

MDPI

Article

A Federated Blockchain Approach for Fertility Preservation and Assisted Reproduction in Smart Cities

Da-Yin Liao

Straight & Up Intelligent Innovations Group Co., San Jose, CA 95113, USA; eliao@miicg.com

Abstract: Modern life is making people infertile. Giving birth later in life is wreaking havoc on our fertility and threatening human survival. Smart cities intend to optimize the quality of life of their citizens by utilizing technology for smarter living. This research first identifies the requirements and business opportunities of using advanced technology for smarter fertility preservation and assisted reproduction in smart cities. A federated blockchain approach is proposed for the alliance of integrated commercial egg banks (ICEBs). In particular, we designed a membership fee rebate (MFR) mechanism that offers incentives for blockchain creations in the egg banking alliance. We formulated the MFR problem into a leader-followers Stackelberg game whose objectives are (1) to maximize the benefits of forming the alliance (the leader) and (2) to maximize the benefits in each ICEB (the follower). We developed an iterative scheme that utilizes mathematical programming techniques to solve the two-level, Stackelberg game problem. With a given set of parameters of the alliance and membership fee function, and the average number of blocks generated for an oocyte, the iterative scheme achieves the optimal solution for the MFR rate per block created . A numerical example demonstrates the feasibility and applicability of the proposed iterative scheme. Numerical results show that it achieves good solutions in adding a small to medium-sized new ICEB to the existing alliance. The proposed federated approach lays the foundation for developing a blockchain-based egg banking platform.

Keywords: federated blockchain; consortium blockchain; smart cities; fertility preservation; commercial egg bank; membership fee; Stackelberg game



check for

Citation: Liao, D.-Y. A Federated Blockchain Approach for Fertility Preservation and Assisted Reproduction in Smart Cities. *Smart* Cities 2022, 5, 583–607. https:// doi.org/10.3390/smartcities5020031

Academic Editors: Renita Murimi and Zhixiang Fang

Received: 27 February 2022 Accepted: 29 April 2022 Published: 3 May 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

1. Introduction

"I want to be a mom!"—a strong but helpless voice frequently heard in clinical infertility practice. Most people in the world have the strong desire to conceive children during their lifetimes. However, with a trend toward late childbearing, more and more people are suffering from infertility in modern life. The global fertility rate continues to declinin and has hit an all-time low during the COVID-19 pandemic [1]. About half of the world's population lives in low-fertility countries whose fertility rates are less than replacement level—the average number of children born per woman needed to replace a population from one generation to next generation [2]. In the United States, about 15% of couples have infertility problems [3]. The contributing factors, including giving birth later in life, air pollution, human-made chemicals, tobacco or alcohol use, overweight or underweight, diabetes and more, are wreaking havoc on our fertility and threatening human survival [4]. Women are deferring child birth until their thirties and forties. This has led to female age-related infertility, the most common cause of infertility today [5].

While many countries and municipalities have embraced the concept of smart cities [6,7] for years, a precise definition of "smart cities" has remained elusive. Tech giants have imagined the way that technology could be used to make cities smart. City majors and people running for election want smart cities to attract more businesses and talent to make their cities more prosperous, more livable and more job-rich. Their dream for smart cities is to fulfill the needs of their citizens while optimizing the quality of life

of their citizens by utilizing technology for smarter living [8–12]. Among modern citizens' needs, fertility preservation and assisted reproduction [13,14] are crucial considerations for smart cities.

Fertility preservation and assisted reproduction help reproductive-aged young women retain their fertility to have biological children in the future. Thanks to the advance of vitrification technology [15], efficient and safe oocyte cryopreservation [16] (or egg freezing [17]) is considered the most applicable option for fertility preservation. The situations in which women demand egg freezing are various. The female may expect future reproduction prior to cancer treatment or be at risk for a medical condition that may impact fertility in future. Alternatively, there may be extra embryos left during an *in vitro* fertility (IVF) cycle. Oocyte donation to donor egg banks for IVF is another one. Finally, the female may extend childbearing years in order to counter future infertility [18]. Egg freezing empowers women to preserve their eggs either for use when they are ready to have babies; or for donation or sale of unused eggs to infertile women. Analysis of the U.S. National Assisted Reproduction Technology (ART) data during period of Years 2013 through 2015 indicates that utilization of traditional fresh oocyte donation rapidly declined by 32.9%, whereas frozen oocyte donation increased by 44.4% [19]. The egg banking system was thus developed and is a kind of insurance against the female biological clock.

An egg bank [20], also called "donor egg bank" or "commercial egg bank" (CEB), is a commercial repository that saves cryopreserved human eggs with the purpose of female fertility preservation for future use. An egg bank is an entity which provides cryopreserved oocytes to intended recipients of egg donation. In addition to oocyte cryostorage for fertility preservation, it offers strong benefits in terms of scheduling flexibility, improved clinical efficiencies and a wider immediate inventory choice. As shown in Figure 1, the CEB is a part of the landscape in integrated commercial egg banking (ICEB) whose functions cover cryopreservation, ART services portal, extensive medical assessment, rigorous donor screening, networking of affiliated IVF centers, medical training and surrogate agency. There are several parties involved in an ICEB, including intended parents, donors of eggs, IVF laboratories, partnered CEBs, courier services providers and transportation, lodging and foods providers. Effective fertility preservation and assisted reproduction demand high quality environment control of temperature, pH and osmolality; low oxygen, volatile organic compounds and particulate matter; and low aspiration pressure [21,22]. IoT (Internet of Things) or AIoT (Artificial Intelligence of Things) sensors are used to monitor and measure many sources of data for environment control in IVF clinics, laboratories and egg banks. Sensors are crucial to the operations of the IVF clinical instruments, laboratory, egg banking facilities and devices for cryopreservation.

