

Research Article

Development of the Air Flow and Biological Model for a Hospital for the Protection of Immune Compromised Patients

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Abstract

The purpose of this paper is to outline the theoretical development of an air flow and biological control model for a new hospital. Immune compromised patients represent an increasing subset of patients in major hospitals. These patients require intensive treatment and a relatively clean living space in a hospital whether old or new. Fungal spores that enter the clean living space increase the risk of fungal infections for the immune compromised patients. Fungal infections present a significant risk of premature death to the patients. The initial development of a new air flow and biological control model concentrates on the movement of fungal spores, although other contamination sources can be added to the model. The model has a number of significant constraints in algorithmic and computational terms, which are considered in the paper. The results discuss methods to overcome the computational and algorithmic problems in developing a combined air flow and biological control model for a hospital. A simple model can begin to track the incidence of fungal records and fungal infections, and compare the measured fungal spores against a model estimate. The model then provides a data stream for the hospital staff to prioritize interventions in the hospital operational procedures to reduce the level of fungal spores in clean living spaces and potentially reduce mortality rates for immune compromised patients.

Our early research work on fungal spore movement concentrated on the movement of dust from construction sites at existing hospitals. This dust has been shown, by others, to increase the mortality rate from fungal infections. However, research work on the dust issue has shown that a broader category of problem exists, in which dust generation and movement is merely one component.

A ten year study of deaths from fungal infections in a French hospital, by others, clearly illustrates the infection problems facing immune compromised patients who are exposed to fungal spores. A straightforward statistical analysis of the French data, by the author, showed a two month peak in the mortality data for the French hospital that had not previously been identified. This mortality peak is considered to be a result of poor air conditioning maintenance methods, providing a known entry path through the HVAC system that should be controlled.

The current research interest lies in all of the movement paths for fungal spores from the outside world to the clean living spaces. Two movement paths fetch fungal spores into hospitals, the first is the air stream and the second is the human and goods stream. These two flow streams both intersect and may combine to introduce fungal spores into a clean living space. Any numerical model that allows for the two streams will by nature be complex in design and difficult to calibrate, but even a simple model may provide hospital staff with a clearer idea of the combined movement mechanisms for fungal spores and allow methods to be considered to deal with these fungal spores and the reduce the infection rates.

ABBREVIATIONS

FFT: Fast Fourier Transform; OSH: Outside A Hospital; ICO: Infection Control Officer; PM: Project Manager; WCH: Watkins, Carter, Hamilton Architects of Houston; K_t is the product of the Boltzmann constant, k , and the absolute temperature; T : Almost Periodic Function; TB: Tuberculosis; CFD: Computational Fluid Dynamics

INTRODUCTION

Two movement paths fetch fungal spores into hospitals, the first is the air stream and the second is the human and goods stream, assuming the water and gas streams are never contaminated. These two streams intersect, mingle and carry fungal spores into clean living spaces. This paper addresses the conceptual issues in the development of a computational model

that can conceptualize the two streams as a single model and estimate the fungal spore concentrations in the clean living spaces and elsewhere in the hospital. A new hospital development will be used as the example for the development of the model. This paper does not consider the issue of hospital extension that will be the subject of a future paper [1], provide a reasonable view on how the built environment affects patients' medical outcomes. Everything has to come from outside the hospital, OSH, for the development of a new hospital. The model will start from the OSH using this as a source and sink in the traditional modelling sense. Everything within the building fabric of the hospital is made in a manufactured environment and assembled by hand on site by a construction team. It is thus possible to develop a modelling system that allows for the construction and then operation of the hospital, although it will be by nature a complex model. The literature review suggests that key elements of this work are still

missing, [2], are quite specific on this point.

Figure (1) shows the bridge problem of Königsberg [18], that Euler considered in 1736 to develop graph theory as a mathematical tool. Significant advances have been made in graph theory since 1736 and the tool underlies many of the major engineering advances of the last two centuries including circuit theory, water distribution analysis and kinematic catchment models [3]. Graph theory provides the underpinning to the current development of the air flow and biological control model for a hospital. The system is designed ultimately to provide a method to assist in infection control.

