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A double-ended queueing model for dynamic allocation of live organs based on a best-fit criterion

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ABSTRACT

We propose a novel approach, based on a Human Leukocyte Antigen (HLA) best-fit criterion, to dynamically allocate live organs (specifically, kidneys) to candidates needing transplantation. A 'reward' is assigned to each level of HLA fit, such that higher rewards are attributed to transplants between better-matched candidates and kidneys. We also envision future technologies by which it will be possible to store organs so that two queues may form: waiting candidates or stored kidneys. Consequently, a double-ended queue of candidates and kidneys is constructed, where the lifetime of a stored kidney is random, and candidates queueing for transplantation may die ('renege') while waiting. We derive expressions for the probability that a candidate gets a kidney before reneging; for the mean numbers of waiting candidates and of stored kidneys; and for a candidate's or kidney's mean sojourn time. Assuming a best-HLA-fit matching policy, we study three measures of effectiveness: (i) Rate of Reward from Transplantation (RRT); (ii) Expected Reward per Transplantation (ERT), calculated as RRT divided by the rate of performed transplantations, and (iii) Gained rate of reward per one dollar of expenditure. The optimal fraction of kidneys that should be stored so as to maximize the rate of reward per one dollar of expenditure is numerically determined.

1. Introduction

Transplantation of kidneys is the preferred and most effective treatment for patients suffering from end stage renal disease (ESRD). It is considered to be a 'life-saving gift' for these patients, as it reduces their mortality risk and typically allows them to resume regular life activities. Unfortunately, the supply of kidneys for transplantation falls short of the increasing demand [1,2], and even in a hypothetical situation in which the supply of kidneys is ample, there still exists a complex, time-dependent problem of allocating randomly-arriving kidneys to waiting patients ('candidates').

The operations research (OR) literature includes numerous studies that apply OR tools to different problems in healthcare management, and particularly problems related to organ transplantation (see Zahiri et al. [3] for a detailed classification of healthcare-related OR studies; see also a review by Rais and Viana [4]). In general, the process of sequentially allocating randomly-arriving kidneys to candidates depends on various interacting clinical and administrative factors. A key medically-oriented criterion is the immunological compatibility of the donor kidney and the prospective recipient. Such compatibility is measured according to human leukocyte antigen (HLA) matching. Determining the HLA "match-level" between a donor

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and a recipient involves comparing their white blood cells along a set of six proteins, or antigens—two of type A, two of type B, and two of type DR (see, e.g., [5])—and quantifying how many of these antigens are identical between the donor and the recipient (in particular, there are 59 different type-A antigens, 118 different type-B antigens, and 124 different type-DR antigens). It should be noted that, when calculating the HLA match-level between a donor and a recipient, researchers and practitioners may assign different weights to specific antigen matches (see, e.g., [6,7]) on the basis of their prevalence in the population. Extensive clinical research (see, e.g., [8–11]) points to the relevance of HLA matching to transplantation success. According to a review by Takemoto et al. [12], transplantation of kidneys into HLA-matched candidates decreases the risk of graft loss by about 40%. The risk increases with the number of mismatches. The United Network for Organ Sharing (UNOS), the organization that manages the US organ transplant system, lists immunological compatibility as a key consideration when matching between transplantation candidates and donor organs (see https://www.unos.org/transplantation/faqs/). According to Ata, Skaro and Tayur [13], the "current kidney allocation policy of UNOS is a point system that prioritizes the potential transplant candidates based on the points they receive on the following four dimensions: (i) waiting times (ii) antibodies (i.e. whether the patient is sensitized or not); (iii) antigen matches (the quality of tissue match between the donor and candidate) [equivalent to HLA matching]; and (iv) whether the patient is a child". Furthermore, even if a priority is given to, say, a child over an adult, HLA compatibility is an extremely important consideration in selecting the child candidate.

In light of the crucial role of HLA fit in organ–candidate matching, the current paper proposes a new HLA-match-based criterion for allocating randomly-arriving kidneys to randomly-arriving patients. Specifically, according to this criterion, referred to as the *best-HLA-fit rule*, each arriving kidney is assigned to the waiting candidate with the highest number of HLA matches, i.e., the patient for whom the likelihood of transplantation success is highest. Thus, we assign a different 'reward' to each HLA match-level, which we use to assess the performance of the system.

David and Yechiali [14] used the HLA-match-level criterion in a model of a time-dependent stopping problem in which a single candidate is considered. In their model, the decision of whether or not to allocate a randomly-arriving kidney to the candidate depends both on the HLA match-level and on the residual lifetime of the candidate, as well as on the intensity of kidney arrivals. They considered four antigens - two of type A and two of type B - together with their frequencies in the population, and derived formulas to calculate the probability of each match-level (zero, one, two, three or four mismatches) between a random candidate and a random kidney. They showed that the optimal policy for a single candidate is to wait some finite time-interval, t_A, until a kidney with the best possible match arrives, and if no such kidney arrives, to wait another finite time-interval, until t_B ($t_B > t_A$) for either the best or the second-best possible match, and so on, until finally the candidate may accept a kidney with even the lowest possible match-level (zero matches). Righter [15] considered a more general allocation problem in which various parameters change according to an independent random environment Markov process. Her model assumes a finite number of activities that need to be carried out. Each activity requires a single resource, and resources arrive according to a Poisson process. Given that different resources are associated with different costs, and that different activities yield different values, the objective is to assign each arriving resource to an activity so as to maximize total expected return. David and Yechiali [16] further studied a sequential assignment match process with arrivals of both candidates and 'offers', with only one match-level between the two streams (i.e., match or mismatch). Their model assumes that a match results in a high reward R, and that a mismatch results in a much smaller reward $r < R$. The authors showed that the policy that yields the optimal average reward is allocation of offers exclusively to matching candidates. The same authors further studied a one-attribute sequential assignment process in discrete time, where M randomly-arriving offers are sequentially assigned to N candidates [17]. They studied several cases with various assumptions on the problem parameters and on the assignment regime, and derived optimal policies that maximize the total discounted reward. Bendersky and David [7] recently studied a flexible single-candidate model for the kidney allocation problem. Their model considered an HLA system comprising two groups of antigens (corresponding to two classes of the major histocompatibility complex): Class I, containing A, B and C antigens (which are present inside almost all cells in the body), and Class II, containing antigens of the types DP, DR and DQ (which are present only in the membranes of antigen-presenting cells, which are cells responsible for triggering the immune system). Analyzing a broad family of Gamma lifetime distributions, the authors obtained the optimal critical times of acceptance of offers of different qualities.