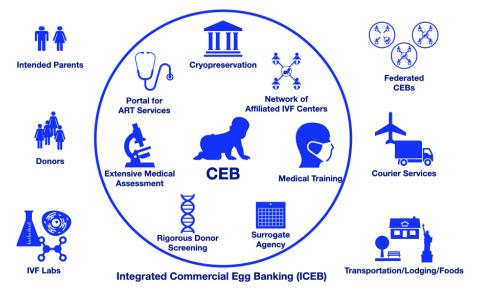


Figure 1. The landscape of an ICEB.

Daily activities in an ICEB use and generate a huge amount of data. In additional to traditional relational databases, an ICEB utilizes NoSQL databases for managing big data analytics. Management of the data in an ICEB involves the integration of various entities with heterogeneous data stored in different relational and NoSQL databases. Storing, updating and replicating these data are restricted to one or a few authorized entities that have to be trusted not to mess up the data or get hacked. Effective integration of these relational and NoSQL databases is quite challenging and can create a big headache for the IT team in an ICEB.

Differently from existing biobanks that collect biological samples of tissue of human beings, an ICEB is novel and focuses on the choice of the depositor, who must invest money and body to obtain the banked entity [23]. In addition to the safety, efficacy and cost of IVF treatments, egg banking also faces many other challenges, such as medical, ethical, moral and social concerns [24,25]. Among these, issues of integrity, consistency, privacy and physical protection of eggs and their associated data are mostly addressed along the entire egg banking process—from the retrieval of an egg to its successful placement in the uterus, or the eventual death by discard or removal from its egg banking.

Blockchain technology [26] uses a distributed data structure in creating the digital ledger of data and sharing it among a network of participating nodes. It uses cryptography and allows each participant in the network to maintain the digital ledger in a secure way. Blockchain technology is useful for applications that need redundant copies in multiple distributed computers, trust among all the participants and lack a trusted third party [27]. Compared to the traditional databases, blockchain technology is good at the integration of systems in supply chain management system or in a federated consortium of independent parties where there is more than one authorized entity and there is a trust deficit between the parties [28]. The advantages of using blockchain technology for egg banking are to ensure transparency and security of the operations of eggs and their data in the egg banking process. The decentralized structure of blockchain allows all parties to participate in supply chain management of the eggs. Blockchain can establish an organization-encompassing platform to exchange information to meet the requirements of managing physical eggs and their data in the egg banking process. This paper deals with the coalition of federated ICEBs and presents the preliminary design of an on-going project: a Blockchain-based, Automated, Biomedical Implementation for Egg Saving (BABIES) platform for management of the egg banking operations in the federated ICEBs.

Blockchain technology maintains a distributed ledger of immutable, auditable and single-version-of-truth data. Blockchain technology holds many important advantages in decentralization, data integrity, security, transparency, audibility and automation. It enables simple, traceable and trustworthy data sharing in a data ecosystem. A blockchain is a decentralized tamper-proof ledger which keeps an append-only, sequenced set of transactions. Before adding a transaction to a blockchain, a new block is created for the transaction and the block for the transaction has to be verified through a decentralized consensus process among the nodes in the blockchain network. Blockchain technology has a wide range of applications in smart cities [29–31]. In this paper, a node that participates in the consensus process is called a *block creator* or a *creator*. Such operations are called *block creation* or *creation*. A prime creator is a creator that receives a request for creating a new block and creates the new block. In this paper, only the prime creator can receive an incentive for each block creation.

While public blockchain networks suffer from high costs and long delays in creation and synchronization of new blocks, private blockchain networks allow only invited (or permissioned) participants to join, with access being controlled by a single organization. Compared to public and private blockchain networks, federated blockchain (also knows as consortium blockchain) [32] networks are managed by consortia of pre-selected participants or organizations. A federated blockchain has the advantages of modest cost and computing requirements, good scalability and short delay. However, allying a blockchain consortium demands cooperation among a number of participants or organizations. A participant or

organization that considers teaming up with its partners or even its competitors, must weigh the potential benefits of cooperation and the possible conflicts of interest. Each participant or organization requires sufficient motivation and incentive to join the alliance and remain faithful to the alliance.

This research deals with the smart application that utilizes blockchain technology for egg banking of fertility preservation and assisted reproduction in smart cities. We first identify the requirements and business opportunities involved in using advanced technology for smarter egg banking. Then, we propose a federated blockchain approach for the alliance of ICEBs. In particular, we focuse on the optimal design of an incentive mechanism for blockchain operations of egg banking, from which a decision-making problem to find the best membership fee rebate (MFR) rate per block creation is modeled. We formulate the MFR optimization problem into a leader–followers Stackelberg game whose objectives are to maximize the benefits of forming the alliance (the leader) and to maximize the benefits in each ICEB (the followers). We developed an iterative scheme that utilizes mathematical programming techniques to solve the two-level cooperative game problem. With a given set of parameters of the alliance and membership fee function, and the average number of blocks generated for an oocyte, the iterative scheme achieves the optimal solution for the MFR rate per block creation.

The main contributions of this paper are fivefold:

- (1) We propose a novel federated business model for ICEBs and utilize blockchain technology to ensure safe and secure egg banking operations for fertility preservation and assisted reproduction in smart cities. To the best of found knowledge, there are no research results or clinical applications using blockchain technology for safe and secure data exchange in egg banking.
- (2) We developed an MFR mechanism for the incentives for blockchain operations of egg banking.
- (3) We formulated the MFR problem as a two-level Stackelberg game between the egg banking alliance and the ICEBs. We utilized mathematical programming techniques to find the optimal MFR rate for the incentives of blockchain operations in egg banking.
- (4) We developed a federated egg banking incentive solution (FEBIS) algorithm to determine the optimal MFR rate per block creation and the optimal number of oocytes in each ICEB to participate the egg banking alliance.
- (5) This paper presents the preliminary design, components and functionalities of the developing Blockchain-based, Automated, Biomedical Implementation for Egg Saving (BABIES) platform.