A hospital can be viewed in the algorithmic modelling sense as a collection of patient and other rooms, and each room can be treated as a node point. A node point can also be a corridor, an operating theater, a kitchen and so on. Rubin and Owens show two figures representing typical rooms in a hospital. Figure (2) shows a critical care room incorporating environmental strategies to promote a quiet place to recover. The drawing was prepared by Watkins, Carter, Hamilton Architects of Houston. Figure (3) shows an operating room incorporating environmental strategies for providing music during surgery also by WCH. These figures show the spaces can be modeled as nodes in the hospital system. A set of links connects each node to create a graph. The graph forms the basis of the conceptual model for the hospital air flow and biological control model.

The paper presents the materials and methods for the study. The key methods are space syntax modelling, air flow, fungal transport and model development. The next stage presents the results and discussion that centers on the implementation of the system and the conclusions summarize the development of the system.

MATERIALS AND METHODS

This section of the paper outlines the theoretical development of the model and the application of the model to a modern hospital. The key objective of the work is to develop an algorithm to model risk to immune compromised patients who are resident in a new hospital. In reality the model will allow ultimately the IFC to address most infectious and contaminating agents in the air and human/goods movement stream.

Each network, as for the Königsberg Bridge problem, has a particular topology. Each hospital will have a different topology, except for a few special cases, such as the standard Australian Army hospital developed during WWII for use in the islands.

The topological layout of hospitals has been the subject of intense study as improved health and operating cost outcomes are sought by the community interested in medical care [1]. The point of interest from this research is not the patient outcomes, but the configuration of rooms and hall ways for a modern hospital, so that a complex movement model can address the vexing issue of fungal infections of immune compromised patients, although ultimately the model can address other contaminate sources [4], demonstrates the use of space syntax in describing the topology of a 1921 house. He shows human and room connectedness to the OSH for the house to provide a view as to the social interaction and human movement. In a topological sense [5], demonstrate the development of the root node concept and the tree diagram



Figure 1 Euler's Königsberg graph theory problem from (Wikipedia contributors. 2016). This theory provides the basis for all network modelling methods used air flow handling, water supply and traffic systems.

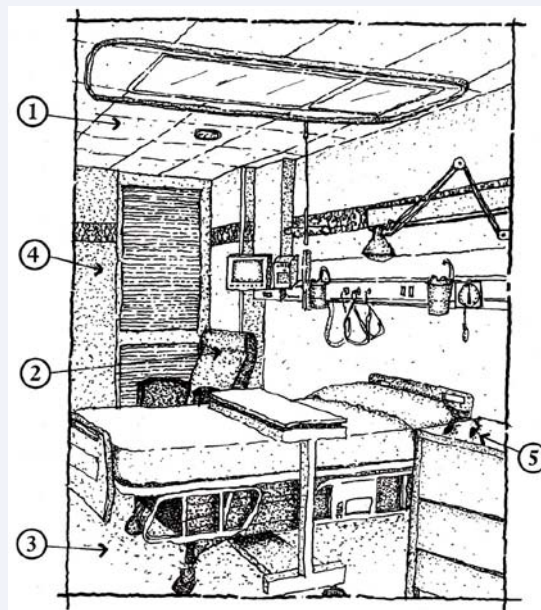


Figure 2 Critical care room incorporating environmental strategies to promote quiet (courtesy Watkins, Carter, Hamilton Architects). This type of room represents a node in a model of the air and good movement system, in reality it is likely a terminal node in the system.

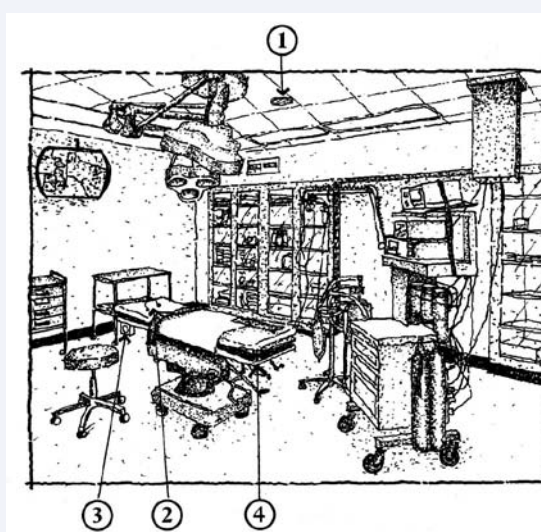


Figure 3 An operating room incorporating environmental strategies for providing music during surgery (courtesy Watkins, Carter, Hamilton Architects). This room is not likely to be a terminal node as patients move in and out of this node in a consistent stream.

