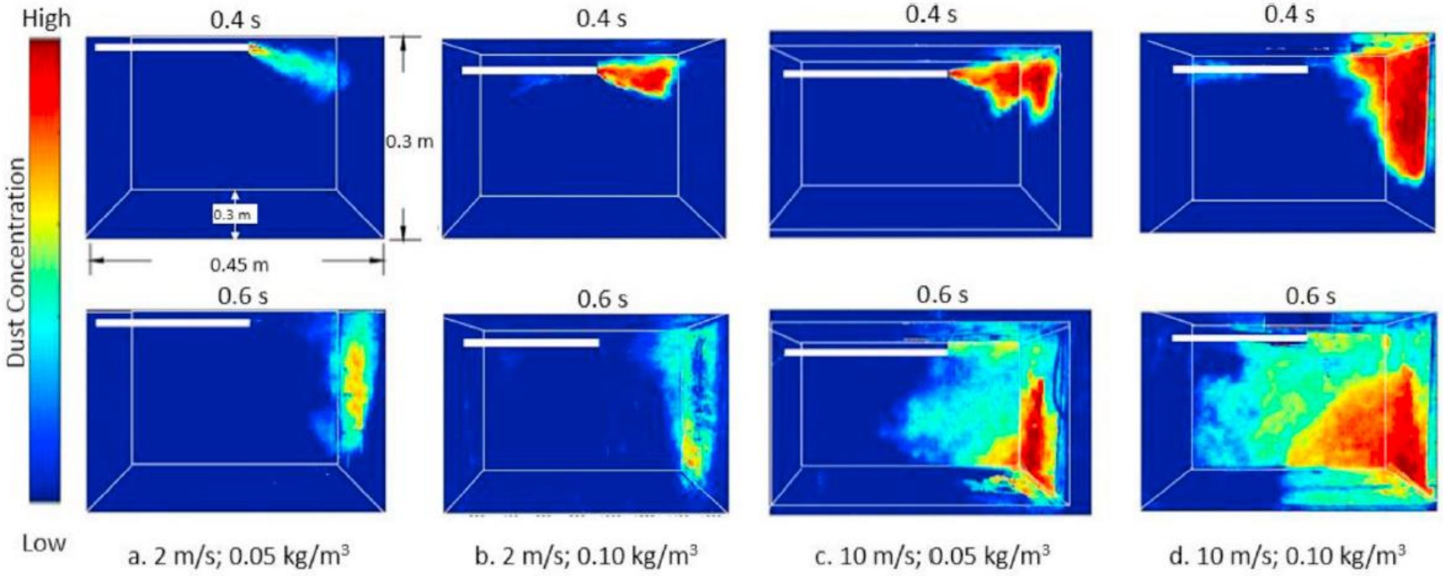
Opportunities for Research
Simulation

CFD Simulation

Zhao, Y., & Ambrose, R. K. (2019). Modeling dust dispersion and suspension pattern under turbulence. *Journal of Loss Prevention in the Process Industries*, *62*, 103934.

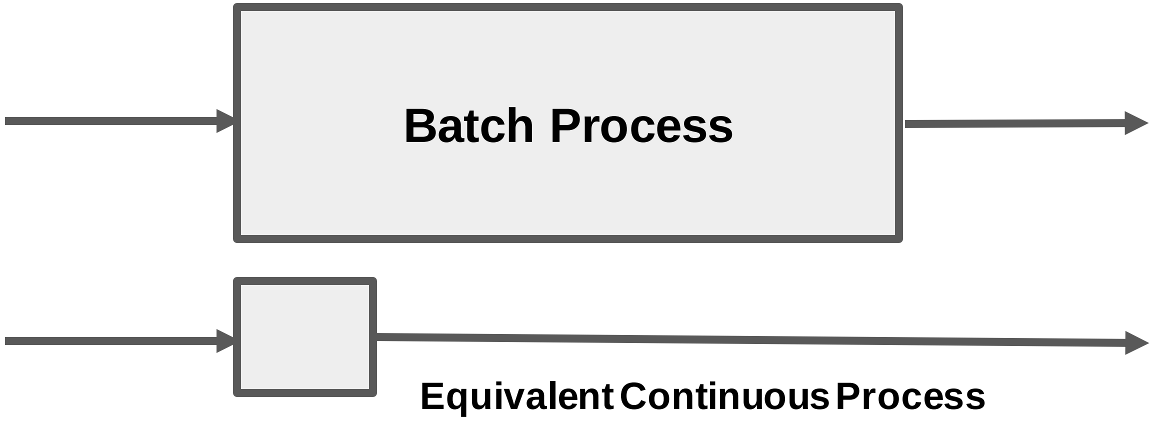
1. What is the critical enclosure volume and geometry for each operation mode?
2. Is there a critical size distribution to keep a powder processing facility safe?