The remainder of this paper is organized as follows. Section 2 reviews the related works of fertility preservation, applications of blockchain in the healthcare domain and game-theoretic incentive mechanisms for blockchains. Section 3 identifies the requirements and business opportunities of egg banking, presents the alliance business model of ICEBs and proposes the federated blockchain approach for egg banking. In Section 4 we develop the optimal design of an MFR mechanism for blockchain operations. Section 5 reports the numerical tests and analysis of the results. Section 6 presents the system architecture and software stack of the Blockchain-based, Automated, Biomedical Implementation for Egg Saving (BABIES) platform. Section 7 concludes this paper.

2. Related Works

Since the birth of the first "test tube baby" in 1978, medical research and clinical efforts have devoted in ART and helped millions of desperate-for-babies people to conceive [33]. In the United States, ART accounted for 2.1% of all infants born in 2019 [34]. As the most effective form of ART, IVF deals with complicated procedures to help people with fertilization, embryo development and implantation for the conception of babies. IVF can be done either with fresh donor oocytes or through cryopreservation and thaw cycles of donor oocytes [35]. As cryopreservation techniques have evolved, vitrification has played a vital part in contemporary ART. The success rates with donor oocyte vitrification show similar clinical efficiency to that of

IVF with fresh donor oocytes [36]. Oocyte vitrification and saving provides an efficient option for fertility preservation for young women under 38 years old [37]. Egg saving empowers women to continue their careers and find their right partners with no fear of jeopardizing fertility. Like egg donation, egg saving has faced ethical, legal and religious concerns [38]. A growing and diverse transformation on technical, regulatory and commercial aspects has reshaped the assisted reproduction landscape [39].

The establishment of an egg banking facility requires an expert team of fertility specialists, embryologists and skilled laboratory operators in oocyte vitrification; and a complex support team dealing with legal, recruiting, compliance and marketing tasks [40]. Effective egg banking demands a set of optimized ART protocols that are implemented in a smart, automated and integrated biomedical platform both for safe, reliable and secure oocyte storage and transport during cryopreservation, and for data security, privacy and analytics of bioinformatics.

Over the last decade, CEBs have emerged and been evolving into several operational models—affiliated, networked and central [41,42]. In the affiliated model, the CEB only works with its affiliated IVF clinic. In the networked model, the CEB works with the network of affiliated IVF clinics. In the central model, the CEB works with any interested IVF clinic if it is technically, legally and commercially feasible. All these operational models are centered on only a single CEB. While egg banking is now gaining more professional and public acceptance, CEBs are grasping the great opportunity. However, existing CEBs are facing severe challenges of operational inefficiency, high costs and low customer satisfaction. The emergence of ICEB demands a paradigm shift for more collaboration and coalition among egg banking facilities to create high economic efficiency, lower operating costs and provide high customer satisfaction.

Applications of blockchain technology in the healthcare sector have been emerging for years [43–45]. Hickman et al. [46] provided a systematic review of the use of blockchain technology in the healthcare industry and found no solutions proposed for IVF or fertility. Benchoufi and Ravaud [47] explored the core functionalities of blockchain applied to clinical trials. The use of artificial intelligence and big data in reproductive medicine has just begun [48]. Blockchain-based data sharing in ART is promising to promote collaborative research and innovation while reducing the costs of validation and implementation of artificial intelligence [49]. Yaqoob et al. [50] considered the application of blockchain for healthcare data management systems to stimulate innovations and bring major improvements. A thorough search of this relevant topic shows that there are no research results or clinical applications using blockchain technology for safe and secure data exchange throughout the egg banking process.

Numerous research efforts have adopted game theory as the analytic tool to elucidate various facets in blockchain-related issues, such as security challenges, computational power allocation, incentive consensus and energy trading [51]. Researchers have developed Stackelberg game [52] models to formulate the interactions in distributed blockchain networks. Bai et al. [53] proposed a hybrid consortium blockchain architecture for public participation in smart city governance. To deal with the risks of malicious attacks, they developed a Stackelberg-game-based incentive mechanism to encourage public participation in the transaction verification process. Xiong et al. [54] used a two-stage Stackelberg game model to deal with the interactions between the cloud/fog computing providers and the block creators in the blockchain consensus process. By applying the pricing policy of the same price to all creators, they validated the uniqueness of the Stackelberg equilibrium and identified the best response strategies of the creators. Ding et al. [55] dealt with the pricing and budget allocation problem between edge servers and IoT devices, whose interactions were modeled as a multi-leader, multi-follower Stackelberg game. Hu et al. [56] designed a novel autonomous client participation scheme to incentivize a federation of clients to train a machine learning model. Their minority-game-based client participation scheme can boost utility by 39% to 48% and reduce volatility by 51% to 100%. We aimed to design

an optimal incentive mechanism for blockchain operations in the alliance of ICEBs, where the optimal incentive problem is modeled as a two-level Stackelberg game problem.

3. Federated Blockchain Approach for Egg Banking

3.1. Needs of Advanced Technology and Integration for Egg Banking

Successful egg banking services encompass a wide variety of activities, operations and functions covering many domains, including environmental control, technology innovation, service optimization, compassionate care, partnership management and continuous improvements. Figure 2 illustrates the activities, operations and functions for egg banking services



Figure 2. Activities, operations and functions for successful egg banking services.

People spending their time and money on egg banking are looking for fertility preservation and expect someday to have *healthy babies*—the ultimate value of egg banking. To let people have healthy babies, egg banking must provide careful, legal, safe, predictable, quality and friendly operations and services. In ART practice, egg banking uses many applications and systems to support its activities, operations and functions, including hospitality services, protocol management, a picture archiving and communication system (PACS), access control, digital identity, analytics, intelligent medicine, automation, laboratory integration, a laboratory information management system (LIMS), a hospital information system (HIS), a portal and case management. However, most of these systems are poorly integrated and composed of silos of raw health data.