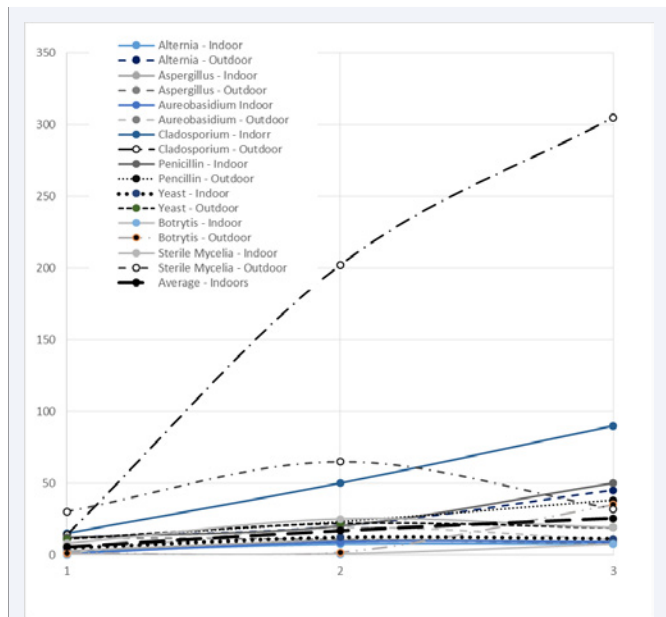


Figure 4 Winter (1), Spring (2) and Autumn (3) concentrations in CFU/m³ for indoor and outdoor air quality adapted from Salonen, Duchaine et al. (2015). The data shows the seasonal variation in fungal colony forming units for particular climate zones, it is informative rather than definitive.

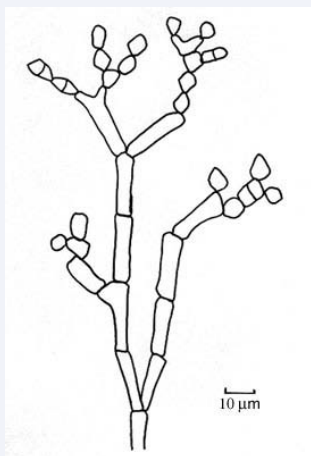


Figure 5 *Cladosporium* spp. Courtesy of Sydney University (2016). The sketch shows the small scale of the fungi.

for a network. They show the development of the mathematical model that underlies such a system and how to execute the model in LISP. The conceptual methods used for space syntax will be applied to this hospital air flow and biological contamination model to create the complex flow patterns in a form that can be represented in a mathematical model.

This research work establishes the broad configuration of an air flow and contamination model for fungi. A formal computer model represents a significant research undertaking past the intent of this paper.

RESULTS AND DISCUSSION

This section outlines the conceptual ideas required for the

development of an air flow and contamination model program for fungi and other contaminants. The key tools are the graph theory to study the topology of the hospital, a contamination model, a movement model and an air flow model. The interesting challenge is the overall model calibration given the significant number of variables, although the work of [6], provide clear guidance in this matter.

Model development flows from using the mathematical technique of starting from a single entity; let us define a node N_i as a patient's room in a hospital. Figure (2) shows a somewhat typical room, which is defined as a node, N_{100} . A group of nodes

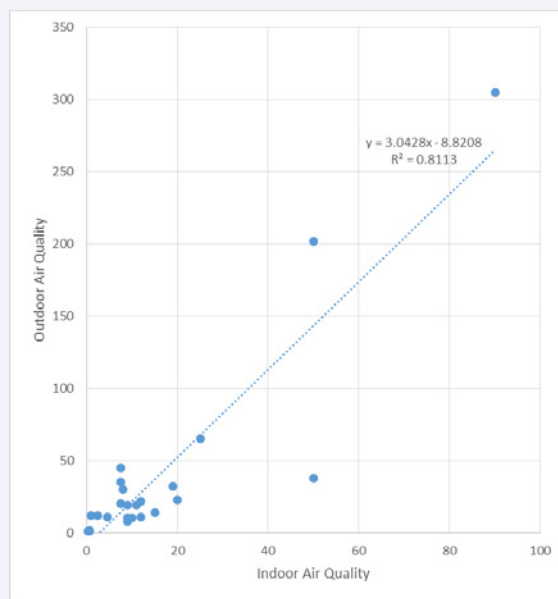


Figure 6 Plot of the ratio of Outdoor Air Concentrations to Indoor Air Concentrations for all samples. A linear regression curve shows a reasonable but not brilliant relationship between the indoor to outdoor air quality, given the likely fall in concentrations as one moves away from windows and doors the test data is controlled by the relative test locations.

