SRYAHWA PUBLICATIONS

Research Journal of Food and Nutrition
ISSN: 2637-5583 | Volume 8, Issue 2, 2025
https://doi.org/10.22259/2637-5583.0802002

REVIEW ARTICLE

Models for Mold Infection and Mycotoxin Production and Influencing Factors: A Review

Huy L. Nguyen[1], Janie M. Moore[1], Binh C. Nguyen[3], Hong M. X. Nguyen[2*]

[1]Department of Biological and Agricultural Engineering, Texas A&M University
[2]Department of Food Biochemistry and Human Nutrition, Faculty of Chemical Engineering and Food Technology, Nong Lam University, Ho Chi Minh City, Vietnam.
[3] Ho Chi Minh City University of Industry and Trade

Received: 22 October 2025 Accepted: 10 November 2025 Published: 11 November 2025

Corresponding Author: Hong M. X. Nguyen, Department of Food Biochemistry and Human Nutrition, Faculty of Chemical Engineering and Food Technology, Nong Lam University, Ho Chi Minh City, Vietnam.

Abstract

Mold infection and mycotoxin production, driven by fungi such as *Aspergillus*, *Fusarium*, and *Penicillium*, pose significant threats to global food safety, contributing to 25% of crop losses annually [Eskola et al., 2020]. This review synthesizes mathematical modeling approaches—empirical, mechanistic, and artificial intelligence (AI)-based—for predicting mold growth and mycotoxin contamination in food systems. Empirical models, like polynomial regressions, offer simplicity but limited generalizability, while mechanistic models, such as the Baranyi-Roberts framework, provide biological insights yet demand detailed data. AI-driven models, including deep learning, achieve up to 95% predictive accuracy by capturing nonlinear environmental interactions (e.g., temperature, water activity) [Mateo et al., 2021]. Key factors influencing contamination—temperature, moisture, pH, oxygen, and substrate—are analyzed, with AI enhancing real-time risk assessment. Challenges include data scarcity, model interpretability, and high costs, particularly in developing regions like Vietnam. By integrating hybrid AI-mechanistic models and leveraging IoT for real-time monitoring, future strategies can reduce mycotoxin risks, supporting safer storage and sustainable food systems. This review guides researchers and policymakers in advancing predictive tools for food safety management.

Keywords: Artificial Intelligence (AI), Food Safety, Mold Infection, Mycotoxins, Predictive Modeling.

1. Introduction

Mold contamination and mycotoxin production are significant concerns in global food and feed supply chains, particularly in cereal grains and other staple commodities. Molds cause post-harvest losses through spoilage and pose serious health risks due to their ability to produce toxic secondary metabolites known as mycotoxins. These substances are often heat-stable and resistant to conventional food processing and have been linked to a wide range of acute and chronic health issues, including carcinogenicity, immunosuppression, endocrine disruption, and other adverse animal health effects associated with significant economic impacts [1-2] [24].

Fungi such as *Aspergillus*, *Fusarium*, and *Penicillium* are the primary culprits responsible for mold infection and mycotoxin biosynthesis. Their growth and toxin production are influenced by a complex interplay of factors, including temperature, moisture content (water activity), relative humidity, pH, substrate composition, and storage conditions [3-4]. Climate change has further complicated this issue by altering fungal ecology and extending the geographical range of toxigenic species, leading to increased risks in previously less-affected regions [5]. Recent assessments predict that warming climates will increase mycotoxin prevalence in many temperate regions, with shifts in fungal populations and mycotoxin patterns resulting from changing

Citation: Huy L. Nguyen, Janie M. Moore, Binh C. Nguyen, *et al*. Models for Mold Infection and Mycotoxin Production and Influencing Factors: A Review. Research Journal of Food and Nutrition. 2025;8(2):14-25.

climatic conditions. However, impacts will vary by region and are challenging to predict due to complex multi-factor interactions [6] [25].

In response to these challenges, various models have been developed to predict mold growth and assess the risk of mycotoxin contamination. These range from empirical models based on observed data to mechanistic models that simulate underlying biological and environmental processes. More recently, machine learning and AI-driven modeling approaches have emerged, offering powerful tools to handle multidimensional data, uncover non-linear patterns that improve predictive accuracy, and enhance overall mycotoxin management at pre- and post-harvest levels [7-8] [26].

This review provides a comprehensive overview of current modeling approaches for mold infection and mycotoxin production. It explores the strengths and limitations of each modeling category, highlights recent advancements, and identifies gaps in current research. The goal is to guide future efforts in developing robust, reliable, and practical models to support food safety management and post-harvest decision-making.

2. Selected Equations for Qualifying Fungal Growth

Quantifying fungal growth is fundamental for predicting mold behavior in food systems, where proliferation can lead to spoilage and mycotoxin accumulation. Mathematical models provide a structured approach to describe and predict fungal growth under different environmental conditions. Models are classified into primary (time-dependent growth under constant conditions), secondary (environmental effects on growth parameters), and tertiary (integrated tools for practical application).

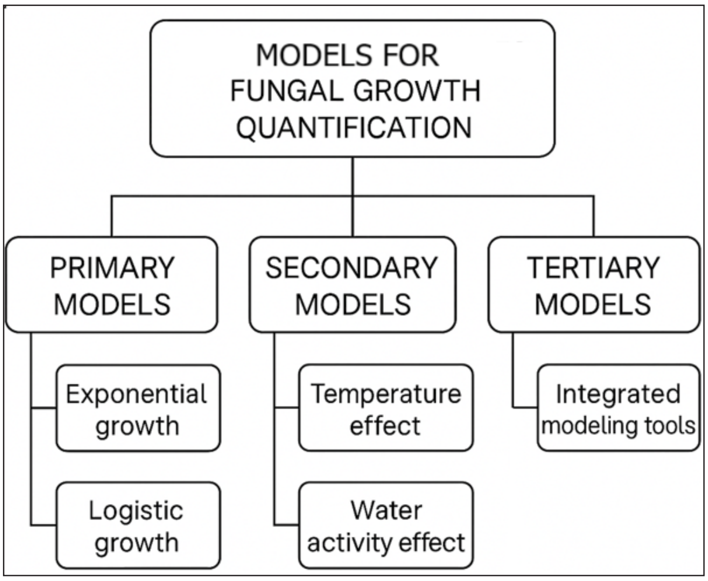

Figure 1. *Conceptual framework used to quantify fungal growth*

Below, key equations, their applications, and limitations, with updates from recent studies, are outlined.