To achieve seamless integration of the systems, egg banking is embracing advanced technology for its system integration and operations automation [57,58]. This research envisions the opportunities for the amalgamation of different cutting-edge technologies with smarter operations for better egg banking services. Promising technologies for effective egg banking include blockchain technology, X-as-a-Service, Artificial Intelligence of Things (AIoT), edge computing, security, radio frequency identification (RFID), statistical learning, machine learning, knowledge inferencing, end-to-end tracking, automated loading and unloading, Open Platform Communications Unified Architecture (OPC UA), small cells, microservices and so on.

3.2. Federated Egg Banking Business Model

We propose a federated operational business model for egg banking. As shown in Figure 3, two or more ICEBs form a federated egg banking ecosystem. Each ICEB

established on its own protocols, defines its own performance indicators and provides egg banking services to its affiliated IVF clinics or fertility centers. An IVF clinic or fertility center may belong to one or more ICEB, depending on its operational efficiency and effectiveness. In the federated ecosystem, each ICEB can exchange secured medical data and provide frozen oocytes to other ICEBs for commercial purposes.

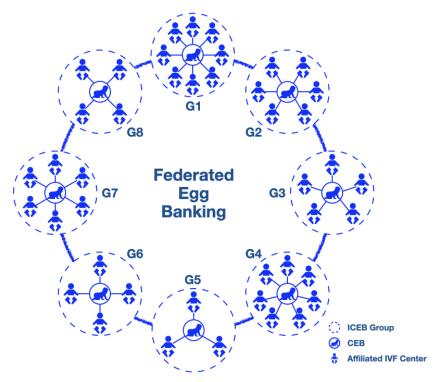


Figure 3. The federated egg banking business model.

Differently from the existing affiliated, networked and central CEB operational models [20,41,42], the proposed federated business model extends the boundaries and flexibility of the egg banking business. It allows each ICEB to make use of the ecosystem for its own benefit while collaborating with other ICEBs in the ecosystem. However, many challenges arise with the federated business model. There are concerns of data integrity, security, visibility and ownership for data exchange among the ICEBs in the ecosystem. There are also issues of oocyte safety, identification and consistency in storage and transportation along the whole egg banking process. This paper adopts blockchain technology to tackle the challenges of data integrity, security, visibility and ownership for data exchange among the ICEBs. Additionally, blockchain technology facilitates the safety, identification and consistency of oocytes along the entire egg banking process.

The key to the proposed federated egg banking business model is to form the egg banking alliance (EBA). An EBA is a strategic alliance of a number of ICEBs that cooperate in terms of sharing resources (i.e., oocytes and their data in each ICEB) to achieve some specific goals. The main purpose of the EBA is to increase the market demands for the alliance members, i.e., the ICEBs. For a participating ICEB, the EBA offers a great opportunity to expand its economies of scope through diversification of available oocytes. The member ICEB can extend its existing capabilities by providing a wider variety of oocytes available for patients to choose. A primitive motivation for an ICEB to join the EBA is the benefits from increasing its profits through resource sharing. Managing interactions among the ICEBs from the EBA is challenging. Fair allocation of benefits and obligations is the key to establishing and sustaining the EBA. In order for a participating ICEB to remain faithful to the alliance, the EBA should share the benefits from cooperation fairly among its member ICEBs and apply fair membership rules to its member ICEBs.

We developed a two-level Stackelberg game to formulate the interactions between the EBA and the ICEBs in the proposed federated egg banking business model. In the upper level, the goal of the EBA is to maximize the joint economies of scope of the alliance, while allocating a portion of benefits from cooperation to its member ICEBs as incentives. On the other hand, in the lower level, the goal of each ICEB is to maximize its benefits to join and remain in the alliance, while keeping its expenses lower than its budget. For an ICEB, its benefits from cooperation include the gain of its extra economies of scope and the sharing of benefits of cooperation. In the model, knowledge about other participants is available to all the participants, making it a game with complete information.

3.3. Federated Blockchain Approach

Blockchain enables distributed trust over the Internet and simplifies complex transactions. Based on the proposed federated egg banking business model, this section presents a federated blockchain approach for egg banking of fertility preservation and assisted reproduction in smart cities. The federated blockchain approach adopts the federated blockchain (or consortium blockchain) technology [32]. A federated blockchain is a permissioned blockchain that can offer the advantages of faster speed, higher throughput, privacy and low power consumption, compared to permissionless public blockchain technology (e.g., Bitcoin and Ethereum). The federated blockchain approach defines two types of participants: (1) blockchain users and (2) block creators. Only verified blockchain users are allowed to have their own individual copies of the blockchain; and only preselected block creators can participate in the consensus mechanism in the blockchain, i.e., maintaining and determining the true state of the blockchain. Federated blockchain technology is useful for the egg banking ecosystem where the identity of each participant—the ICEB, intended parent, donor, IVF lab, surrogate agent, courier service provider or transportation/lodging/foods provider—can be pre-determined and easily verified. In the federated blockchain approach, all the verified participants in the egg banking ecosystem are blockchain users, but only the preselected ICEBs from the alliance EBA are block creators. Figure 4 shows the block creators (the ICEBs) and blockchain users (all the participants in egg banking activities) in the federated egg banking blockchain system.

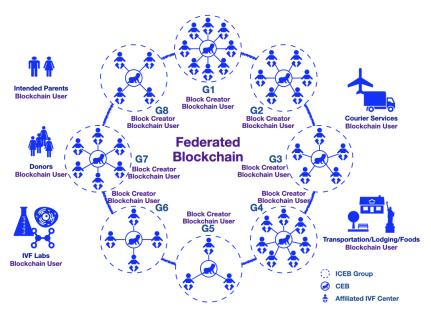


Figure 4. Block creators and blockchain users in the federated egg banking blockchain system.