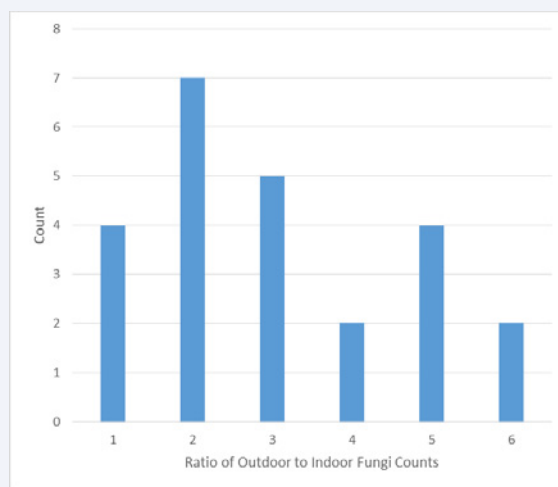


Figure 7 *Cladosporium* spp. Courtesy of Sydney University (2016).

comprises a ward. We define a ward as $W = \sum_{i=1}^n N_i$. In reality,

a set of rooms in a ward is connected with a corridor or wide hallway. The corridor C_k forms part of the ward so that now

$W = \sum_{i=1}^n N_i + C$. There are the ancillary rooms, A_j , so that the

result is $W_k = \sum_{i=1}^n N_i + C_k + \sum_{j=1}^m A_j$.

A hospital is collection of wards, $H = \sum_{k=1}^p W_k$, with additional

ancillary rooms that serve all wards, such as the kitchen, morgue and so on, defined as major corridors, MC_l , ancillary rooms, AR_g , and external door, D_f so that

$$H = \sum_{k=1}^p W_k + \sum_{l=1}^q MC_l + \sum_{g=1}^r AR_g + \sum_{f=1}^t D_f$$

* MERGEFORMAT (1)

This system describes a network, although the network is a partial network at this stage.

The root node is the OSH and the exterior as described by Glowacki. In a water distribution network it represents the water supply source, although in this case the root node is the outside air space. Water distribution networks have a distinct advantage in that water elevations are simple to measure and observe, air pressure is significantly more difficult to measure and observe [7]. Defines the **OSH** pressure as P_o and for this paper assumes the **OSH** air velocity is zero. A zero air velocity implies that Brownian motion dominates the air and contaminate movement [8]. There are specific reasons to start with this assumption and relax it in future work.

A reviewer asked for comment on the assumption of zero air velocity. Wind velocity is a Gumbel distribution. This distribution is dominated by low wind velocities, except in a few distinct and usually non-inhabited regions. Most US and European hospitals have controlled access doors so that the inflow of air from wind driven events is likely to be difficult to assess until this matter has been researched. However, the reviewer's point is taken and the model should include an anemometer and a wind direction vane coupled to measurements of the door open events to provide a differential inflow depending on wind speed and direction [9]. Demonstrate the form of a biological control model for a French hospital used as a coarse indicator of infection. Their original work clearly identified peak frequencies in the data stream, but the author, using a technique developed by [10], showed the existence of a two month peak that is most likely human rather than weather related.

The development of a model requires calibration for the movement of particles both air and contaminates. The fungal data from the [2], has been statistically analyzed to allow for the conceptual development of the biological model to accompany

the air flow model [2]. Completed a review of the airborne viable fungi in school environments for a set of distinct climatic regions. The data from the numerous papers referenced by [2], includes data for winter, spring and autumn for a single climatic region, in this case from a continental climate area. This data shows the type of information available for the **OSH** area, which will provide the baseline data for the model. As an example, Figure (4) shows the data for the concentrations of eight common fungal types for indoor and outdoor air quality for winter (1), Spring (2) and autumn (3) [2]. Note that the *Cladosporium spp.* Have the greatest concentrations for these sets of measurements with a peak of approximately 300 cfu/m³. This is a common fungi type both out and indoors.