Various papers in the literature explicitly account for fairness and medical efficiency in the kidney allocation process. Zenios et al. [18] addressed a dynamic kidney allocation problem with three objectives: maximizing the 'quality-adjusted life expectancy' of transplant candidates; maximizing a linear function of the likelihood of transplantation of the various types of candidates; and minimizing a quadratic function that quantifies the differences in mean waiting times across candidate types. Su and Zenios [19,20] analyzed the kidney allocation process while considering the perspective of society, as well as the perspective of an individual candidate. The same authors [21] studied the sequential assignment problem with the objective of determining an organ allocation policy that maximizes the total expected reward. Their stochastic model seeks to create a more efficient and equitable system, while providing candidates with some flexibility to decide whether or not to accept specific organs. Bertsimas et al. [22] developed models in which, instead of making specific assumptions about fairness principles or priority criteria, the decision maker has the flexibility to select his desired criteria and fairness constraints from a broad class of allowable constraints. A point system is generated based on the selected priority criteria, and the model then approximately maximizes medical efficiency, i.e., life-year gains from transplantation, while simultaneously enforcing the selected fairness constraints. Drekic et al. [23] developed a self-promoting priority queueing model for patients' waiting times, which takes into account changes in health status over time. The model allows patients both to renege from the queue and to self-promote to an urgent status. The authors obtained the waiting time distributions

and their moments, the queue length distributions, and the reneging probabilities. Recently, Bloch and Cantala [24] analyzed dynamic assignment of randomly-arriving kidneys to patients organized in a waiting list. Each time a new kidney becomes available, it is offered to a patient according to a fixed sequence, and the patient decides whether to accept it or not. Three efficiency criteria are considered, and it is argued that waiting time should be used as a primary criterion in the order of allocation. In the US, the current organ allocation policy (established by UNOS) has a geographically-tiered structure (https://www.unos.org/transplantation/matching-organs/): An available organ is offered first within the region in which the donor is located (Donor Service Area, DSA). Ata et al. [13] recently explored a means of amending this potential source of inequity. Specifically, they proposed offering affordable jet services (OrganJet) to candidates on the transplant waiting list, effectively enabling these candidates to be included in multiple DSAs. The authors evaluated how many patients might utilize this service and studied how its availability would affect waiting times, the number of organs harvested, and mortality rates.

As noted above, drawing from the idea that a higher number of HLA matches results in a superior transplantation outcome [12], we expand the scope of studies on the kidney allocation problem by proposing a novel approach for allocating arriving kidneys to waiting candidates (or of matching an arriving candidate with a stored kidney): If there is a queue of candidates, an arriving kidney is allocated to the waiting candidate with the best HLA match-level, or if there is a queue of stored kidneys, an arriving candidate is matched with the best-fit kidney. In this approach, a reward is assigned to each match according to the HLA match-level. The reward can be operationalized in different ways. For example, one option is to use the candidate's expected quality-adjusted life years after transplantation (see, e.g., [19]). Given a set of rewards, we define three measures of effectiveness. The first is the Rate of Reward from Transplantation (RRT) realized under the best-HLA-fit rule. The second is Expected Reward per Transplantation (ERT) under the best-HLA-fit rule; this measure corresponds to the RRT divided by the rate of performed transplantations. The third measure is the gained rate of reward per one dollar of expenditure. We note that, in contrast to some of the works cited above, our model does not accommodate individual decisions on whether to accept or reject an offered kidney. Rather, the goal is to maximize overall societal benefit, by introducing an objective criterion—the best-HLA-fit rule—according to which the decision maker determines who receives each kidney.

Another contribution of our work is the fact that it considers the possibility of organ preservation. The ability to preserve organs outside the body has played a major role in the development of transplant services worldwide over the last four decades. At present, hypothermic storage is the most common storage method used, and organs are typically stored for periods of 24 hours or less, depending on the organ in question. The science of organ preservation is constantly being updated with new knowledge and ideas, so as to meet the growing demand for high-quality organs for transplantation. In particular, the kidney, which is the most widely transplanted organ, also has the longest history of preservation research (see [25]), and kidney storage has been at the focus of many developments in the field. Accordingly, we envision future technologies by which it will be possible to store kidneys for longer periods of time.

Thus, we consider a double-ended queueing model that incorporates two independent streams: a stream of randomly-arriving patients (candidates) needing transplantation, and a stream of randomly-arriving kidneys. Double-ended queues were first introduced by Kashyap [26] to analyze the taxi-passenger problem, where taxis wait for passengers and passengers queue for taxis. Since then, numerous works have considered double-ended queues, in a variety of applications. For example, Takahashi et al. [27] considered a double-ended queue consisting of two buffers with finite capacities. Conolly et al. [28] studied the effect of impatient behavior on various outcomes in double-ended queues, under the assumption of Poisson arrivals and exponential patience. Crescenzo et al. [29] considered a double-ended queue with catastrophes and repairs and obtained steady-state and failure-state probabilities. Recently, Liu et al. [30] developed fluid and diffusion models for double-ended queues with renewal arrivals and exponential patience times.

In this paper we assume that a kidney that arrives when candidates are waiting for transplant is immediately allocated to the candidate with whom it has the best HLA fit. On the other hand, a kidney that arrives when the queue of candidates is empty is stored with a given probability (that may depend on the number of stored kidneys) for possible future allocation. Similarly, a candidate arriving when the candidate queue is empty and there are stored kidneys will be matched with the best-HLA-fit kidney.

In line with Conolly et al. [28] and Shin and Choo [31], who studied the reneging phenomenon as an important component of queueing models, we further take into account the realistic scenario in which a candidate queueing for transplantation may die while waiting. Several studies have considered such 'reneging' from the transplantation queue, including the works of Zenios [32], Boxma et al. [33], and Drekic et al. [23]; those studies, however, applied first-come-first-serve (FCFS) allocation policies (or variations of FCFS), rather than the HLA-match-based allocation approach we propose herein. Notably, Boxma et al. [33] also took into account the capacity to store kidneys. Whereas that study assumed a constant storage period, we attribute a probability distribution function to the lifetime of a stored kidney.

Analyzing the steady-state probabilities of our double-ended queueing system, we identify, for each level of stored kidneys, the optimal fraction of kidneys that should be stored so as to maximize the gained rate of reward achieved per dollar of expenditure, under the best-HLA-fit criterion. By evaluating the rate of reward obtained per dollar spent, we address the universal social dilemma of how much to spend in order to provide transplantation candidates with a better quality of life and to increase their life expectancy. Using numerical analysis, we find that the optimal kidney storage policy varies according to the measure being optimized: the optimal fraction of kidneys that should be stored when seeking to maximize cost-effectiveness (gained rate of reward per one dollar of expenditure) is always higher than that

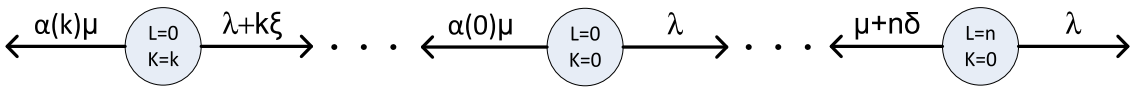

Fig. 1. Transition-rate diagram.

obtained when the objective is to minimize the sum of candidates' waiting costs and kidney storage costs per unit of time.