3.4. Federated Egg Banking Blockchain

The federated egg banking blockchain is a blockchain of oocytes which are created, stored and maintained in the federated, blockchain-based egg banking system. The federated egg banking blockchain records all the transaction data of every oocyte, starting

from oocyte retrieval to fertilization, if the oocyte is lucky enough to survive to the end. In the egg banking system, a transaction is an activity or information update of an oocyte. Each transaction creates and appends a new block to the blockchain. In practice, dozens of transaction records are generated along the egg banking lifecycle of an oocyte. Figure 5 illustrates a typical egg banking workflow for an oocyte.

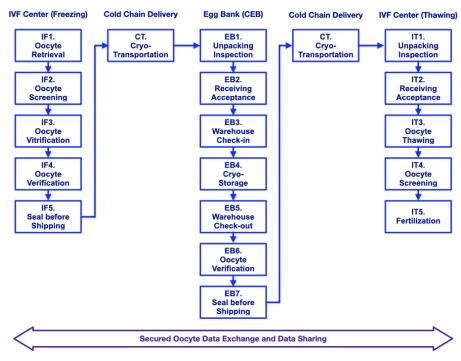


Figure 5. A typical egg banking workflow from oocyte retrieval to fertilization.

The federated egg banking blockchain stores a cascade of blocks of oocytes' transactions in the egg banking system. Each block contains a block header and a body. A block header is composed of the hash of its previous block, the Merkle root, a timestamp of the block and nonce (number only used once) used by creators. The body in a block stores a Merkle tree of transaction data. In the body, transaction data are hashed first, paired with one another and structured into a Merkle tree. The root of the Merkle tree is called the Merkle root, which has all the information of the transaction data in the block. Due to its tree structure, verification with a Merkle tree is very efficient.

The federated egg banking blockchain system adopts the Practical Byzantine Fault Tolerance (PBFT) [59] consensus protocol in appending a new block. In the consensus process, only block creators can participate. The creation of a new block is successful only after the majority of the block creators (more than two-third of the creators) agree upon the new block. For each block creation, the federated egg banking blockchain system provides an incentive to the prime creator that receives the request of a transaction and creates the new block.

The blockchain operations in the federated egg banking blockchain system can be summarized as follows:

- (1) A blockchain user initiates a request to a prime creator for a new transaction for an oocyte.
- (2) The prime creator disseminates the transaction into a block.
- (3) The prime creator multicasts the new block to the federated blockchain system.
- (4) All blockchain creators verify the block and multicast to the other creators.
- (5) The majority of block creators reach a consensus and agree upon the new block.
- (6) The new block is appended to the blockchain. Every blockchain user updates its local replica of the blockchain.

(7) Only the prime creator of the new block receives an incentive.

Figure 6 depicts the blockchain operations in the federated egg banking blockchain system with *I* blockchain creators.

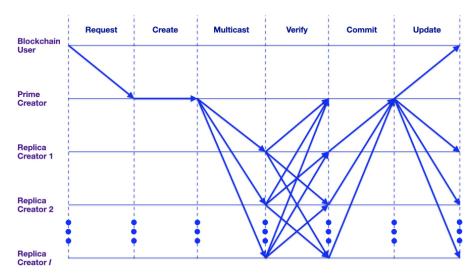


Figure 6. The blockchain operations in the federated egg banking blockchain system.

In the federated egg banking blockchain system, the success of a consensus process requires all the distributed block creators (the ICEBs in the EBA) to participate and reach an agreement on whether to accept a new transaction of an oocyte or not. Completing a consensus process demands computing power from the block creators. In the EBA, every ICEB has to spend capital on information technology (IT) to support the blockchain operations. We designed a membership fee rebate (MFR) mechanism as the incentive to financially motivate the ICEBs for their contributions to blockchain operations in the EBA.

4. Optimal Incentive Design for Egg Banking Blockchain Operations

We propose an incentive mechanism that offers a membership fee rebate (MFR) to the prime creator of a new block in egg banking blockchain operations. The rebate is paid to each creator (the ICEB) annually and on a *pro rata* basis according to the total number of new blocks created by the creator during the past year. The effectiveness of the proposed incentive mechanism depends on the selection of a good MFR rate to encourage the ICEBs to contribute to egg banking blockchain operations. The higher the MFR rate is, the more the ICEBs will be willing to participate in the alliance. However, on the other hand, the alliance has to pay more for MFRs with a higher rebate rate. Selection of a good rate for MFR must leverage between the cooperation benefits vs. costs. This section presents the optimal design for the MFR rate as the incentive for blockchain operations in the federated egg banking blockchain system.

4.1. Problem Formulation

Consider a federated egg banking blockchain system with a number of block creators (the ICEBs) that are interested to form the alliance (the EBA). Define customer satisfaction as a function of number of candidate oocytes for patients to choose. Additionally, define member participation as a function of MRF rate (i.e., the average MFR per block creation). The goal to form the alliance is to maximize the overall customer satisfaction and member participation from cooperation of the member ICEBs. The objective of each ICEB is to maximize its profit from joining the alliance and its received MFRs as the incentive for its blockchain operations. Each ICEB decides on the number of its oocytes participating in the alliance. Membership fees are collected from every member ICEB to establish the alliance and support the alliance service. Some of the membership fees are rebated as the incentives to member ICEBs for their support to the blockchain operations. The amount of

the membership fee paid by an ICEB depends on its number of oocytes participating in the alliance.

To continue the development of the optimal incentive design, assumptions and notation are listed as follows:

Assumptions:

- (1) All the decisions of the ICEBs are economically rational.
- (2) All the ICEBs have perfect information.
- (3) All the ICEBs have freedom of choice to join or not to join the alliance.
- (4) The decision for an ICEB to join the alliance only depends on the MFR rate and its number of oocytes participating in the alliance.
- (5) Each oocyte is unique and distinct.