2.1 Primary Models – Describing Growth over Time

Primary models depict the growth of fungal biomass, colony diameter, or toxin levels as a function of time under constant environmental conditions. These models often assume a sigmoidal growth curve composed of lag, exponential, and stationary phases.

2.1.1 Exponential Growth Model

$$N(t) = N_0.e^{\mu t}$$

where N(t) is the fungal population (e.g., CFU, mg biomass, or colony diameter) at time T; N_0 is the initial population; and μ is the specific growth rate. It is used in the early stages of mold growth, limited by the assumption of constant resources.

2.1.2 Logistic Growth Model

The logistic growth model is a foundational equation in population biology. It describes how a microbial or fungal population grows over time when resources are limited. It improves upon the exponential model by incorporating a carrying capacity, which is the maximum population the environment can sustain. This is especially relevant for fungi when nutrients, space, or moisture are depleted or when inhibitory metabolites accumulate. The classical logistic growth equation is written as:

$$N(t) = \frac{K}{1 + \left(\frac{K - N_0}{N_0}\right) e^{-\mu t}}$$

where N(t) is the fungal biomass or colony size at time t; N_0 is the initial population (e.g., spore count or diameter); K is the carrying capacity (maximum attainable size, e.g., colony diameter or biomass); μ is the specific growth rate (h^{-1} or mm/day); and e is Euler's number (2.718).

2.1.3 Modified Gompertz Model

The Gompertz model is a sigmoidal (S-shaped) model initially developed for human mortality statistics but later adapted to describe microbial growth curves, including fungi. Its modified version is widely used in predictive microbiology due to its mathematical flexibility and biological interpretability. The most common form of microbial growth is:

$$\log N(t) = A + D.\exp\left(-\exp\left[\frac{B.e}{D}(M - t) + 1\right]\right)$$

where log N(t) is the log population (or colony diameter) at time t; A is the lower asymptote (initial value); D is the number of log units of growth; B is the relative growth rate at the inflection point; M is the time to reach maximum growth rate (inflection point); and e is Euler's number (2.718). It captures asymmetry in microbial growth, where growth increases quickly then decelerates more slowly.

2.1.4 Baranyi and Roberts Model

The Baranyi and Roberts model is a more mechanistic sigmoidal model. It was built to improve upon the Gompertz and logistic equations by explicitly describing the lag phase as a physiological adaptation process. It is one of the most widely used models in predictive microbiology and food safety modeling. The equation is described as:

$$N(t) = N_0 + \mu_{max}A(t) - \ln\left(1 + \frac{e^{\mu_{max}A(t)} - 1}{e^{N_{max} - N_0}}\right)$$

with the adaptation function:

$$A(t) = t + \frac{1}{\mu_{max}} \ln\left(\frac{e^{-\mu_{max}t} + q_0}{1 + q_0}\right)$$

where N(t) is the log microbial population at time t; N_0 is the initial log population; N_{max} is the maximum population; μ_{max} is the maximum specific growth rate; and q_0 is the physiological state of cells at inoculation.

2.2 Secondary Models – Describing environmental effects

Secondary models explain how ecological parameters affect the growth rate (μ) or other outputs of primary models. They are usually empirical or semi-mechanistic and include temperature, water activity (aw), pH, oxygen, or substrate type functions.

2.2.1 Ratkowsky Square-Root Model (for temperature) (Ratkowsky et al., 1983)

$$\sqrt{\mu} = b(T - T_{min})$$

where T is the environmental temperature; T_{min} refers to the minimum temperature for growth. The model is ideal for sub-optimal temperature ranges.

2.2.2.Cardinal Temperature Model with Inflection (CTMI)

$$\mu(T) = \mu_{opt} \cdot \left(\frac{T - T_{min}}{T_{opt} - T_{min}}\right)^{\alpha} \cdot \left(\frac{T_{max} - T}{T_{max} - T_{opt}}\right)^{\beta}$$

where μ(T) is the specific growth rate at temperature T; μ_{opt} is the maximum growth rate at the optimal temperature; T_{min} is the minimum temperature for growth; T_{opt} is the optimum temperature for growth (where $\mu=\mu_{opt}$; T_{max} is the maximum temperature for growth; α, β are shape parameters that determine the slope before and after the optimum. This model accounts for the asymmetry typically observed in microbial growth: the increase in growth rate from T_{min} to T_{opt} is often more gradual, while the decrease from T_{opt} to T_{max} is steeper due to heat stress and denaturation processes.

2.2.3 Polynomial Models

Polynomial models are commonly used as secondary models in predictive microbiology to describe the nonlinear effects of environmental variables, such as water activity (a_w) and pH, on molds' specific growth rate (μ) or lag phase duration. Unlike more mechanistic models, like Ratkowsky or CTMI models, polynomial equations are typically empirical, meaning they are fit directly to experimental data without assuming specific biological mechanisms.

For a single variable, a second-order polynomial is most often used as:

$$\mu = a_0 + a_1 x + a_2 x^2$$

where μ is the specific growth rate (e.g., mm/day for radial growth or h^{-1} for biomass increase); x is the environmental variable (e.g., a_w or pH); a_0, a_1, a_2 are regression coefficients fitted from experimental data. Applications in the food systems are described in Table 1.

Table 1. *Application of polynomial models in food systems*

Mold Species	Variable	Substrate	Outcome
Aspergillus flavus	a_w	Maize	Defined aflatoxin risk zones
Penicillium expansum	pH	Apples	Modeled the patulin production onset
Fusarium graminearum	a_w	Barley	Fitted growth/no-growth interfaces
Aspergillus ochraceus	pH, a_w	Dry-cured meats	Described the ochratoxin A production

2.3 Tertiary Models – Integrating Models for Practical Use

Tertiary models combine primary and secondary equations into user-accessible platforms. They are embedded in software tools, databases, and decision-support systems that allow users to simulate mold growth under changing environmental conditions.