The remainder of this paper is organized as follows: In Section 2 we formulate the queueing model and derive the steady-state probabilities of the system. Section 3 develops expressions for three types of queuing system performance measures: (i) the probability that a candidate gets a kidney before reneging; (ii) mean number of candidates and mean number of kidneys in the system; and (iii) mean sojourn times of candidates and kidneys in the system. We note that these expressions are independent of the allocation rule used (e.g., best-HLA-fit or FCFS). However, according to our approach, different allocation methods may differ in terms of the probability distributions of sojourn times and in terms of the quality of the transplantation outcome (reflected in our proposed 'reward' measures). In Section 4 we investigate the system's properties under the FCFS allocation rule. In Section 5 the best-HLA-fit allocation rule is analyzed. Section 6 addresses the question of whether "to store or not to store" and finds the optimal fraction of kidneys to be stored in various scenarios. Section 7 concludes the paper.

2. Model formulation

We assume that candidates for live-organ transplantation arrive according to a Poisson process with rate λ. Each candidate waits in queue until either receiving a graft (i.e., a kidney) or reneging from the system (willingly or due to death) after an exponentially-distributed length of time with parameter δ. In parallel, kidneys arrive according to a Poisson process with rate μ and are allocated to waiting candidates. Thus, one 'side' of the process can be considered as a single-server queue in which the inter-arrival time of kidneys is equivalent to service duration, so that when there are $L=n$ candidates in the system, the overall service rate is state-dependent and equals $\mu+n\delta$.

As discussed above, we consider a scenario in which organ preservation technologies have developed sufficiently to enable kidneys to be stored for a relatively substantial period of time. Accordingly, our model assumes that if a kidney arrives when the queue of candidates is empty, it is stored for possible future allocation with probability $0 \le \alpha(k) \le 1$, where $\alpha(0)=\alpha$ and $\alpha(k)$ is a monotone decreasing function of k, the number of inventoried kidneys stored in the system. The kidney is lost with the complementary probability.

In addition, we assume that the lifetime of a stored kidney is exponentially distributed with parameter ξ. Hence, the other 'side' of the system can be looked upon as a state-dependent Markovian single-server queue with arrival rate $\alpha(k)\mu$ and service rate $\lambda+k\xi$ when there are k stored kidneys and no candidates. Note that the above state-dependent rates ($\mu+n\delta$ and $\lambda+k\xi$) are each independent of the inner order of the corresponding queues (candidates or kidneys).

Let $L=n$, $n=0, 1, 2, 3, \ldots$ denote the number of candidates in the system. Also, when $L=0$, denote by K the number of kidneys waiting to be allocated to arriving candidates. Note that the numbers of candidates and kidneys in the system are independent of the allocation policy, since it is assumed that a kidney that arrives when candidates are waiting is immediately allocated to a candidate. Similarly, a candidate arriving when the candidate queue is empty and there are stored kidneys will instantaneously be matched with a kidney. Thus, we define a double-ended queue with state space $\{L, K\}$, where the possible states are $\{\{L=n,\ n\ge 1;\ K=0\}, \{L=0;\ K=k,\ k\ge 1\}, \{L=0,\ K=0\}\}$. The transition rates between the system's states are depicted in Fig. 1.

In what follows, the analysis is conducted on the basis of the steady-state analysis of the process, since the transient solution is difficult to obtain. Moreover, such processes reach equilibrium quite rapidly.

2.1. Derivation of the steady-state probabilities

For $n \ge 1$, let $p_n=P(L=n,\ K=0)$; and for $k \ge 1$, let $q_k=P(L=0,\ K=k)$. Also, let $p_0=P(L=0,\ K=0)$. Constructing the balance equations, we obtain

$$p_n = p_0 \prod_{i=1}^{n} \left(\frac{\lambda}{\mu + i\delta} \right),\ n = 1, 2, 3, \ldots \tag{1}$$

and

$$q_k = p_0 \prod_{i=1}^{k} \left(\frac{\alpha(k)\mu}{\lambda + i\xi} \right),\ k = 1, 2, 3, \ldots \tag{2}$$

Summing up all probabilities and equating to one, we get

$$p_0 = \left[1 + \sum_{n=1}^{\infty}\prod_{i=1}^{n}\left(\frac{\lambda}{\mu+i\delta}\right) + \sum_{k=1}^{\infty}\prod_{i=1}^{k}\left(\frac{\alpha(k)\mu}{\lambda+i\xi}\right)\right]^{-1}. \tag{3}$$

We start with the special case where the probability of storing a kidney is constant ($\alpha(k)=\alpha$); This assumption enables us to obtain closed-form solutions. The case where $\alpha(k)$ depends on the number of kidneys currently being stored ($\alpha(k)=\frac{\alpha}{k}$, $k=1, 2, 3, \ldots$) is addressed in Section 6.3.

For $\alpha(k)=\alpha$ we have

$$\frac{\sum_{n=1}^{\infty} p_n}{p_0} = \sum_{n=1}^{\infty}\prod_{i=1}^{n}\left(\frac{\lambda}{\mu+i\delta}\right) = \lambda^{-\frac{\mu}{\delta}}\delta^{\frac{\mu}{\delta}}e^{\frac{\lambda}{\delta}}\left(\Gamma\left(\frac{\delta+\mu}{\delta}\right) - \Gamma\left(\frac{\delta+\mu}{\delta}, \frac{\lambda}{\delta}\right)\right) \tag{4}$$

and

$$\frac{\sum_{k=1}^{\infty} q_k}{p_0} = \sum_{k=1}^{\infty}\prod_{i=1}^{k}\left(\frac{\alpha\mu}{\lambda+i\xi}\right) = \mu^{-\frac{\lambda}{\xi}}\xi^{\frac{\lambda}{\xi}}e^{\frac{\alpha\mu}{\xi}}\left(\Gamma\left(\frac{\xi+\lambda}{\xi}\right) - \Gamma\left(\frac{\xi+\lambda}{\xi}, \frac{\alpha\mu}{\xi}\right)\right), \tag{5}$$

Where $\Gamma(\alpha, y) = \int_y^{\infty} t^{\alpha-1}e^{-t}dt$ is the upper incomplete Gamma function.

In the next section we will use Eqs. (4)–(5) to calculate various performance measures.

3. Performance measures

We now calculate various performance measures: (i) the probability that an arbitrary candidate gets a kidney before reneging; (ii) mean number of candidates and mean number of kidneys in the system; and (iii) mean sojourn times of candidates and kidneys in the system. We note that, the mean waiting time of a candidate (kidney), in a so called 'work-conserving' and non-preemptive single-server queue, is independent of the order of service (see [34]: Theorems 29.2 and 29.3 in pages 478 and 479), as it is the mean of sum of interchangeable identical random variables divided by the number served. Since the state-dependent service rates are independent of the inner order of queues, and since a transplantation is performed instantaneously, these performance measures are independent of the allocation policy (e.g., FCFS, random selection, or best-HLA-fit allocation).