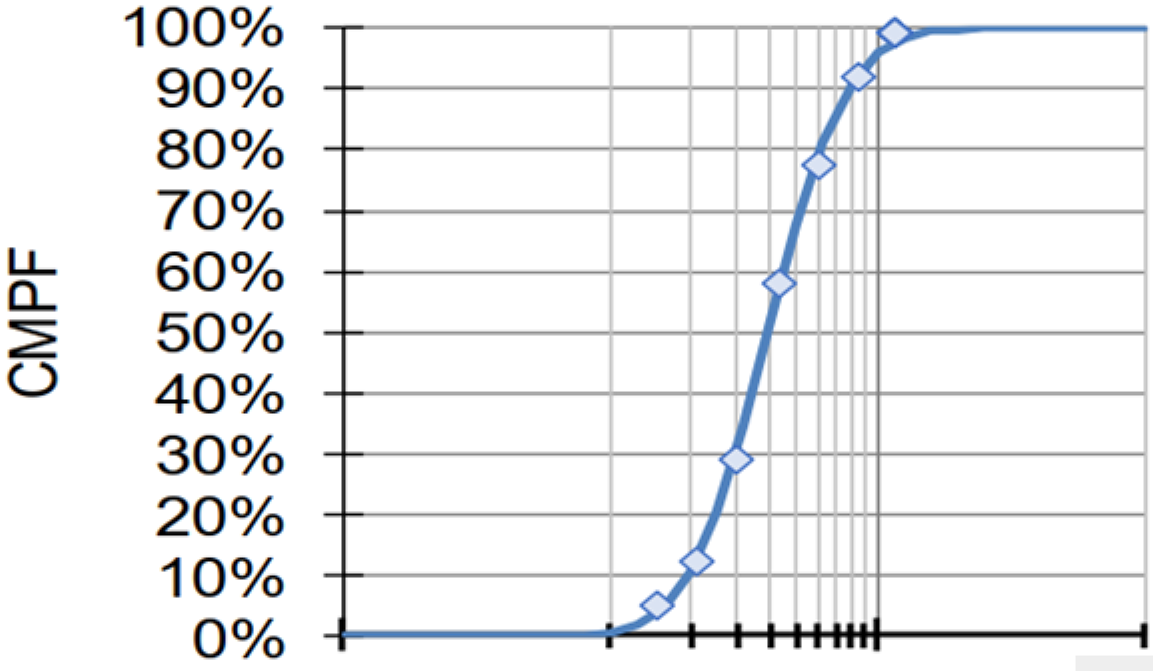


Opportunities for Research
CFD Simulation and Probabilistic Modeling

What is the critical enclosure volume and geometry for each operation mode?



Is there a critical size distribution to keep a powder processing facility safe?



Conclusion

- Showed the advantages of a Probabilistic Condition Monitoring Model for a Roller Compactor.
- Demonstrated the use of Factor Graphs to create a Dust Safety Monitoring Model for a Pharmaceutical Powder Processing Facility.
- Discussed research opportunities that are essential for the development of the model:
    - Development and Testing of Novel Sensors: Dust Concentration (Regular Camera), Particle Size Distribution (Eyecon2)
    - CFD Simulations: Produce Training Data for the Probabilistic Condition Monitoring Model, Batch vs Continuous Mode Confinement Dilemma, Critical Particle Size Distribution Determination.

Future Work

- Train and improve the Probabilistic Condition Monitoring Model.
- Determine feasibility of novel sensors for condition monitoring: Regular Camera and Eyecon2

Ideas for your Safety Problem

Acknowledgements

Thank you for your attention.

Any questions?

Email: rlagare@purdue.edu, lagare.rb@gmail.com