3. Factors Influencing Mold Infection and Mycotoxin Production

3.1 Temperature

Temperature plays a crucial role in regulating fungal growth and mycotoxin production by influencing biological processes such as enzyme activity and nutrient transport. Each fungal species operates within a specific thermal range defined by minimum, optimum, and maximum temperatures. Various models have been created to quantify how temperature impacts fungal behavior. The Cardinal Temperature Model with Inflection (CTMI), introduced by Rosso et al. (1993) [9], remains a cornerstone in predictive mycology:

$$\mu(T) = \mu_{opt}\left(\frac{T - T_{min}}{T_{opt} - T_{min}}\right)^{\frac{T_{opt}-T_{min}}{T_{max}-T_{min}}} \cdot \left(\frac{T_{max} - T}{T_{max} - T_{opt}}\right)^{\frac{T_{max}-T_{opt}}{T_{opt}-T_{min}}}$$

This model allows for estimating specific growth rate ($\mu(T)$) at any temperature within the permissible range. For conditions where temperatures are suboptimal, the Ratkowsky square-root model (Ratkowsky et al., 1983)[10] is widely used:

$$\sqrt{\mu} = b(T - T_{min})$$

This equation is particularly effective for describing microbial growth between T_{min} and T_{opt}, with b as an empirical constant. Modern applications often couple these secondary models with primary growth equations like the Baranyi and Roberts model[11], integrating both lag and exponential phases. Under dynamic temperature regimes, the Baranyi model adapts well by adjusting the growth rate as a function of time-varying temperature inputs:

$$\frac{dy}{dt} = \mu\big(T(t)\big).y(t)$$

A recent study by Boaventura et al. (2025)[12] investigated *Cordyceps javanica*, revealing optimal growth at 25–30°C and no development at ≥ 33°C, which reinforced and expanded upon these models. Their application of the nonlinear Ratkowsky model [10] confirmed the species' narrow thermal growth window, emphasizing the importance of precision in selecting biological control strains. This highlights how even moderate increases in temperature can impair fungal pathogenicity in ecological systems.

The interplay between temperature and mycotoxin biosynthesis is particularly nuanced. For *Aspergillus flavus*, aflatoxin B1 production peaks around 28–30°C, slightly below the organism's optimal biomass accumulation temperature. Pitt (1993) [13] developed a mechanistic model linking fungal biomass (C_{mold}), toxin concentration (C_{toxin}) through growth rate and toxin yield, accounting for temperature-modulated degradation, and dead cell-mass concentration (C_{dead}) as the concentration of non-viable or lysed fungal biomass in the medium:

$$\frac{dC_{mold}}{dt} = \mu.C - m.C$$

$$\frac{dC_{toxin}}{dt} = Y_p.\mu.C_{mold} - k_d.C_{toxin}.C_{dead}$$

Here, m represents the maintenance rate, Y_p is the toxin yield coefficient, and k_d is the degradation rate, which increases with temperature via an Arrhenius-like relationship. These models have been crucial for understanding how thermal conditions impact food safety, particularly in cereal grains.

More broadly, rising global temperatures are expected to reshape fungal biogeography and pathogenic potential. Casadevall et al. (2019)[14] proposed that *Candida auris*, a multidrug-resistant fungus now found globally, emerged in part due to selective pressure from rising ambient temperatures, allowing it to adapt to mammalian body heat. This hypothesis, if generalized, implies that other fungal species may follow similar thermal adaptation trajectories.

In indoor environments, Rowan et al. (1999)[15] proposed temperature-relative humidity isopleths for fungi like *Stachybotrys chartarum* and *Aspergillus versicolor*, using polynomial surfaces such as:

$$RH = a_1T^3 + a_2T^2 + a_3T + a_4$$

Such models delineate the minimal combinations of RH and temperature that support growth, allowing environmental engineers and storage managers to establish fungal-free thresholds.

In summary, Temperature is a key regulator of fungal growth, virulence, and distribution. Models like CTMI and Ratkowsky are crucial for quantifying growth, while recent studies explore climate-related impacts on fungal ecology. With rising global temperatures, using these models for prediction is vital to protect food safety and public health.

3.2 Water activity (a_w)

Water activity (aw) is a crucial factor affecting mold growth and mycotoxin production, as it indicates the availability of free water for microbial activity. Molds tolerate lower aw than bacteria, enabling growth in drier conditions, though each species has its own optimal range. For example, *Aspergillus flavus* can grow at a_w = 0.80–0.85, but mycotoxin production usually needs aw ≥ 0.90.

Experimental studies have consistently shown that there is a distinct nonlinear relationship between a_w and both fungal growth rate and toxin synthesis. In a classic study by Gibson et al. (1994)[16] , *A. flavus*, *A. parasiticus*, and *A. oryzae* were grown across ten water activity levels ranging from 0.810 to 0.995. Colony diameter was used to assess growth, and a modified Baranyi growth model was applied:

$$y(t) = y_0 + gA(t) - \ln\left(1 + \frac{e^{gA(t)} - 1}{e^{y_{max} - y_0}}\right)$$

where g is the maximum growth rate, y_0 is the initial colony diameter, and A(t) is the adjusted time function incorporating lag and curvature parameters. Their analysis showed a sharp decline in radial growth below 0.90 a_w, confirming that although xerotolerant molds may survive at low a_w, active proliferation and colonization require higher values.

To model this response, a transformed water activity term to stabilize variance was developed:

$$b_w = \ln\left(\frac{1}{1 - a_w}\right)$$

and fitted a quadratic equation:

$$\ln(g) = C_0 + C_1 b_w + C_2 b_w^2$$

This equation allowed the estimation of the optimum a_w for maximum growth rate such as:

$$b_{w,opt} = -\frac{C_1}{2C_2}$$

$$a_{w,opt} = 1 - e^{-b_{w,opt}}$$

In their results, the optimum a_w for *A. flavus* was between 0.98 and 0.99, aligning with peak aflatoxin production ranges reported by other studies[13] [17]. This supports the widely accepted view that toxin production often peaks at slightly lower a_w than required for maximal growth.

Regarding mycotoxin synthesis, water activity modulates fungal biomass accumulation and triggers or represses the biosynthetic pathways of secondary metabolites. Pitt (1993) modeled aflatoxin formation using a yield coefficient-based approach, incorporating a_w-dependent growth and toxin formation:

$$\frac{dC_{toxin}}{dt} = Y_p.\mu(a_w).C - k_d.C_{toxin}.C_{dead}$$

where $\mu(a_w)$ is the specific growth rate at a given water activity, Y_P is a function dependent on environmental conditions. Toxin production declines sharply below a_w = 0.90, even if growth persists, due to downregulating key regulatory genes like *aflR* and *aflD* [18].

Storage fungi such as *Penicillium verrucosum*, which produces ochratoxin A, behave similarly. Through logistic regression that the probability of exceeding the European OTA limit (5 µg/kg) is directly related to both water activity and fungal colony count, using the equation:

$$\ln\left(\frac{P}{1 - P}\right) = c_0 + c_1.logCFU + c_2.a_w + c_3(CFU.a_w)$$

where P is the probability of OTA levels exceeding the threshold. Their results showed that increasing a_w from 0.85 to 0.95 drastically raised the likelihood of OTA accumulation, especially when fungal counts were high.