3.1. Probability that a candidate receives a kidney before reneging

Regardless of the allocation policy, a transplantation is performed either in the case when a candidate arrives and finds an available kidney (which occurs with probability $\sum_{k=1}^{\infty} q_k$), or when a kidney arrives and finds waiting candidates (an event occurring with probability $\sum_{n=1}^{\infty} p_n$). Thus, Lemma 1 below states the rate of performed transplantations.

Lemma 1. The rate of performed transplantations is given by: $\lambda\sum_{k=1}^{\infty} q_k + \mu\sum_{n=1}^{\infty} p_n$,

where $\frac{\sum_{k=1}^{\infty} q_k}{p_0}$ is given by (5), and $\frac{\sum_{n=1}^{\infty} p_n}{p_0}$ is given by (4).

Note that in the special case when $\delta=0$ and $\lambda < \mu$, the rate of performed transplantations equals λ.

Next, the probability that an arbitrary candidate gets a kidney before reneging, denoted by $P(G)$, is given in Proposition 1.

Proposition 1. $P(G) = \sum_{k=1}^{\infty} q_k + \frac{\mu}{\lambda}\sum_{n=1}^{\infty} p_n$.

Proof.

$$P(G) = \sum_{k=1}^{\infty} q_k q(G|K=k) + \sum_{n=0}^{\infty} p_n P(G|L=n) \tag{6}$$

Now, for $=1, 2, 3, \ldots$, $P(G|K=k)=1$, while for $n \geq 1$,

$$P(G|L=n) = \left(\frac{(n+1)\delta}{(n+1)\delta+\mu}\cdot\frac{n}{n+1} + \frac{\mu}{(n+1)\delta+\mu}\right)\cdot P(G|L=n-1) = \frac{n\delta+\mu}{(n+1)\delta+\mu}\cdot P(G|L=n-1)$$

The above follows since when a candidate arrives and finds $L=n$ candidates in queue, he/she joins and increases L to $n+1$. The term $\frac{(n+1)\delta}{(n+1)\delta+\mu}$ is the probability that one of the candidates reneges before a kidney arrives. This probability is multiplied by the probability, $\frac{n}{n+1}$, that the reneging candidate is one of the other n candidates. The term $\frac{\mu}{(n+1)\delta+\mu}$ is the probability that a kidney arrives before a reneging occurs and the kidney is assigned to the first candidate in line.

For $n=0$, $P(G|L=0) = \frac{\mu}{\mu+\delta}$. Then, iterating, we obtain

$$P(G|L=n) = \frac{\mu}{(n+1)\delta+\mu} \tag{7}$$

Substituting Eq. (7) in Eq. (6) leads to

$$P(G) = \sum_{k=1}^{\infty} q_k + \sum_{n=0}^{\infty} p_n \frac{\mu}{(n+1)\delta + \mu}. \tag{8}$$

Using $\lambda p_n = [(n+1)\delta + \mu]p_{n+1}$, $n = 0, 1, 2, \ldots$, leads to $\sum_{n=0}^{\infty} p_n \frac{\mu}{(n+1)\delta+\mu} = \frac{\mu}{\lambda}\sum_{n=1}^{\infty} p_n$, which completes the proof. □

Note that, since the arrival rate of candidates is λ, Proposition 1 can also be derived by using Lemma 1 and applying the mean value argument, namely, dividing the performed rate of transplantation by λ. Note also that in the special case in which $\delta = 0$ and $\lambda < \mu$, the probability that a candidate gets a kidney equals one.

3.2. Mean numbers and mean sojourn times of candidates and kidneys in the system

The mean number of candidates and the mean number of kidneys in the system are obtained by $E[L] = \sum_{n=1}^{\infty} np_n$ and $E[K] = \sum_{k=1}^{\infty} kq_k$, respectively. Explicit (though cumbersome) expressions of those means are given in Appendix A.

For the special case in which both $\delta = 0$ and $\xi = 0$, while $\alpha\mu < \lambda < \mu$, we obtain simpler expressions:

$$E[L] = \frac{\lambda - \alpha\mu}{(\mu - \lambda)(1-\alpha)} \tag{9}$$

and

$$E[K] = \frac{\alpha(\mu - \lambda)}{(\lambda - \alpha\mu)(1-\alpha)}. \tag{10}$$

Let us assume that each waiting candidate inflicts a waiting cost of C_L per time unit, and that C_K is the cost rate of storing a kidney. Thus, the total cost (sum of candidates' waiting costs and kidneys' storage costs) per unit of time is $C_L E[L] + C_K E[K]$.

As indicated above, $E[W]$, the mean sojourn time of a candidate in the system until either receiving a kidney or reneging, is independent of the allocation policy. Thus, we claim:

Proposition 2.

$$E[W] = E[W_{FCFS}] = \frac{1}{\mu + \delta} p_0 + \sum_{n=1}^{\infty} \left(\frac{n+1}{\mu + (n+1)\delta} \right) p_0 \prod_{i=1}^{n} \left(\frac{\lambda}{\mu + i\delta} \right)$$

Proof. Under the FCFS allocation rule,

$$E[W_{FCFS}] = \sum_{n=0}^{\infty} p_n E[W_{FCFS} | L = n] + \sum_{k=1}^{\infty} q_k E[W_{FCFS} | K = k].$$

Clearly, for $k \geq 1$, $E[W_{FCFS}|K = k] = 0$. When the system is in state $(L = 0,\ K = 0)$, an arriving candidate joins the queue and waits until either an arrival of a kidney, or his own reneging, whichever occurs first. Thus, $E[W_{FCFS}|L = 0,\ K = 0] = \frac{1}{\mu+\delta}$.

For $(L = n \geq 1)$,

$$\begin{aligned} E[W_{FCFS}|L = n] = {} & \frac{1}{\mu + (n+1)\delta} + \frac{\mu}{\mu + (n+1)\delta} E[W_{FCFS}|L = n-1] \\ & + \frac{(n+1)\delta}{\mu + (n+1)\delta} \cdot \left(\frac{1}{n+1} \cdot 0 + \frac{n}{n+1} \cdot E[W_{FCFS}|L = n-1] \right) \end{aligned} \tag{11}$$

When a candidate arrives and $L = n$, he joins the queue and increases L to $n+1$. The first term in Eq. (11) is the mean time until either an arrival of a kidney or a reneging of one of the $n+1$ candidates occurs. The second term deals with the case in which a kidney arrives first (with probability $\frac{\mu}{\mu+(n+1)\delta}$) and is allocated to the first candidate in line. The third term deals with the case in which a reneging occurs before a kidney's arrival (with probability $\frac{(n+1)\delta}{\mu+(n+1)\delta}$). Then, with probability $\frac{1}{n+1}$, the reneging candidate is either the one who has just arrived and his additional waiting time is zero, or, with the complementary probability, the reneging candidate is one of the other n candidates. Iterating (where $E[W_{FCFS}|L = 0,\ K = 0] = \frac{1}{\mu+\delta}$), we obtain:

$E[W_{FCFS}|L = n] = \frac{n+1}{\mu+(n+1)\delta}$, $n = 0, 1, 2, \ldots$ Thus, using Eq. (1), the claim is proved. □

For the special case in which both $\delta = 0$ and $\xi = 0$, while $\alpha\mu < \lambda < \mu$,

$$E[W] = \frac{\lambda - \alpha\mu}{\lambda(\mu - \alpha)(1-\alpha)}.$$

Let S denote the sojourn time of a kidney before being allocated or becoming obsolete. Proposition 3 below states the mean value of S, $E[S]$. Where, again, $E[S] = E[S_{FCFS}]$.