Figure (5) shows a line drawing with dimensions for the *Cladosporium* species. The spore size will be less than 10 μm . This size of particle settles slowly and is affected by Brownian motion.

Figure (6) shows the plot of the indoor to outdoor concentrations for the three seasons, Winter, Spring and Autumn for the eight fungal types for a single climate type. A linear regression curve is fitted to the data on Figure (6). The ratio of outdoor concentrations to indoor concentrations has an average slope on the linear regression curve of 3 ± 0.3 with a $[P < 0.05]$. As a secondary statistical check a histogram for the relative ratio between the outdoor and indoor air quality is shown in Figure (7). The rather interesting results show a two mode distribution, which suggests that different fungi have different movement patterns and models. The biological model for the fungal movement can in the early air flow model be a simple concentration model. This type of model is typical in water distribution systems.

A simple space syntax model can be established, Figure (8a) shows a simple network, representative of a small country hospital. The network has a root node [0.1], where [a.b] means node level a and b is the node number at that level. The node level depth is 9. The breadth is five, the model is reasonably representative of a small hospital. It is anticipated that the likely spore concentrations will depend to some extent on the node level, so the root node [0.1] will likely have higher concentrations

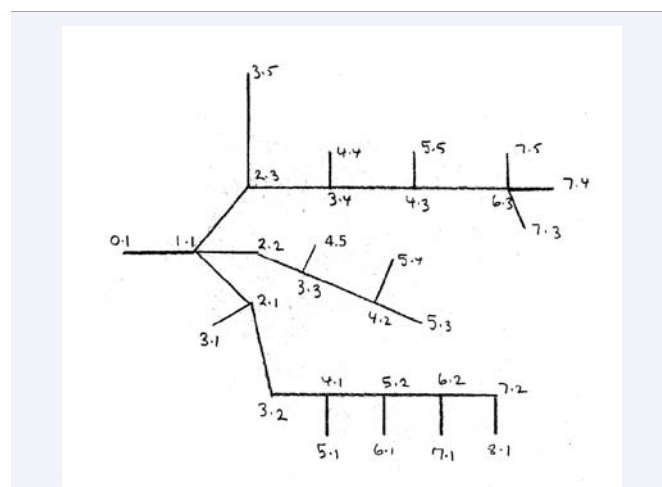


Figure 8 Simple Hospital Network of Corridors and Rooms.

of spores than say node [4.5].

Figure (9) shows the node density or count at each node level. Figure (9) is a critical figure in understanding the very real network problems in developing an air handling system. The system has a major objective of reducing the incidence of fungal infections for immune compromised patients and other infections that will infect normal patients.

The air handling system designer is trying to ensure that that flows follow a fairly standard pattern and the amount of direct **OHS** air is limited in immune compromised patient areas. The node density and depth introduces problems with the air flow caused by cross flows between spaces and potential contamination movement in the cross flows [11]. Provides excellent recommendations for the conceptual design of this type of system. However, there are physical and engineering constraints that exist that limit the ability of any designed system to meet the objective of providing clean air to all immune compromised patients. An understanding is required of these limitations and allowance made for them in developing a set of guidelines for the design of a hospital HVAC system and for the development of the airflow and biological contamination model.

The first limitation is Brownian motion [12]. Shows how this motion can move even items that are many times larger than fungal size. This flows from the fundamental laws of thermodynamics that higher pressures will always seek to flow to areas of lower pressures or concentrations, so that a concentration of fungal spores at say 300 cfu/m³ at node [0.1] and of say 30 cfu/m³ at node [8.1], will result in a movement in spores from [0.1] to [8.1] purely by Brownian motion, even if the nominal air flow is from [8.1] → [0.1] Kappler clearly showed at the macroscopic scale that this due to a Gaussian variation in **kT** with time. Even uniform pressures, where there are differential concentrations of some media, such as fungal spores, will move out to achieve a “uniform” distribution given enough time. In real terms, if a two cubic meter space exists and two fungi spores are released into one side, call it side A, then given sufficient time, the fungi will spend 50% of their time on each side, assuming that