Notations:

A : set of the Federated Egg Banking Alliance, i.e., the EBA

I: total number of ICEBs in A

 \mathbb{B}_i : *i*th ICEB, $i = 1, \dots, I$

 O_i : number of oocytes in \mathbb{B}_i , $O_i > 0$

 C_i : budget limit of \mathbb{B}_i for membership fee expenditure

N: average number of blocks generated by an oocyte in \mathbb{A} , N > 0

 α : weighting factor for the satisfaction function, $\alpha > 0$

 β : weighting factor for the utility function for profit, $\beta > 0$

 ρ : ratio of membership fees allocated for rebate, $0 \le \rho \le 1$

a : constant coefficient of the satisfaction function, a > 0

b : constant coefficient of the participation function, b > 0

m, n: constant coefficients of the membership fee function, m > 0, n > 0

r: constant coefficient of the utility function for profit, r > 0

<u>Decision Variables</u>

 u_i : number of oocytes in \mathbb{B}_i to participate in \mathbb{A} , $0 \le u_i \le O_i$

v: MFR rate per block creation, v > 0

Without loss of generality, assume that all the ICEBs in the alliance \mathbb{A} are sequenced in an ascending order according to their numbers of oocytes in the ICEBs, that is, $\{\mathbb{B}_i|O_1\leq O_2\leq \cdots \leq O_I\}$.

Let $W_{-1}(xe^x) = x \le -1$, $-\frac{1}{e} \le xe^x < 0$ denote the second branch of the Lambert W function.

This paper adopts the following four functions to model the objectives of the optimal incentive problem:

(i) The *satisfaction* function $\phi(x)$ for customer satisfaction from the egg banking service with x participating oocytes:

$$\phi(x) = \ln(1 + ax), \quad \text{where } x \ge 0; \tag{1}$$

(ii) The *participation* function for an MFR rate of *x* per block creation:

$$\eta(x) = bx, \quad \text{where } x \ge 0;$$

(iii) The *membership fee* function $\xi(x)$ for participating x oocytes in \mathbb{A} :

$$\xi(x) = m \ln(1 + nx), \quad \text{where } x \ge 0; \tag{3}$$

(iv) The *utility* function for profit $\psi(x)$ of participating x oocytes in \mathbb{A} :

$$\psi(x) = \frac{1}{1 + e^{-rx}}, \text{ where } x \ge 0.$$
 (4)

Note that all the above four functions, Equations (1)–(4) are strictly increasing on $x \ge 0$. The second derivatives of $\phi(x)$, $\xi(x)$ and $\psi(x)$ are negative and the second derivative of $\eta(x)$ is 0. The above four functions are strictly concave on $x \ge 0$.

For ICEB \mathbb{B}_i , the total amount of its MFR for blockchain operations can be calculated by vNu_i . This amount is capped by a predefined ratio ρ of its membership fee paid to \mathbb{A} . That is, $vNu_i \leq \rho \xi(u_i)$.

The objective of the federated egg banking alliance, \mathbb{A} , is to maximize the benefits by forming the alliance, i.e., the total customer satisfaction and member participation, while offering MFRs for federated blockchain operations. Mathematically, it is formulated as the following program:

maximize
$$\alpha \phi \left(\sum_{i=1}^{I} u_i \right) + \eta(v)$$
 (5)

subject to:

$$vNu_i \le \rho \xi(u_i), \forall i = 1, \cdots, I,$$
 (6)

$$0 \le u_i \le O_i, \forall i = 1, \cdots, I, \tag{7}$$

$$v > 0. (8)$$

For ICEB \mathbb{B}_i , its motivation to join \mathbb{A} and remain faithful to the alliance is to maximize its profit after joining the alliance and the collective MFRs for its contributions to blockchain operations, while satisfying its budget limit for membership expenditure. The following program describes the mathematical model:

$$\underset{u_i,v}{\text{maximize}} \ \beta \psi(u_i) + v N u_i \tag{9}$$

subject to:

$$\xi(u_i) - vNu_i \le C_i, \tag{10}$$

$$0 \le u_i \le O_i, \forall i = 1, \cdots, I, \tag{11}$$

$$v > 0. (12)$$

We adopted the Stackelberg game approach [52] to formulate the interactions between the alliance \mathbb{A} and the ICEBs $\{\mathbb{B}_i, i=1,\cdots,I\}$. The interactions follow a leader–followers decision making mechanism. At the leader level, the alliance \mathbb{A} offers to the ICEBS an MFR rate per block creation. At the follower level, the ICEBs determine their strategies to maximize their profits according to the offered MFR rate. In the Stackelberg game model, the alliance \mathbb{A} is the leader that determines the MFR rate per block creation, v. Additionally, each ICEB, \mathbb{B}_i , is the follower that determines its optimal number of participating oocytes for the coalition, u_i , to respond to the given MFR rate per block creation. Mathematically, the optimization problem is formulated as follows:

subject to: $vNu_i \le \rho \xi(u_i), \forall i = 1, \cdots, I,$ (13)

$$v > 0. (14)$$

Followers
$$(PB-i, i=1, \cdots, I)$$
: maximize $\Psi(u_i) \equiv \beta \psi(u_i) + vNu_i$

subject to:

$$\xi(u_i) - vNu_i \le C_i,\tag{15}$$

$$0 \le u_i \le O_i. \tag{16}$$

The above leader–followers problem forms a Stackelberg game whose objective is to find the Stackelberg equilibrium point of the game. For $\{u_i, i=1,\cdots,I\}$ and v satisfying Equations (13)–(16), the point $(\{u_i^*\}, v^*)$ is the Stackelberg equilibrium point if the following two conditions are satisfied:

$$\Phi(\{u_i^*\}, v^*) \ge \Phi(\{u_i^*\}, v),\tag{17}$$

$$\Psi(u_i^*) \ge \Psi(u_i), \quad \forall i = 1, \cdots, I. \tag{18}$$

4.2. Solution Methodology

4.2.1. Solution to the Leader Optimization Problem (PA)

As $\frac{\partial^2\Phi(v)}{\partial v^2}<0$, $\Phi(v)$ is strictly concave. The leader optimization problem (PA) is a convex optimization problem. The optimal solution to (PA) must satisfy the Karush–Kuhn–Tucker (KKT) conditions [60], the first-order necessary conditions for an optimal solution to a convex optimization problem.