Proposition 3.

$$E[S] = E[S_{FCFS}] = \frac{1}{\lambda+\xi}p_0 + \sum_{k=0}^{\infty}\left(\frac{k+1}{\lambda+(k+1)\xi}\right)p_0\prod_{i=1}^{k}\left(\frac{\alpha\mu}{\lambda+i\xi}\right)$$

Proof. Since the process of waiting kidneys is symmetric with respect to the process of waiting candidates, the claim is proved by Proposition 2 when performing the necessary parameter interchanges. □

For the special case in which both $\delta=0$ and $\xi=0$, while $\alpha\mu < \lambda < \mu$, $E[S] = \frac{\mu-\lambda}{\mu(\lambda-\alpha\mu)(1-\alpha)}$.

4. Probability distributions of sojourn times under the FCFS allocation rule

Since waiting time is an important parameter in transplantation priority systems, the FCFS allocation rule (in which an arriving kidney is allocated to the first candidate in line when $L \geq 1$) is common in the literature and also serves as a benchmark for other allocation policies (see, e.g., [13,19]). Therefore, in this section we characterize the system under the FCFS allocation rule.

When a candidate arrives while $\{L=0,\ K \geq 1\}$, the candidate receives a kidney instantaneously. The probability distribution functions of the sojourn times of a candidate and of a kidney under the FCFS allocation rule are given in the propositions below.

Proposition 4. For the special case in which $\delta=0$, $\lambda < \mu$, the probability distribution function of W_{FCFS} is given by $P(W_{FCFS} \leq t) = \sum_{k=1}^{\infty} q_k \cdot 1 + p_0^{\delta=0}\frac{\mu}{\mu-\lambda}(1-e^{-(\mu-\lambda)t})$, where $\sum_{k=1}^{\infty} q_k$ can be extracted from Eq. (5) with $p_0 = p_0^{\delta=0}$, $p_n^{\delta=0} = p_0^{\delta=0}(\frac{\lambda}{\mu})^n$ and

$$p_0^{\delta=0} = \left[\frac{\mu}{\mu-\lambda} + \sum_{k=1}^{\infty}\prod_{i=1}^{k}\left(\frac{\alpha\mu}{\lambda+i\xi}\right)\right]^{-1}.$$

Proof. The proof uses standard queueing arguments and is given in Appendix B.

Consider now S_{FCFS}, the sojourn time of a kidney under the FCFS allocation rule.

Proposition 5. For the special case in which $\xi=0$, $\alpha\mu < \lambda$, the probability distribution function of S_{FCFS} is given by

$$P(S_{FCFS} \leq t) = \sum_{n=1}^{\infty} p_n^{\xi=0}\cdot 1 + \left(1-\alpha e^{-\lambda t}\right)p_0^{\xi=0} + \alpha\lambda\left(e^{-\lambda t} - e^{-(\lambda-\alpha\mu)t}\right)p_0^{\xi=0},$$

where $p_0^{\xi=0} = [\frac{\lambda}{\lambda-\alpha\mu} + \sum_{n=1}^{\infty}\prod_{i=1}^{n}(\frac{\lambda}{\mu+i\delta})]^{-1}$ and $p_n^{\xi=0}$ can be extracted from Eq. (1) with $p_0 = p_0^{\xi=0}$.

Proof. The proof relies on arguments similar to those used in the proof of Proposition 4 and is given in Appendix C.

5. Best-HLA-fit allocation policy

As outlined in the introduction, we propose a new policy for allocating kidneys to candidates based on best HLA-fit between kidneys and candidates. Specifically, when a kidney arrives at a non-empty queue of waiting candidates, it is assigned to the candidate with whom it has the smallest number of HLA mismatches (i.e., the highest match-level). Similarly, when a candidate arrives at a queue containing $K=k \geq 1$ kidneys, the candidate is matched to the 'best' available kidney. Thus, heterogeneity across kidneys (and candidates) is captured in the differences among their respective sets of antigens. We note that although heterogeneity also arises with respect to blood type, it turns out that, in practice, a great majority of kidneys in each blood type are transplanted into candidates with the same blood type (see [24]). Thus, we assume that kidneys and candidates are homogeneous with respect to their blood type.

Let the random variable H denote the number of HLA mismatches between a randomly-arriving kidney (candidate) and a random candidate (kidney). Let $f_i = P(H=i)$, $i=0, 1, 2, \ldots, I$, be the probability that a random candidate and a random kidney have i mismatches; and let $F_i = P(H \leq i)$, where $F_I = 1$. Let X be a random variable denoting the 'transplantation reward' realized when a random kidney is assigned to a random candidate (see [14,17,35]). Note that there are I 'values' of rewards, with each reward value corresponding to a different number of mismatches. The value of X for $H = i$ mismatches is denoted by x_i, where if $i < j$, then $x_i > x_j$. Consequently, $P(X=x_i) = P(H=i) = f_i$, and $E[X] = \sum_{i=0}^{I} f_i x_i$.

Consider a random kidney arriving when $L=n \geq 1$ candidates are present in the system. Then, the n possible matches of transplantation rewards corresponding to the n candidates are $X_1, X_2, \ldots, X_n$. Since each HLA match between the arriving organ and each candidate (as discussed in the introduction) corresponds to numerous specific proteins, and since each possible match is between a random kidney and a random candidate, one may assume that $X_1, X_2, \ldots, X_n$ are i.i.d. like X.

Let $X^*_{(n)} = max\{X_1, X_2, \ldots, X_n\}$. Then, with $\bar{F}_i = 1 - F_i$,

$$E\left[X^*_{(n)}\right] = \underbrace{\left(1-\bar{F}_0^n\right)}_{\substack{\text{The probability}\\ \text{that at least one}\\ \text{candidate has}\\ \text{zero mismatches}}} x_0 + \sum_{i=1}^{I} \underbrace{\left((1-\bar{F}_i^n)-(1-\bar{F}_{i-1}^n)\right)}_{\substack{\text{The probability that the candidate}\\ \text{with the best match has}\\ \text{exactly } i \text{ mismatches}}} x_i \tag{12}$$

Similarly, when a candidate arrives to find $K=k \geq 1$, the transplantation reward is $X^*_{(k)}$. Note that $E[X^*_{(1)}] = E[X] = \sum_{i=0}^{I} f_i x_i$.

We calculate the Expected Reward per Transplantation under this best-HLA-fit rule and denote this measure by $ERT_{Best-Fit}$.