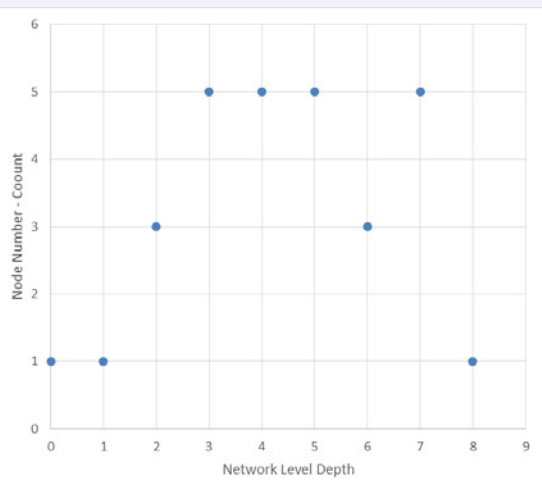


Figure 9 Network Node Density.

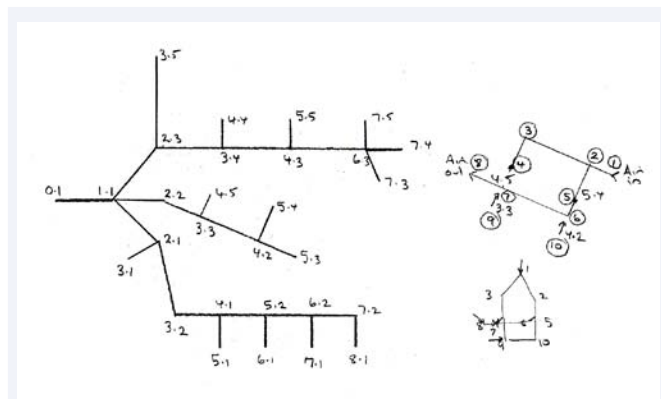


Figure 10 Simple Network Model.

each side has the same probability then one can expect, as for any random game, that 50% of the time the two spores are in different sides, 25% of the time in Side A only and 25% of the time in Side B only. If there are 10 particles then 0.1% of the time theoretically all will be on the same side.

In terms of the biological model the essential element is the transfer function from the **OHS** to the inside, Figure 7 shows that this range from 1 to 7 for a school building in a continental climate, unfortunately this type of data is scarce and to a large extent are site, season and fungal type specific. The measurement of this ratio and the daily variation in this ratio, due to heat, wind and rain is an early critical step in the model development.

The second limitation is the transfer of fungi from the **OHS** to the inside by humans and not as an airborne infection. Human transport is a much smaller cohort than the air mass, but it much harder to assess. One aspect of construction dust may not necessarily be the transport through the air [13], showed how easy it is to stop if filtered properly, but pedestrian foot traffic can move dust particles a long distance in a short time. The movement of spores with humans is not likely to be periodic, humans are not periodic. The application of almost periodic functions provides a starting point that is less constrained than periodic function analysis.

Let us assume that three almost periodic functions exist [14], that will interact in almost periodic manner in accordance with the theorems of almost periodic functions.

The first **APF** is the daily variation in the fungal contamination rate in the **OHS** air, let us define the function $f(x,t)$. It can be measured using either spot measurement, where x,t both vary or be continuous where x is fixed and t is continuous. Of course $f(x,t)$ is affected by the location, weather, fungal and plant species and a multitude of other factors, but periodic measurements allow us to estimate $f(x,t) < \epsilon$, where ϵ is some allowed error. The repeat period is estimated as annual, but issues such as construction may introduce a perturbation to $f(x,t)$, of course the matter of interest is then in the size of the perturbation function, which for simplicity may be $p_{t+\tau} = \alpha f(x,t)$, so for time τ the following applies $p_{\tau+t} - p_t = \alpha p(x, \tau + t) - p(x, t)$. Experimental data is then fitted to a numerical model to

determine the input function to the air and biological model. As further data is collected the model complexity can be changed to allow for the observational data.

The second **APF** is the transfer of the spores from the outside to the inside of the building. This is clearly tied to the network depth and density, such as shown in Figure (8a). One could postulate that the spore concentration in the air at node [8.1] termed [8.1] is less than [0.1], but [0.1] is simply $p_t = \alpha f(x, t)$ at time t as the **OHS** is tied to the root node directly. So the two functions are now related at a point in space and time.