Water activity (aw) influences both mold infection and the activation of toxin-producing pathways, with the highest risks occurring at aw levels of 0.95–0.99. While fungi can survive at lower aw, higher levels favor infection and mycotoxin production. Therefore, controlling aw is essential in food storage, processing, and indoor air quality management to prevent contamination.

3.3 pH

pH is a critical environmental factor that affects fungal growth, infection ability, and mycotoxin production. It influences key processes like enzyme activity, membrane function, and nutrient availability. Most molds grow best in mildly acidic conditions, typically between pH 4 and 6, though this varies by species and substrate

Numerous studies have shown that fungal pathogens such as *Aspergillus flavus*, *Fusarium verticillioides*, and *Penicillium expansum* exhibit maximum radial growth and biomass accumulation within specific acidic pH ranges [19]. For instance, *A. flavus* generally grows best between pH 4.0 and 6.5, while *P. expansum* exhibits vigorous colonization of apple tissue at pH 3.5–5.5, exploiting the acidic microenvironment of fruit surfaces. Deviations from the optimal pH range lead to decreased enzyme efficiency, protein denaturation, and impaired transport processes, ultimately reducing growth rate and conidial production. In predictive microbiology, the pH effect on growth can be modeled using a quadratic function:

$$f(pH) = 1 - \alpha(pH - pH_{opt})^2$$

where f(pH) is the relative growth factor; α is a coefficient indicating sensitivity to pH deviation; and pH_{opt} is the pH at which the growth rate is maximized.

This model has been used to generate growth isopleths when combined with other variables such as temperature and water activity. For example, *A. flavus* exhibits a clear bell-shaped growth curve across pH values, where both strongly acidic (<3.5) and alkaline (>8.0) environments result in negligible development.

The influence of pH on mycotoxin biosynthesis is not always congruent with its effect on biomass growth. Many fungi demonstrate peak toxin production at slightly different pH values than their optimal for growth. Pitt (1993) proposed that aflatoxin production by *A. flavus* peaks at pH 5.0–6.0, even when maximum growth occurs near pH 6.5. Similar observations have been made for ochratoxin A production by *Penicillium verrucosum*, which is highest between pH 4.5 and 5.5, even when growth continues across a broader pH spectrum.

Mechanistically, pH affects transcriptional regulation of toxin biosynthetic genes. For aflatoxin, the expression of key genes such as *aflR* and *aflS* is upregulated in slightly acidic environments, while alkaline pH leads to suppression. This is linked to global regulatory systems such as the PacC transcription factor, which modulates gene expression in response to extracellular pH. Under acidic conditions, PacC remains inactive, allowing toxin gene expression, whereas under alkaline conditions, PacC is activated and represses aflatoxin biosynthesis genes.

Pitt's model (1993) incorporates the effect of pH as a multiplicative modifier of both growth rate and toxin yield:

$$\mu(pH) = \mu_{max} \cdot f_{pH}$$

$$Y_p(pH) = Y_{p,max} \cdot g_{pH}$$

where f_{pH} and g_{pH} are pH-dependent growth and toxin yield functions, respectively. The relative toxin yield function for aflatoxin B_1 was empirically fitted as:

$$g_{pH} = 1 - 0.1048(pH - 6)^2$$

This function suggests a parabolic decline in yield on either side of the optimum (pH 6), with complete suppression of toxin production at strongly acidic (<3) or basic (>8) conditions.

From an applied perspective, manipulating pH is a proven strategy for fungal and mycotoxin control. The acidification of fruit surfaces (e.g., through lactic or acetic acid treatment) can inhibit *Penicillium* spp. during storage. The alkalization of maize and peanuts, common hosts for *A. flavus*, has also been proposed as a postharvest intervention to suppress aflatoxin formation. Moreover, pH adjustment is crucial in fermented food products, where mold contaminants can be introduced during the aging or ripening stages.

In summary, pH exerts a dual influence on mold infection and mycotoxin production, serving both as a physiological regulator of fungal metabolism and a molecular signal influencing secondary metabolite pathways. While most fungi prefer mildly acidic environments for colonization, toxin production may peak within narrower pH ranges due to transcriptional controls. Understanding and modeling these pH dependencies is essential for designing effective fungal growth control measures in food systems and optimizing risk assessment in storage conditions.

3.4 Oxygen level

Oxygen availability plays a vital role in fungal growth, spore germination, and mycotoxin production. Most filamentous fungi are aerobic and depend on oxygen for energy, but varying oxygen levels can affect colonization and toxin gene expression. Understanding oxygen's impact is crucial for effective storage, packaging, and food safety strategies.

Most molds, including *Aspergillus*, *Penicillium*, and *Fusarium*, rely on aerobic respiration and grow well under normal oxygen levels (~21%). Oxygen limitation, as seen in MAP or vacuum-sealed foods, can significantly reduce fungal growth. Studies show growth declines below 5% O_2 and may stop entirely below 1–2%, especially with high CO_2.

Aspergillus flavus and *Fusarium verticillioides* show reduced growth and spore germination under low or no oxygen conditions due to impaired mitochondrial function and lower ATP production. Some fungi can survive in oxygen-poor environments by switching to fermentation, but this pathway is inefficient. As a result, it rarely supports strong fungal colonization.

Mathematically, the influence of oxygen can be integrated into growth rate models using Michaelis-Menten-type kinetics, where oxygen acts as a limiting substrate:

$$\mu(O_2) = \mu_{max} \cdot \frac{[O_2]}{K_O + [O_2]}$$

where $\mu(O_2)$ is the oxygen-dependent growth rate, μ_{max} is the maximum growth rate under full oxygenation, $[O_2]$ is the oxygen concentration, K_O is the half-saturation constant. This model captures the saturation kinetics of fungal response to oxygen, where growth increases sharply with oxygen up to a plateau beyond which it no longer improves.

Oxygen availability influences mycotoxin production in complex, species-specific ways, often more strongly than it affects growth. For example, *Aspergillus flavus* continues to grow under low oxygen but shows reduced aflatoxin B1 production due to downregulation of key genes like *aflR* and *aflS*. Similarly, *Fusarium graminearum* and *F. verticillioides* reduce trichothecene and fumonisin synthesis under oxygen-limited conditions. *Penicillium verrucosum* also shows a sharp decline in ochratoxin A production when exposed to oxygen levels below 2%.