Theorem 1.

$$ERT_{Best-Fit} = \frac{\mu \sum_{n=1}^{\infty} p_n\left(\left(1-\bar{F}_0^n\right)x_0 + \sum_{i=1}^{I}\left(\bar{F}_{i-1}^n - \bar{F}_i^n\right)x_i\right) + \lambda \sum_{k=1}^{\infty} q_k\left(\left(1-\bar{F}_0^k\right)x_0 + \sum_{i=1}^{I}\left(\bar{F}_{i-1}^k - \bar{F}_i^k\right)x_i\right)}{\mu \sum_{n=1}^{\infty} p_n + \lambda \sum_{k=1}^{\infty} q_k}$$

Proof. The rate of kidney arrivals is μ. When $L=n \geq 1$ and a kidney arrives, the match with the best candidate yields $E[X^*_{(n)}]$. In all other states, no transplantation can be performed and the kidney joins the queue. Similarly, the rate of candidate arrivals is λ. When $K=k \geq 1$ and a candidate arrives, the match with the best kidney yields $E[X^*_{(k)}]$. The claim is proved since the rate of performed transplantations is given in Lemma 1. □

We refer to the numerator of $ERT_{Best-Fit}$ (i.e., the numerator on the right-hand side of Theorem 1) as the Rate of Reward from Transplantation, $RRT_{Best-Fit}$, realized under the best-HLA-fit rule, where

$$RRT_{Best-Fit} = \mu \sum_{n=1}^{\infty} p_n \left(\left(1-\bar{F}_0^n\right)x_0 + \sum_{i=1}^{I}\left(\bar{F}_{i-1}^n - \bar{F}_i^n\right)x_i\right) + \lambda \sum_{k=1}^{\infty} q_k \left(\left(1-\bar{F}_0^k\right)x_0 + \sum_{i=1}^{I}\left(\bar{F}_{i-1}^k - \bar{F}_i^k\right)x_i\right) \tag{13}$$

The corresponding ERT under the FCFS rule is given in the following proposition.

Proposition 6.

$$ERT_{FCFS} = E[X].$$

Proof. The proposition follows directly from the definitions above. □

It is clear that $ERT_{Best-Fit} \geq ERT_{FCFS}$ since $E[X^*_{(n)}] \geq E[X^*_{(1)}] = E[X]$.

6. To store or not to store

In this section, we study how storing kidneys affects the various performance measures of the system, and we identify the optimal fraction of stored kidneys, α^*. Sections 6.1 and 6.2 present the case in which the probability of storing a kidney is fixed, whereas Section 6.3 presents the case in which the probability of storing a kidney depends on the current size of the queue of stored kidneys.

6.1. A numerical example

Since the mathematical expressions are cumbersome, we first demonstrate the results using a numerical example with the set of values $\mu=1$, $\xi=0.5$, $\lambda=1.4$ and $\delta=0.05$. Note that since $\delta > 0$, λ/μ can exceed 1, which reflects the realistic scenario in which the rate of candidate arrival is higher than the rate of kidney arrival. Also, we assume that $C_L=0.3$ and that $C_K=2$, as technologies that enable kidneys to be stored are likely to be expensive (see [36]). To calculate the rate of reward from transplantation, $RRT_{Best-Fit}$, we use the following data: $I=6$, f_i= [0.0001, 0.0031, 0.0285, 0.1306, 0.3103, 0.3632, 0.1642], and x_i= [0.850, 0.833, 0.818, 0.802, 0.786, 0.771, 0.750] (based on UNOS data and HLA mismatch computations from [17]). Fig. 2 depicts the total cost as a function of α.

Fig. 2 shows that the total cost function is concave in α with a minimum cost of 2.555 at $\alpha^* \cong 0.3$. Note that the total cost function is a weighted sum of $E[L]$, a monotone decreasing function of α, and $E[K]$, a monotone increasing function of α.

We note that $RRT_{Best-Fit}$ increases in α, as a result of the fact that the presence of a larger number of kidneys in the system allows for better matches.

Given that the $RRT_{Best-Fit}$ measure does not account for waiting times and for storage costs, we propose a cost-effectiveness measure that is likely to be of practical value to decision makers. Specifically, we analyze the gained rate of reward per one dollar of expenditure. Fig. 3 depicts this ratio as a function of α.

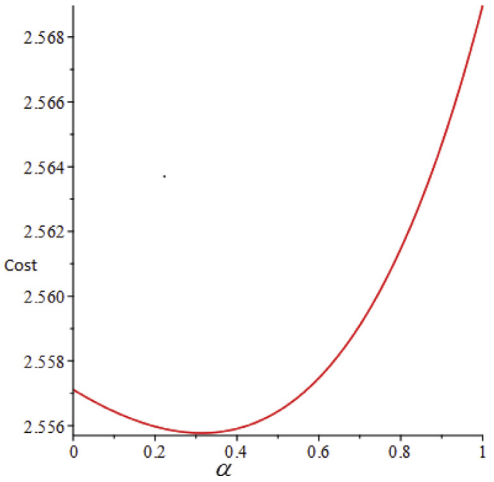

Fig. 2. Total cost $C_L E[L] + C_K E[K]$ as a function of α.

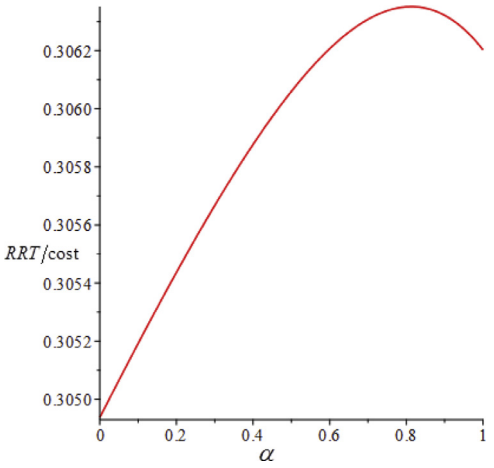

Fig. 3. The ratio $RRT_{Best-Fit}/[C_L E[L] + C_K E[K]]$ as a function of α.

The optimal value of α that maximizes the rate of reward per dollar of expenditure (under the best-HLA-fit allocation rule) is $\alpha^* \cong 0.8$ at $\frac{RRT_{Best-Fit}}{C_L E[L]+C_K E[K]} = 0.3063$. When we compare the optimal values of α in Fig. 2 and in Fig. 3, we observe that the optimal fraction of stored kidneys in the latter case — i.e., when attempting to optimize the cost-effectiveness measure $\frac{RRT_{Best-Fit}}{C_L E[L]+C_K E[K]}$ — is higher than that in the former case — i.e., when attempting merely to minimize costs. In other words, under the best-HLA-fit policy, the benefit obtained from performing more transplantations justifies the extra cost resulting from storing kidneys.