Define the Lagrangian function L_A as:

$$L_A(\{\lambda_i\}) = -\alpha \phi \left(\sum_{i=1}^{I} u_i\right) - \eta(v) + \sum_{i=1}^{I} \lambda_i [vNu_i - \rho \xi(u_i)], \tag{19}$$

where $\{\lambda_i | \lambda_i \ge 0, i = 1, \dots, I\}$ are the Lagrange multipliers associated with the conditions in Equation (13).

The KKT conditions, in addition to the constraint Equation (14), are:

$$\frac{\partial L_A(\{\lambda_i\})}{\partial v} = -b + \sum_{i=1}^{I} \lambda_i N u_i = 0, \tag{20}$$

and:

$$\lambda_i[vNu_i - \rho\xi(u_i)] = 0, \forall i = 1, \cdots, I.$$
(21)

As b>0, according to Equation (20), $\exists u_j>0$ and $\exists \lambda_j=\frac{b}{Nu_j}>0$. In Equation (21), $vNu_j-\rho\xi(u_j)=0$ or $v=\frac{\rho\xi(u_j)}{Nu_j}>0$. For $i=1,\cdots,I$, if $u_i\neq u_j,\lambda_i=0$. Hence, Equations (20) and (21) of the KKT conditions and Equation (14) are satisfied. To satisfy Equation (13), for $i=1,\cdots,I,i\neq j,vNu_i\leq \rho\xi(u_i)$. Therefore, $v\leq\min\left\{\frac{\rho\xi(u_i)}{Nu_i},\forall u_i>0,i\neq j\right\}$. Combining with $v=\frac{\rho\xi(u_j)}{Nu_j},u_j>0$, the following lemma holds:

Lemma 1. For a given set of $\{u_i|u_i>0, i=1,\cdots I\}$, $v^*=\min\left\{\frac{\rho\xi(u_i)}{Nu_i}, i=1,\cdots,I\right\}$ is the optimal solution to the leader optimization problem (PA).

Note that $v \leq \min\left\{\frac{\rho\xi(u_i)}{Nu_i}, \forall u_i > 0\right\} = \min\left\{\frac{\rho\xi(u_i)}{Nu_i}, \forall u_i \geq 1\right\} \leq \frac{\rho\xi(1)}{N} = \frac{\rho m \ln(1+n)}{N}.$ That is, this value of $\frac{\rho m \ln(1+n)}{N}$ provides an upper bound to v. Consider the set of $\{u_i = O_i, \forall i = 1, \cdots, I\}$. Since $0 < O_1 \leq O_2 \leq \cdots \leq O_I$ and the function of $\frac{\rho\xi(u_i)}{Nu_i}$ monotonically decreases, for $O_i \leq O_j, \frac{\rho\xi(O_j)}{NO_j} \leq \frac{\rho\xi(O_i)}{NO_i}$. From Lemma 1, $v^* = \frac{\rho\xi(O_I)}{NO_I}$ is the optimal solution to the leader optimization problem (PA). As the leader of the Stackelberg game model, the alliance \mathbb{A} , therefore, offers $v^* = \frac{\rho\xi(O_I)}{NO_I}$ as the MFR rate per block creation to the ICEBs.

4.2.2. Solution to the Follower Optimization Program (PB - i)

As $\frac{\partial^2 \Psi(u_i)}{\partial u_i^2} < 0$, $\Psi(u_i)$ is strictly concave, the follower optimization problem (PB-i) is a convex optimization problem. The optimal solution to (PB-i) must satisfy the KKT conditions.

Define the Lagrangian function $L_B(\pi)$ as:

$$L_B(\pi) = -\beta \psi(u_i) - vNu_i + \pi [\xi(u_i) - vNu_i - C_i], \tag{22}$$

where $\pi \ge 0$ is the Lagrange multiplier associated with the condition in Equation (15). The KKT conditions, in addition to the constraint Equation (16), are:

$$\frac{\partial L_B(\pi)}{\partial u_i} = -\frac{\beta r e^{-ru_i}}{(1 + e^{-ru_i})^2} - vN + \pi \left(\frac{mn}{1 + nu_i} - vN\right) = 0, \tag{23}$$

and:

$$\pi[\xi(u_i) - vNu_i - C_i] = 0. \tag{24}$$

For
$$-\frac{1}{e} \le -\frac{vN}{mn}e^{\left(-\frac{vN}{mn} + \frac{C_i}{m}\right)} < 0$$
, let $W_{-1}^{PB_i} = W_{-1}\left[-\frac{vN}{mn}e^{\left(-\frac{vN}{mn} + \frac{C_i}{m}\right)}\right] \le -1$. That is,
$$\left(-W_{-1}^{PB_i}\right)e^{\left(W_{-1}^{PB_i}\right)} = \left(\frac{vN}{mn}\right)e^{\left(-\frac{vN}{mn} + \frac{C_i}{m}\right)}. \tag{25}$$

Taking the logarithm of the both sides of Equation (25) yields that:

$$\ln\left(-W_{-1}^{PB_i}\right) + W_{-1}^{PB_i} = \ln\left(\frac{vN}{mn}\right) - \left(\frac{vN}{mn}\right) + \frac{C_i}{m}.$$
 (26)