These observations suggest that mycotoxin biosynthesis is oxygen-sensitive and regulated at transcriptional and enzymatic levels. The likely mechanism involves the activity of oxygen-dependent monooxygenases and oxidoreductases essential in toxin biosynthetic pathways. Aflatoxin B_1 biosynthesis, for example, consists of a cytochrome P450 monooxygenase step that requires molecular oxygen as a substrate.

An empirical representation of the oxygen effect on mycotoxin production rate (R_p) can be modeled as:

$$R_p = R_{max} \cdot \frac{[O_2]}{K_T + [O_2]}$$

where R_{max} is the maximum toxin production rate and K_T oxygen level at which half-maximal toxin synthesis occurs. Technologies like controlled atmosphere storage, nitrogen flushing, and vacuum packaging reduce oxygen levels to suppress fungal growth and mycotoxin production. Lowering oxygen to 1–2% with CO_2 levels of 20–60% effectively limits *A. flavus* and aflatoxin in peanuts and maize. Hermetic storage also creates oxygen-deficient conditions that naturally inhibit spoilage and extend shelf life. Integrating oxygen control into predictive models and storage strategies can greatly reduce contamination risks.

3.5 Nutrient availability

Fungi need balanced nutrients—mainly carbon and nitrogen sources, plus micronutrients like trace metals and vitamins—to support growth and mycotoxin production. Simple sugars such as glucose and fructose promote rapid fungal development, while complex or limited carbon sources slow growth. Nitrogen type also matters; *Fusarium verticillioides*, for example, grows faster and produces more fumonisins with amino acids like glutamate. Modifying nutrient availability is a potential strategy to control mold growth and toxin contamination in food systems.

The Monod equation is commonly used to model microbial growth under nutrient-limited conditions:

$$\mu(S) = \mu_{max} \cdot \frac{S}{K_S + S}$$

where $\mu(S)$ is the specific growth rate at substrate concentration S, μ_{max} is the maximum growth rate under nutrient saturation, K_S is the half-saturation constant (the value of S at which $\mu = 0.5\mu_{max}$).

This model has been used to describe fungal growth on substrates such as grains and syrups, where nutrient diffusion affects colonization. Notably, maximum mycotoxin production often occurs under nutrient-limited conditions rather than peak growth. Nitrogen depletion or C:N imbalance can trigger increased secondary metabolite synthesis. This shift reflects a fungal survival strategy, redirecting energy from growth to defense and competition.

In the model by Pitt (1993) (present in your uploaded document), nutrient limitation is incorporated through a function dependent on mold biomass approaching a carrying capacity:

$$f_{mold} = \frac{K_p}{K_p + C_{mold}}$$

where f_{mold} is a growth-limiting factor that adjusts the effective growth rate based on current mold biomass; K_p is a constant (with units of g/g medium) that reflects the substrate saturation coefficient and represents the level of mold biomass at which the growth rate is half of its maximum due to substrate limitation; and C_{mold} is the concentration of live mold biomass in the substrate (g/g medium). The equation represents a Monod-like saturation curve where substrate availability decreases as the mold population increases. When $C_{mold} \rightarrow C_{max}$, growth slows, but toxin biosynthesis may accelerate, supported by findings that aflatoxin and ochratoxin production is upregulated under stationary phase conditions.

At the molecular level, nutrient availability influences the expression of global regulators such as AreA (nitrogen metabolism) and CreA (carbon catabolite repression), which in turn modulate secondary metabolite gene clusters like the aflatoxin cluster (*aflR, aflS*) or the fumonisin gene cluster (*FUM1–FUM21*). Under nutrient-rich conditions, these regulators may repress toxin biosynthesis, while nutrient scarcity lifts this repression and triggers the activation of biosynthetic genes. For instance, in *Aspergillus flavus*, nitrogen starvation triggers aflatoxin biosynthesis by derepressing *aflR* expression.

Understanding the nutrient-dependent dynamics of fungal growth and toxigenesis is essential in practical food safety management. Postharvest environments rich in broken kernels, sugars, or proteins (e.g., bruised fruits, insect-damaged grains, syrupy residues) provide ideal nutrient-rich zones for fungal colonization. Conversely, drying, cleaning, and removing fines from grain can reduce nutrient availability and lower contamination risk. Fermentation and ripening environments can also be optimized by manipulating the C:N ratio to favor desired molds (e.g., *Penicillium camemberti* in cheese) while suppressing toxin-producing invaders. Furthermore, synthetic growth media in laboratory or industrial fermentation often use precisely adjusted nutrient formulations to study or inhibit mycotoxin biosynthesis.

3.6 Substrate Composition

Substrate composition, including its chemical nutrients (like sugars, proteins, and minerals) and physical traits (such as texture and porosity), plays a key role in mold growth and mycotoxin production. Nutrient quality, complexity, and bioavailability influence fungal adhesion, colonization, and metabolism. Molds favor easily digestible carbon sources, while complex macromolecules may require specific enzymes to utilize. Structural features like porosity and surface roughness affect fungal penetration, oxygen flow, and moisture retention, shaping infection dynamics. Natural substrates with microdamage or rich starch content, like maize or fruit, can significantly increase contamination risk.

Substrate composition affects growth and strongly modulates secondary metabolism, particularly mycotoxin production. Complex or low-nitrogen substrates often lead to increased expression of toxin biosynthetic genes. Pitt (1993) and other researchers observed that aflatoxin production by *A. flavus* was significantly higher on natural substrates like maize and peanut meals than on synthetic media, even when moisture, pH, and temperature were controlled. This indicates that chemical signals from the substrates, such as polyphenols, fatty acids, or stress-inducing compounds, may act as inducers or derepresses of toxin biosynthesis.

The influence of substrate on toxin output can be modeled by introducing a substrate coefficient S_f into generalized toxin yield equations:

$$R_{toxin} = Y_p.\mu.C.S_f$$

where Y_p is the yield coefficient for toxin per unit biomass, μ is the specific growth rate, C is the fungal biomass, and S_f is the substrate-dependent modulation factor (empirically derived).

Even if two substrates support similar fungal growth, their ability to promote toxin production can vary due to differences in metabolite signaling and gene regulation. Substrate composition influences both colonization and mycotoxin synthesis by combining nutritional and structural factors. Effective modeling must consider real-world substrate properties, including temperature, water activity, chemistry, and biochemical signals.