6.2. A simple case

Next, we analyze the special case in which both $\delta = 0$ and $\xi = 0$. In this case, the stability condition $\alpha\mu < \lambda < \mu$ must hold. Since transplant waitlists are almost never empty, it is appropriate to assume that $\lambda = 0.95$and $\mu = 1$ (see [37]). Under these simplifying assumptions, some of the results can be obtained analytically. Specifically, for any values of $C_L$and C_K, where $E[L]$ and $E[K]$ are given by Eqs. (9) and (10), respectively, the optimal value of α that minimizes the total cost rate is

$$\alpha^* = \frac{C_L\lambda\mu - \sqrt{C_K\lambda\mu(\mu-\lambda)^2\,(C_L+C_K)}}{\mu[(C_L+C_K)\mu - C_K\lambda]} \tag{14}$$

Clearly, in the case where $\alpha = 0$, the total cost is $C_L E[L] = \frac{C_L\lambda}{\mu-\lambda}$. When $C_L = 0.3$ and $C_K = 2$ then $\alpha^* = 0.451$, as depicted in Fig. 4.

Fig. 5 depicts the ratio $RRT_{Best-Fit}/[C_L E[L] + C_K E[K]]$ as a function of α.

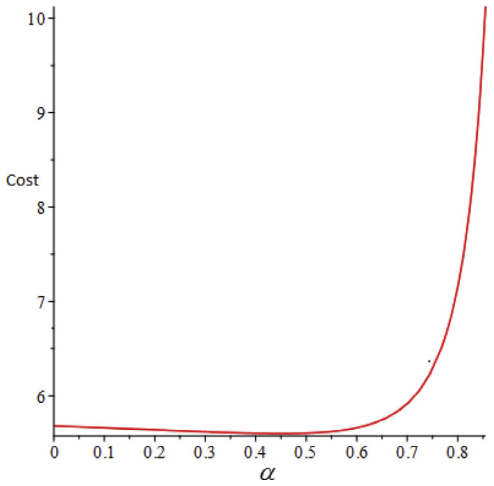

Fig. 4. Total cost $C_L E[L] + C_K E[K]$ as a function of α for the special case.

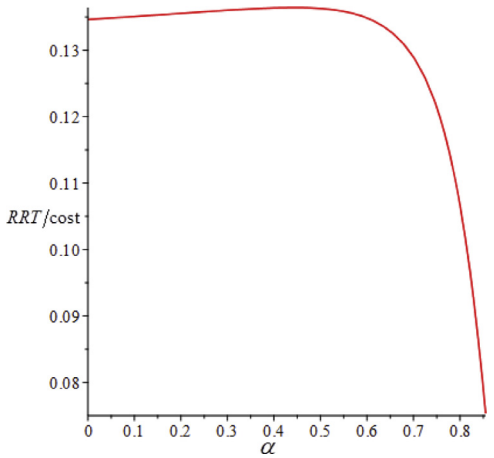

Fig. 5. The ratio $RRT_{Best-Fit}/[C_L E[L] + C_K E[K]]$ as a function of α for the special case.

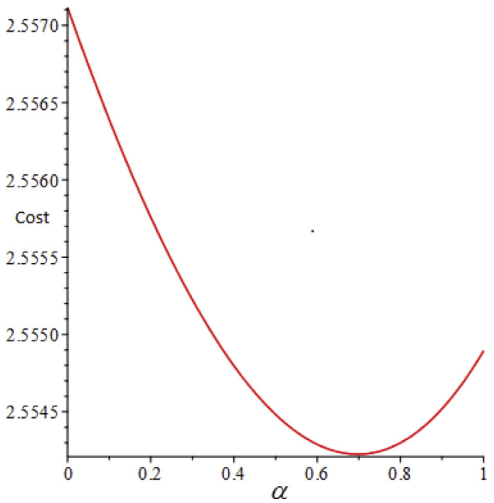

Fig. 6. Total cost $C_L E[L] + C_K E[K]$ as a function of α when $\alpha(k) = \frac{\alpha}{k}$ for values of example 6.1.

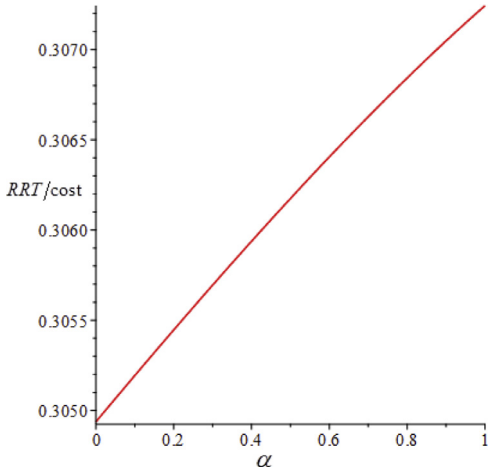

Fig. 7. The ratio $RRT_{Best-Fit}/[C_L E[L] + C_K E[K]]$ as a function of α when $\alpha(k) = \frac{\alpha}{k}$ for values of example 6.1.

In this case, the optimal value of α is $\alpha^* \cong 0.55$. Again, consideration of the rate of reward per dollar spent—as opposed to mere cost minimization—results in a higher value of α.

6.3. Probability of storing a kidney depending on the system-state

We now examine a case in which the probability of storing a kidney depends on the size of the queue of stored kidneys. It seems reasonable to assume that $\alpha(k)$ should decrease with k, the number of kidneys being stored in anticipation of candidates' arrival. Thus, we assume that $\alpha(k) = \frac{\alpha}{k}$. Using the same data given in the example in Section 6.1, Fig. 6 depicts the total cost as a function of α, and Fig. 7 shows the ratio $RRT_{Best-Fit}/[C_L E[L] + C_K E[K]]$ as a function of α.

Fig. 6 shows that the optimal value that minimizes the total cost is $\alpha^* \cong 0.7$, so that $\alpha^*(k) \cong \frac{0.7}{k}$.

Fig. 7 shows that the optimal value that maximizes the ratio $RRT_{Best-Fit}/[C_L E[L] + C_K E[K]]$ is $\alpha^* = 1$, so that $\alpha^*(k) \cong \frac{1}{k}$.

7. Conclusions

This work proposes and analyzes a novel approach for allocating randomly-arriving live organs (specifically, kidneys) to candidates waiting for transplantation. The method is based on the principle of best-HLA-fit. Specifically, an arriving organ is allocated to the candidate with whom its HLA match-level is highest among all waiting candidates, regardless of how long each candidate has been waiting for transplantation. Correspondingly, when it is possible to preserve kidneys and a queue of stored kidneys forms, an arriving candidate is matched with the best-fit kidney. We assign a transplantation reward to each HLA match-level, and introduce three new measures: $ERT_{Best-Fit}$ (Expected Reward per Transplantation under the best-HLA-fit rule), $RRT_{Best-Fit}$ (Rate of Reward from Transplantation realized under the best-HLA-fit rule), and $RRT_{Best\text{-}Fit}$ per dollar spent in candidate waiting costs and in kidney storage costs.