Let us define the **APF** for the transfer function as $g(x, t) = \beta_i([i, j_c] - [i-1, k_c])$ where node [i-1,k] is the linking node from node [i,j], example [0.1] → [1.1]. The question then relates to the form of β , so in moving air and fungi either in the air or on other vectors from [0.1] → [8.1] do we have $\beta_F = \prod_{i=0}^8 B_i$ so if the transfer function from [0.1] → [1.1] is 0.8 then the [0.1] → [8.1] might be 0.162, which trends to zero very slowly. Data collection will allow the form of the β to be established.

The third **APF** is the HVAC system used to provide “clean” air to the hospital. We can define three room types, isolation room such as for **TB** patients, where the air flow is into the room, In the 20th century, these patients were often isolated from the general population and from other patients, the Rankin Park Hospital in Newcastle, NSW, Australia is an example of this type of facility. Normal patient rooms, where the need is for the air to change over in the room regularly and for the flow to be “reasonably” clean and the third is immune compromised patient where we want clean air in only.

In real terms, the measurable **APF** functions are the fatality function for the immune compromised patients and $f(x, t)$, all else is a conceptual idea for a flow and contamination model and will require significant calibration data [14]. Demonstrates the proof that an **APF** can be a Fourier series [15], building on the seminal work by [9], showed that the fatality rate is an **APF** using a Fourier analysis.

At this point, the numerical development of an air and contamination model is a reasonably self-evident task, given the availability of model forms, a Hardy Cross system would suffice as a simple starting point, as shown in [16]. The three **APF** need to be incorporated into the model. Data collection is a simple, yet time consuming task and model calibration is straight forward [17].

The real task understands the complex and required engineering relationships to ensure that clean air is delivered to the immune compromised patients and compromised air is removed from the area of **TB** patients.

The real issue is to define clean. If we define clean as zero fungal spores near the patient, then we need to define near and so on. In reality, a target contamination rate must be set, although

[2], indicate that this has not been studied at that time. However, let us assume a target contamination of λ cfu per day. λ can

now be broken into three parts, $\lambda = \sum_{i=1}^3 \lambda_i$, where λ_1 is the

air contamination from the HVAC system, which means that the HVAC if delivering γ m³ of air per day then the contamination

rate for the air stream is $\frac{\lambda_1}{\gamma}$ cfu/m³. The HVAC specialist can now design the system.

There are however modelling problems in verifying the concentrations are achieved in all rooms. An example of this problem follows, which is not uncommon in water supply modelling systems and that can lead to interesting numerical and thus design issues.

Let us assume that node [4.5] is an immune compromised patient room. A simple HVAC system may have air delivered as shown in Figure (8b), with the same air stream supplying air to nodes [5.4] and [4.5]. A conventional network topology has been developed and is shown on Figure (8b). A simple network analysis model was developed to try and balance this air flow system. Node 1 is a source from the HVAC system, Node 9 is a source from the corridor system, Node 8 is the HVAC air out, 4 and 5 represent the rooms. An analysis of this type of system shows a significant number of problems in balancing the flows and the pressures. The critical problems are:

1. Node 4 and 5 represent Nodes [4.5] and [5.4]. The flow at Node 9 or effectively through the doorway provides a significant and variable flow that is difficult to control [19], studied this problem and obtained a non-Gaussian distribution of flows for a closed door depending on the door gap size distribution. The patient safety is now significantly affected by the standard of construction of the doorway in terms of gap dimensions. The medical community is probably completely unaware of this need for door gap control for air flow control at the contract implementation stage for engaging a design team.

2. Air flow out from Node 6 to 7 is very sensitive to the relative pressures in the two rooms and small changes would see air flowing from room [5.4] to [4.5]. Brownian motion also means that any contamination in [5.4] could be discharged into [4.5] even if the net flow is outward if there are differential concentrations of fungi.

λ_2 is human contamination movement of fungi along the corridors. This is part of the second **APF** and requires a systematic contamination study as shown by [9], for the French hospital. This is a reasonably standard epidemiological study.

λ_3 is the effective removal rate for the fungi that have entered a room such as [4.5]. Removal can be by cleaning, natural death of the fungal spores or removal in the HVAC system. However, the four fundamental laws of thermodynamics clearly imply that λ will not be zero for the patient without complete isolation. There are of course social issues with complete isolation [1], although it will work. But no-one in the modern era would follow this procedure for these patients, except in extreme cases.