4. Model for Aflatoxin and Fumonisin Production

Aflatoxins and fumonisins are among the most harmful mycotoxins produced by fungi, notably *Aspergillus flavus* and *Fusarium verticillioides*, respectively. These secondary metabolites are potent carcinogens and have severe implications in food safety, trade, and public health. Mathematical modeling of their biosynthesis allows researchers and food safety regulators to predict contamination risk, especially under changing environmental or storage conditions.

The production of aflatoxins and fumonisins is typically linked to the growth kinetics of the producing mold but also exhibits behaviors that are independent of biomass accumulation. Pitt (1993) proposed a mechanistic model where the rate of toxin accumulation is dependent on the live biomass, growth rate, and degradation dynamics. The general form is: $\frac{dC_{toxin}}{dt} = Y_p.\mu.C_{mold} - k_d.C_{toxin}.C_{dead}$

where C_{toxin} is the toxin concentration at time t; Y_p is toxin yield coefficient (affected by environmental conditions); μ is specific growth rate; C_{mold} is Live fungal biomass; C_{dead} is Dead biomass (affects degradation); and k_d is degradation rate constant.

To simulate the effects of the environment, Pitt further multiplied the growth rate and yield by modifiers:

$$\mu = \mu_{opt}.f_T(T).f_{a_w}(a_w).f_{pH}(pH)$$

Garcia et al. (2013) [20] developed a 2D predictive model for aflatoxin B_1 production by *A. flavus* on maize-based media. They incubated the fungus under combinations of temperature (20–40°C) and water activity (0.85–0.99), fitting the aflatoxin data with a response surface model:

$$\ln(AFB_1) = a_0 + a_1T + a_2a_w + a_3T^2 + a_4a_w^2 + a_5T.a_w$$

that represented how temperature and water activity (a_w) affect aflatoxin B_1 (AFB_1) production by *Aspergillus flavus*. Aflatoxins, carcinogenic mycotoxins produced by Aspergillus flavus, pose severe health and economic risks to Texas corn production. Castano-Duque et al. (2025) integrated mechanistic models, including the Aflatoxin Risk Index (ARI) based on temperature and humidity, with machine learning approaches like gradient boosting, neural networks, and random forests. The neural network model excelled, achieving 73% accuracy in forecasting high-risk events, which underscored the complex interactions among soil, weather, and plant health. This result urged Texas growers to adopt targeted mitigation strategies, such as biocontrol and resilient varieties, for sustainable farming. Table 2 describes some prediction models that optimized the conditions and approaches of mycotoxin production by different fungi [27].

Table 2. *Mycotoxin Production by Fungi with optimal conditions and modeling approaches*

Toxin	Fungus	Optimal Conditions	Model Type Used
Aflatoxin B_1	*Aspergillus flavus*	30-33°C; $a_w > 0.97$	Polynomial and Cardinal Temperature
Fumonisin B_1	*Fusarium verticillioides*	25-30°C; $a_w = 0.95 – 0.98$	Polynomial and Time-dependent kinetic
Ochratoxin A	*Penicillium verrucosum*	20°C; $a_w = 0.98$	Logistic regression
Aflatoxin	*A. flavus*	Variable climate	ML and Mechanistic

Ochratoxin A (OTA) by *P. verrucosum* in stored grains is another well-studied scenario. OTA models often use logistic regression to predict whether contamination exceeds legal limits based on temperature and moisture, focusing on binary risk outcomes. In contrast, aflatoxin and fumonisin models use continuous outputs and have shown reliable predictions when validated in field and storage conditions [21-22]. *Fumonisin* models are used in some countries to anticipate when the Fusarium ear rot might lead to high fumonisins, informing timely harvests or the use of fungicides. The integration of mechanistic and empirical models (like using mechanistic models to generate data for empirical surface fits) has improved robustness.

In conclusion, various modeling approaches effectively capture the dynamics of mycotoxin production. Mechanistic models offer detailed insights and are useful for complex scenarios, while empirical models are simpler and more accessible for stakeholders. Both approaches agree on key trends: aflatoxin B1 thrives in hot, humid conditions; fumonisin favors cooler, moist environments; and ochratoxin A is linked to cold, damp storage. These models turn observations into quantitative tools that support informed mycotoxin management decisions.

5. Further Research

Looking ahead, there are several promising directions to advance the modeling of mold infection and mycotoxin production, driven by technological innovations and an increasing recognition of the complexity of real-world systems.

5.1 Integration of AI with Mechanistic Models (Hybrid Modeling)

A promising direction is to integrate mechanistic modeling with machine learning to leverage the strengths of both. Mechanistic models can generate synthetic data for training ML models, enabling fast and accurate predictions across diverse scenarios. In turn, ML can refine mechanistic models by analyzing large datasets to improve parameter estimation or model structure. These hybrid approaches, though still emerging, offer strong potential for creating robust and interpretable predictions, such as ensuring that zero growth aligns with zero toxin production.

5.2 Climate-based forecasting and Early warning systems

As climate variability grows, future research aims to develop real-time forecasting models that link weather data with mycotoxin risk. Recent efforts in Europe combine satellite sensing of crop stress with predictive tools to map toxin risks across entire regions [6]. Machine learning can enhance these systems by continuously learning from new climate and contamination data, improving accuracy each season. In the coming decade, more early warning systems are expected, especially in vulnerable regions like Sub-Saharan Africa and Southeast Asia. Future models must also address extreme weather and simulate climate scenarios to guide policy and risk management [5][23].

5.3 Real-Time Sensing and Internet of Things (IoT)

An emerging area is combining predictive models with real-time sensing technologies. Modern sensors can monitor conditions like temperature, humidity, and CO_2 in silos, while optical tools detect early fungal signs. Integrating these data streams enables dynamic risk assessment, with AI models offering timely alerts and recommendations. This paves the way for smart storage systems that adapt management in real time to prevent contamination.

5.4 Improved Model Validation and Interdisciplinary Collaboration

Future research should prioritize validating models under real-world conditions through field trials and interdisciplinary collaboration. Teams of microbiologists, food technologists, and data scientists can design experiments that test key model assumptions. Integrating One Health perspectives is essential, as mycotoxin risks span agriculture, environment, and human health. Comprehensive models could link contamination predictions to dietary exposure and guide both prevention and post-harvest mitigation strategies.