Organ preservation technology has an important role to play in increasing the number of available organs for transplantation. Our model explores a future scenario in which it will be possible to store kidneys for future transplantations, such that kidneys that arrive at an empty queue of candidates need not go to waste. By maximizing the rate of reward per one dollar of expenditure, reflected in the ratio $RRT_{Best-Fit}/[C_L E[L] + C_K E[K]]$, we have identified the optimal fraction of kidneys to be stored. Our numerical analysis shows that this optimal fraction depends on the decision maker's objective: Specifically, more kidneys should be stored when cost-effectiveness is the objective rather than mere cost minimization (i.e., minimization of $C_L E[L] + C_K E[K]$, which is the sum of candidates' waiting costs and kidneys' storage costs per unit of time).

One possible extension of our model is to consider multiple-type double-ended queues, where candidates are distinguished not only by their HLA compatibility, but also by their blood type. Studies by Stanford et al. [37] and recently by Perlman et al. [35] have taken a first step in this direction, studying two blood types in a one-sided queue, where unmatched kidneys are lost and cannot be stored.

Appendix A

$$E[K] = \frac{E[K]_{num}}{E[K]_{den}},$$

where

$$E[K]_{num} = \left(\frac{\lambda}{\delta}\right)^{\frac{\delta+\mu}{\delta}} \delta(\delta+\mu)\left(\frac{\alpha\mu}{\xi}\right)^{\frac{\lambda+\xi}{\xi}} \xi\alpha\mu \left(\frac{\lambda+\xi}{\xi} + \frac{(\alpha\mu-\lambda)\Gamma\left(\frac{\lambda+2\xi}{\xi}\right)\left(\frac{\alpha\mu}{\xi}\right)^{1-\frac{\lambda+2\xi}{\xi}}}{\xi} e^{\frac{\alpha\mu}{\xi}} + \frac{1}{\xi^2}\left(\left(-\alpha\mu\lambda - \alpha\mu\xi + \lambda^2 + \lambda\xi\right)\left(\frac{\alpha\mu}{\xi}\right)^{1-\frac{\lambda+2\xi}{\xi}} e^{\frac{\alpha\mu}{\xi}} \Gamma\left(\frac{\lambda+2\xi}{\xi} - 1, \frac{\alpha\mu}{\xi}\right)\right)\right),$$

and

$$E[K]_{den} = (\lambda+\xi)\begin{pmatrix} \xi\left(\frac{\alpha\mu}{\xi}\right)^{\frac{\lambda+\xi}{\xi}}\left(\left(\frac{\lambda}{\delta}\right)^{\frac{\delta+\mu}{\delta}}\delta(\delta+\mu) - \left((\delta+\mu)\Gamma\left(\frac{\delta+\mu}{\delta}, \frac{\lambda}{\delta}\right) - \delta\,\Gamma\left(\frac{2\delta+\mu}{\delta}\right)\right)\lambda e^{\frac{\lambda}{\delta}}\right) \\ -\mu\left(\frac{\lambda}{\delta}\right)^{\frac{\delta+\mu}{\delta}}\alpha\delta e^{\frac{\alpha\mu}{\xi}}(\delta+\mu)\left(\Gamma\left(\frac{\delta+\xi}{\xi}, \frac{\alpha\mu}{\xi}\right) - \Gamma\left(\frac{\delta+\xi}{\xi}\right)\right) \end{pmatrix}.$$

$$E[L] = \frac{E[L]_{num}}{E[L]_{den}},$$

where

$$E[L]_{num} = \lambda\left(\frac{\lambda}{\delta}\right)^{\frac{\delta+\mu}{\delta}} \delta\left(\frac{\alpha\mu}{\xi}\right)^{\frac{\lambda+\xi}{\xi}} \xi \left(\frac{(\lambda-\mu)\Gamma\left(\frac{2\delta+\mu}{\delta}\right)\left(\frac{\lambda}{\delta}\right)^{1-\frac{\mu+2\delta}{\delta}}}{\delta} e^{\frac{\lambda}{\delta}} + \frac{1}{\delta^2}\left(\left(-\delta\lambda + \delta\mu - \lambda\mu + \mu^2\right)\left(\frac{\lambda}{\delta}\right)^{1-\frac{\mu+2\delta}{\delta}} e^{\frac{\lambda}{\delta}} \Gamma\left(\frac{\mu+2\delta}{\delta} - 1, \frac{\lambda}{\delta}\right)\right)\right),$$

and

$$E[L]_{den} = (\delta+\mu)\begin{pmatrix} \xi\left(\frac{\alpha\mu}{\xi}\right)^{\frac{\lambda+\xi}{\xi}}\left(\left(\frac{\lambda}{\delta}\right)^{\frac{\delta+\mu}{\delta}}\delta(\delta+\mu) - \left((\delta+\mu)\Gamma\left(\frac{\delta+\mu}{\delta}, \frac{\lambda}{\delta}\right) - \delta\,\Gamma\left(\frac{2\delta+\mu}{\delta}\right)\right)\lambda e^{\frac{\lambda}{\delta}}\right) \\ -\mu\left(\frac{\lambda}{\delta}\right)^{\frac{\delta+\mu}{\delta}}\alpha\delta e^{\frac{\alpha\mu}{\xi}}(\delta+\mu)\left(\Gamma\left(\frac{\delta+\xi}{\xi}, \frac{\alpha\mu}{\xi}\right) - \Gamma\left(\frac{\delta+\xi}{\xi}\right)\right) \end{pmatrix}.$$

Appendix B

Proof of Proposition 4. When $K \geq 1$, an arriving candidate gets a kidney immediately (i.e., with probability 1). This occurs with probability $\sum_{k=1}^{\infty} q_k$. When $(L=n \geq 0,\ K=0)$ an arriving candidate joins the queue in position $n+1$ and resides in the system for a length of time drawn from an Erlang distribution with parameter μ and $n+1$ stages. Using $\sum_{n=0}^{\infty} p_n^{\delta=0} \int_{x=0}^{t} \frac{\mu^{n+1}x^n}{n!} e^{-\mu x} dx = p_0^{\delta=0} \frac{\mu}{\mu-\lambda}(1 - e^{-(\mu-\lambda)t})$ completes the proof. □

Appendix C

Proof of Proposition 5. The proof relies on arguments similar to those used in the proof of Proposition 4. $P(S_{FCFS} \leq t) = \sum_{n=1}^{\infty} p_n^{\xi=0} \cdot 1 + (1-\alpha)p_0^{\xi=0} \cdot 1 + \alpha p_0^{\xi=0}(1 - e^{-\lambda t}) + \alpha \sum_{k=1}^{\infty} q_k^{\xi=0} \int_{x=0}^{t} \frac{\lambda^{k+1}x^k}{k!} e^{-\lambda x} dx$, where the integral in the fourth term of the right-hand side is the Erlang pdf. Using $q_k^{\xi=0} = (\frac{\alpha\mu}{\lambda})^k p_0^{\xi=0}$ and some algebra the claim is proved. □

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