The model needs to incorporate the almost periodic functions that control each of the elements of the hospital air and contamination delivery system. The fatality function derived from the French data shows that the fatality model is an almost periodic function, and the three proposed **APF** functions for the model are individually reasonably simple to code in FORTRAN or C++, the interaction of the model and the calibration are the issues of interest to the broader biological control community. Of course a small amount of funding would help develop the models.

There are a number of hypotheses to be tested for this model. These hypotheses are:

Fungal spores move at a uniform rate from the **OHS** to the inside at a concentration rate, β , that is dependent on network depth

Fungal spores will move into a room even if the air flow is against the movement due to Brownian motion

A concentration of λ cfu per day in the patients room will result in κ patients (immune compromised) being infected per day

The fatality model is an **APF**

Each fungal types follows an **APF**

Model calibration will require estimation of the fatality function and then comparison to reality

Air handling unit filter change kills the bulk of immune compromised patients who acquire fungal infections

Figure (2), showing a hospital patient room can be configured to minimize fungal spore residence time in the room

A simple experimental program has been proposed for TAMU involving a model HVAC and corridor/room system to measure the movement of the fungal spores, determine β for Texas. The second stage would involve immune compromised mice to measure the λ rate for the mice for different fungal exposure levels. The most interesting challenge in this work is not the research, it is determining the authority with jurisdiction or group for funding the research. We have not found them yet.

CONCLUSION

Immune compromised patients will become more and more common as the population aging moves to a mature level and as there is an increased use of transplants. This research work started with an interest by Bassett into the movement of dust from construction sites into hospitals. The follow on research has shown a very complex engineering problem exists developing a modelling system to control fungal spore movement to clean living spaces.

But, as Weary Dunlop is reputed to have opined engineers have saved more lives than doctors. In this case it is clearly better to avoid the problem with engineering than treat an infected patient.

In the case of a new hospital, technology now exists that will allow for the development of an operational control model for new hospitals as a starting point. The control program will model the interaction between the different air streams and the human/

good stream to estimate the movement of fungal spores to the node points in the model. The model work requires an episodic monitoring program for fungal spores to identify concentrations in the different nodes and links. The model then provides a tool to estimate the likely paths from the **OSH** to the clean living spaces. This is of course a significant statistical problem, although one that is achievable given modern technology and the Internet of Things.

Whilst complete three dimensional model using **CFD** software is attractive it is computationally and time wise expensive, nor is it warranted at this point in time. The space syntax modelling provides elements that can be represented using a node and link system and a simpler modelling program that is essentially similar to standard engineering models, where the node points can be treated as reservoirs at each time step. This simpler system will ultimately lead to a 3D **CFD** model, but one needs the underlying **APFs** to be mature to make reasonable progress with a 3D **CFD**.

The proposed model will require a parallel set of statistical studies.

The first study continues the French work on hospitals to determine the rate of inflow and outflow of fungal spores present in each room or node when compared to the **OHS**. This data provides the basis for the derivation of the almost periodic function for fungal spore movement. The second study will look to use a control agent to compare the relative movement of HVAC and OHS air into the room systems.

Once the almost periodic functions are established, a mathematical model based on one of the standard numerical modelling techniques can be used to model the system at very fine time steps, say 100 times per second. It is trivial although not cost free to supply the data collection systems in a new hospital to monitor the reality of the pressures and airflows and adjust the model. The model should be able to pick up dynamic fluctuations in the HVAC system and allow fungi movement modelling. If the **AFP** model system can be shown to work then a hospital needs install a complete pressure and flow velocity measurement system to calibrate the model developed from the **APF's**. The air moving into a room can be treated as mass, rather than as a space and the analysis in terms of cfm/kg provides a simple system to track fungal concentrations. One would then move to the Deep Learning System to determine how best to manage patient location and HVAC operation. The modelling is straightforward, the calibration techniques are relatively simple and the necessary laboratory studies easily accomplished at a Tier 1 University, of course the issue is money.

This is not rocket science, the major engineering tools required for this work were invented in the 1930's, and the computer technology now exists. The issue is a community one of finding the funding source and not in the engineering.

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drawings used in Figures (2,3).

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