Table 3. *Future Research Directions in Modeling of Mold Infection and Mycotoxin Production*

Focus Area	Research Objective	Opportunities / Advantages	Challenges / Limitations	References
Integration of AI with Mechanistic Models (Hybrid Modeling)	Combine mechanistic understanding with machine learning to improve prediction accuracy and interpretability.	Generates synthetic training data; enhances prediction under variable conditions.	Requires interdisciplinary expertise and large datasets.	Focker et al., 2025 [26]
Climate-Based Forecasting and Early Warning Systems	Link climatic and satellite data with fungal/toxin risk models.	Enables proactive monitoring at regional and global scales.	Uncertainty from climate variability; limited regional data.	Battilani et al., 2016 [5]; Kos et al., 2024 [6]
Real-Time Sensing and IoT Integration	Use sensors to monitor temperature, humidity, CO_2, and optical fungal markers.	Provides dynamic, real-time contamination alerts.	Sensor cost, calibration, and data integration.	Mateo et al., 2021 [7]; Tarazona et al., 2021 [8]
Model Validation and Interdisciplinary Collaboration	Conduct field-scale validation and integrate One Health perspectives.	Improves model reliability and cross-sector adoption.	Expensive and time-intensive field testing.	Garcia et al., 2009 [20]
Multi-Toxin and Multi-Species Modeling	Develop models capturing interactions among multiple fungi/toxins (*A. flavus* and *F. verticillioides*).	Reflects realistic storage/field ecosystems.	Complex parameterization with competition modeling.	Castano-Duque et al., 2025 [27]
Stress Factor and Environmental Dynamics Modeling	Examine effects of CO_2, UV, and fluctuating humidity/temperature.	Extends models to real-world stress cycles.	Limited experimental data and standardization.	Casu et al., 2024 [25]
User-Friendly Platforms and Big-Data Analytics	Deploy predictive dashboards, mobile apps, and cloud-based systems.	Broad accessibility for policymakers and farmers.	Data security, interoperability, and maintenance.	Focker et al., 2025 [26]; Goda et al., 2025 [24]

5.5 Model Expansion to Multi-Toxin and Multi-Spaces Scenarios

Many models focus on a single fungus–toxin scenario. Future models will address multiple fungi and toxins concurrently, reflecting reality where several species coexist. For example, *A. flavus* (aflatoxin), *F. verticillioides* (fumonisin), and *Penicillium* spp are stored in a stored corn ecosystem. (ochratoxin) might all be potential players. Mechanistic interspecific models might use competition terms, such as Lotka–Volterra equations in ecology, to predict which fungus will prevail under what conditions. This is a challenging area, but very relevant to holistic risk assessment.

5.6. Enhanced Validation and Refinement of Stress Factor Models

Some environmental factors remain underexplored in modeling, such as elevated CO_2 levels or UV exposure affecting surface contamination. Fluctuating conditions like wet-dry cycles or temperature swings may influence toxin production more than constant environments. Future research should replicate these dynamics to develop models that reflect real-world variability.

5.7 User-friendly model deployment and big data analytics

A key direction for future research is making models accessible through user-friendly platforms and harnessing big data. Cloud computing enables the use of massive datasets, like decades of weather and mycotoxin records, for AI-driven pattern detection. Open databases of mold and toxin data could support transparency and crowd-sourced model refinement. Practical deployment may include mobile apps or web dashboards that provide real-time risk scores using satellite, weather, and historical inputs. The goal is to build predictive, adaptive systems that guide interventions and enhance food safety through interdisciplinary collaboration and real-world usability.

6. Conclusions

Predictive modeling of mold growth and mycotoxin production has evolved into a multidisciplinary field, integrating empirical, mechanistic, and AI-based approaches to address food safety challenges. Empirical models, such as polynomial regressions and response surface methods, provide simplicity and accessibility, making them practical for specific, well-defined conditions. Mechanistic models, grounded in biological principles, offer deeper insights into fungal dynamics and enable predictions beyond experimental data, though they require detailed input parameters. AI-driven models, leveraging machine learning and deep learning, excel in capturing complex, nonlinear interactions among environmental factors like temperature, water activity, and pH, achieving high predictive accuracy. However, each approach has limitations: empirical models lack generalizability, mechanistic models demand extensive data, and AI models face challenges with interpretability and data availability, particularly in resource-constrained regions. Despite these challenges, predictive models are critical tools for designing safer storage systems, optimizing post-harvest management, and reducing mycotoxin risks. They support climate adaptation strategies by informing crop development, harvest timing, and risk mitigation under changing environmental conditions. Hybrid models combining AI with mechanistic frameworks show promise for balancing accuracy and interpretability, while real-time IoT integration enhances their practical utility. Ongoing research is needed to address data scarcity, improve model validation under real-world conditions, and expand models to account for multi-fungal and multi-toxin interactions. By fostering interdisciplinary collaboration and leveraging technological advancements, predictive modeling will continue to enhance food safety, ensuring sustainable and resilient global food systems.

7. References

1. M. Eskola, G. Kos, C. T. Elliott, J. Hajšlová, S. Mayar, and R. Krska, “Worldwide contamination of food-crops with mycotoxins: Validity of the widely cited ‘FAO estimate’ of 25%,” 2020. doi: 10.1080/10408398.2019.1658570.
2. R. L. Latham, J. T. Boyle, A. Barbano, W. G. Loveman, and N. A. Brown, “Diverse mycotoxin threats to safe food and feed cereals,” 2023. doi: 10.1042/EBC20220221.
3. M. Mannaa and K. D. Kim, “Influence of temperature and water activity on deleterious fungi and mycotoxin production during grain storage,” 2017. doi: 10.5941/MYCO.2017.45.4.240.
4. J. Yu, M. Yang, J. Han, and X. Pang, “Fungal and mycotoxin occurrence, affecting factors, and prevention in herbal medicines: a review,” 2022. doi: 10.1080/15569543.2021.1925696.
5. P. Battilani *et al.*, “Aflatoxin B 1 contamination in maize in Europe increases due to climate change,” *Sci. Rep.*, vol. 6, no. March, pp. 1–7, 2016, doi: 10.1038/srep24328.
6. J. Kos *et al.*, “Climate Change and Mycotoxins Trends in Serbia and Croatia: A 15-Year Review,” *Foods*, vol. 13, no. 9, pp. 1–32, 2024, doi: 10.3390/foods13091391.
7. E. M. Mateo, J. V. Gómez, A. Tarazona, M. Á. García-Esparza, and F. Mateo, “Comparative analysis of machine learning methods to predict growth of f. Sporotrichioides and production of t-2 and ht-2 toxins in treatments with ethylene-vinyl alcohol films containing pure components of essential oils,” *Toxins (Basel).*, vol. 13, no. 8, 2021, doi: 10.3390/toxins13080545.
8. [8] A. Tarazona, E. M. Mateo, J. V. Gómez, D. Romera, and F. Mateo, “Potential use of machine learning methods in assessment of Fusarium culmorum and Fusarium proliferatum growth and mycotoxin production in treatments with antifungal agents,”

Fungal Biol., vol. 125, no. 2, 2021, doi: 10.1016/j.funbio.2019.11.006.

9. L. Rosso, J. R. Lobry, and J. P. Flandrois, "An Unexpected Correlation between Cardinal Temperatures of Microbial Growth Highlighted by a New Model," *J. Theor. Biol.*, vol. 162, no. 4, 1993, doi: 10.1006/jtbi.1993.1099.
10. D. A. Ratkowsky, R. K. Lowry, T. A. McMeekin, A. N. Stokes, and R. E. Chandler, "Model for bacterial culture growth rate throughout the entire biokinetic temperature range," *J. Bacteriol.*, vol. 154, no. 3, 1983, doi: 10.1128/jb.154.3.1222-1226.1983.
11. J. Baranyi and T. A. Roberts, "A dynamic approach to predicting bacterial growth in food," *Int. J. Food Microbiol.*, vol. 23, no. 3–4, 1994, doi: 10.1016/0168-1605(94)90157-0.
12. H. A. Boaventura *et al.*, "Temperature-Dependent Modeling and Spatial Predictions for Identifying Geographical Areas in Brazil Suitable for the Use of Cordyceps javanica in Whitefly Control," *J. Fungi*, vol. 11, no. 2, 2025, doi: 10.3390/jof11020125.
13. R. E. Pitt, "A Descriptive Model of Mold Growth and Aflatoxin Formation as Affected by Environmental Conditions," *J. Food Prot.*, vol. 56, no. 2, 1993, doi: 10.4315/0362-028x-56.2.139.
14. A. Casadevall, D. P. Kontoyiannis, and V. Robert, "On the emergence of candida auris: climate change, azoles, swamps, and birds," *MBio*, vol. 10, no. 4, 2019, doi: 10.1128/mBio.01397-19.
15. N. J. Rowan, C. M. Johnstone, R. C. McLean, J. G. Anderson, and J. A. Clarke, "Prediction of toxigenic fungal growth in buildings by using a novel modelling system," *Appl. Environ. Microbiol.*, vol. 65, no. 11, 1999, doi: 10.1128/aem.65.11.4814-4821.1999.
16. A. M. Gibson, J. Baranyi, J. I. Pitt, M. J. Eyles, and T. A. Roberts, "Predicting fungal growth: the effect of water activity on Aspergillus flavus and related species," *Int. J. Food Microbiol.*, vol. 23, no. 3–4, 1994, doi: 10.1016/0168-1605(94)90167-8.
17. S. Marín, C. Colom, V. Sanchis, and A. J. Ramos, "Modelling of growth of aflatoxigenic A. flavus isolates from red chilli powder as a function of water availability," *Int. J. Food Microbiol.*, vol. 128, no. 3, 2009, doi: 10.1016/j.ijfoodmicro.2008.10.020.
18. M. Schmidt-Heydt, A. Abdel-Hadi, N. Magan, and R. Geisen, "Complex regulation of the aflatoxin biosynthesis gene cluster of Aspergillus flavus in relation to various combinations of water activity and temperature," *Int. J. Food Microbiol.*, vol. 135, no. 3, 2009, doi: 10.1016/j.ijfoodmicro.2009.07.026.
19. C. K. Jimdjio *et al.*, "Effect of ambient ph on growth, pathogenicity, and patulin production of penicillium expansum," *Toxins (Basel).*, vol. 13, no. 8, 2021, doi: 10.3390/toxins13080550.
20. D. Garcia, A. J. Ramos, V. Sanchis, and S. Marín, "Predicting mycotoxins in foods: A review," 2009. doi: 10.1016/j.fm.2009.05.014.
21. B. Keller *et al.*, "The potential for aflatoxin predictive risk modelling in sub-Saharan Africa: a review," 2022. doi: 10.3920/WMJ2021.2683.
22. L. Castano-Duque *et al.*, "Prediction of aflatoxin contamination outbreaks in Texas corn using mechanistic and machine learning models," *Front. Microbiol.*, vol. 16, no. March, 2025, doi: 10.3389/fmicb.2025.1528997.
23. J. Pleadin, M. Zadravec, D. Brnić, I. Perković, M. Škrivanko, and D. Kovačević, "Moulds and mycotoxins detected in the regional speciality fermented sausage 'slavonski kulen' during a 1-year production period," *Food Addit. Contam. - Part A Chem. Anal. Control. Expo. Risk Assess.*, vol. 34, no. 2, 2017, doi: 10.1080/19440049.2016.1266395.
24. Goda, A.A., Shi, J., Xu, J., Liu, X., Zhou, Y., Xiao, L., Abdel-Galil, M., Salem, S.H., Ayad, E.G., Deabes, M., Pooe, O., Abou Donia, M.A., Abou-Arab, A.A.K., & Ramzy, S. (2025). Global health and economic impacts of mycotoxins: a comprehensive review. *Environmental Sciences Europe*, 37, 122. doi: 10.1186/s12302-025-01166-x.
25. Casu, A., Leggieri, M.C., Toscano, P., & Battilani, P. (2024). Changing climate, shifting mycotoxins: A comprehensive review of climate change impact on mycotoxin contamination. *Comprehensive Reviews in Food Science and Food Safety*, 23, 2, e13323. doi: 10.1111/1541-4337.13323.
26. Focker, M., Liu, C., Wang, X., & van der Fels-Klerx, H.J. (2025). The use of artificial intelligence to improve mycotoxin management: a review. *Mycotoxin Res*. doi: 10.1007/s12550-025-00602-4.
27. Castano-Duque, L., Avila, A., Mack, B.M., Winzeler, H.E., Blackstock, J.M., Lebar, M.D., Moore, G.G., Owens, P.R., Mehl, H.L., Su, J., Lindsay, J., & Rajasekaran, K. (2025). Prediction of aflatoxin contamination outbreaks in Texas corn using mechanistic and machine learning models. *Front. Microbiol.*, 16, 1528997. doi: 10.3389/fmicb.2025.1528997.