Since
$$W_{-1}^{PB_i} \le -1$$
 and $-\frac{1}{e} \le -\frac{vN}{mn}e^{\left(-\frac{vN}{mn} + \frac{C_i}{m}\right)} < 0$, or $\frac{vN}{mn} \le e^{-\left(1 - \frac{vN}{mn} + \frac{C_i}{m}\right)}$:

$$-\frac{1}{n} - \frac{m}{vN} W_{-1}^{PB_i} = \frac{m}{vN} \left[\left(-\frac{vN}{mn} \right) - W_{-1}^{PB_i} \right] \ge \frac{m}{vN} \left[-e^{-\left(1 - \frac{vN}{mn} + \frac{C_i}{m} \right)} - W_{-1}^{PB_i} \right] > 0. \quad (27)$$

Lemma 2. For $-\frac{1}{e} \le -\frac{vN}{mn}e^{\left(-\frac{vN}{mn} + \frac{C_i}{m}\right)} < 0$, $u_i = -\frac{1}{n} - \frac{m}{vN}W_{-1}^{PB_i} \ge 0$ is a solution to $\xi(u_i) - vNu_i - C_i = 0$.

Proof. Substitute $u_i = -\frac{1}{n} - \frac{m}{vN} W_{-1}^{PB_i}$ into the left-hand side of the equation:

$$\xi(u_{i}) - vNu_{i} - C_{i} = m \ln \left[1 + n \left(-\frac{1}{n} - \frac{m}{vN} W_{-1}^{PB_{i}} \right) \right] - vN \left[-\frac{1}{n} - \frac{m}{vN} W_{-1}^{PB_{i}} \right] - C_{i}
= m \ln \left(\frac{mn}{vN} \right) + m \ln \left(-W_{-1}^{PB_{i}} \right) + \frac{vN}{n} + mW_{-1}^{PB_{i}} - C_{i}
= m \ln \left(\frac{mn}{vN} \right) + \frac{vN}{n} + m \left[\ln \left(-W_{-1}^{PB_{i}} \right) + W_{-1}^{PB_{i}} \right] - C_{i}
= m \ln \left(\frac{mn}{vN} \right) + \frac{vN}{n} + m \left[\ln \left(\frac{vN}{mn} \right) - \left(\frac{vN}{mn} \right) + \frac{C_{i}}{m} \right] - C_{i} = 0$$
(28)

Therefore, for $-\frac{1}{e} \leq -\frac{vN}{mn}e^{\left(-\frac{vN}{mn}+\frac{C_i}{m}\right)} < 0$, $u_i = -\frac{1}{n} - \frac{m}{vN}W_{-1}^{PB_i} \geq 0$ is a solution to $\xi(u_i) - vNu_i - C_i = 0$.

For $u_i = -\frac{1}{n} - \frac{m}{vN} W_{-1}^{PB_i} \ge 0$ and $W_{-1}^{PB_i} \le -1$, $vN(1+nu_i) = mn\left(-W_{-1}^{PB_i}\right) \ge mn$. That is, there exist no solutions for $\pi \ge 0$ such that Equation (23) of the KKT conditions is satisfied.

For
$$W_{-1}^{PB_i} = -1$$
 and $u_i = -\frac{1}{n} + \frac{m}{vN} \ge 0$,

$$\xi(u_{i}) - vNu_{i} = m \ln \left[1 + n \left(-\frac{1}{n} + \frac{m}{vN} \right) \right] - vN \left(-\frac{1}{n} + \frac{m}{vN} \right)$$

$$= m \ln \left[1 + n \left(-\frac{1}{n} - \frac{m}{vN} W_{-1}^{PB_{i}} \right) \right] - vN \left(-\frac{1}{n} - \frac{m}{vN} W_{-1}^{PB_{i}} \right)$$

$$= m \ln \left[-\left(\frac{mn}{vN} \right) W_{-1}^{PB_{i}} \right] + \frac{vN}{n} + mW_{-1}^{PB_{i}}$$

$$= m \ln \left(\frac{mn}{vN} \right) + m \ln \left(-W_{-1}^{PB_{i}} \right) + \frac{vN}{n} + mW_{-1}^{PB_{i}} = C_{i}.$$
(29)

That is, Equation (15) is an active constraint for $u_i = -\frac{1}{n} + \frac{m}{vN} \ge 0$ and $W_{-1}^{PB_i} = -1$. Note that for $W_{-1}^{PB_i} = -1$, $\left(\frac{vN}{mn}\right)e^{\left(-\frac{vN}{mn} + \frac{C_i}{m}\right)} = \frac{1}{e}$.

For $u_i > -\frac{1}{n} + \frac{m}{vN}$, $vN(1 + nu_i) > mn$. That is, there exist no solutions for $\pi \ge 0$ such

that Equation (23) of the KKT conditions is satisfied for $u_i > -\frac{1}{n} + \frac{m}{vN}$. For $0 \le u_i < -\frac{1}{n} + \frac{m}{vN}$ and $W_{-1}^{PB_i} \le -1$, since $\frac{\partial}{\partial u_i} [\xi(u_i) - vNu_i] > 0$, $\xi(u_i) - vNu_i$ is monotonically increasing on $0 \le u_i < -\frac{1}{n} + \frac{m}{vN}$:

$$\xi(u_{i}) - vNu_{i} < m \ln \left[1 + n \left(-\frac{1}{n} + \frac{m}{vN} \right) \right] - vN \left(-\frac{1}{n} + \frac{m}{vN} \right)
\leq m \ln \left[1 + n \left(-\frac{1}{n} - \frac{m}{vN} W_{-1}^{PB_{i}} \right) \right] - vN \left(-\frac{1}{n} - \frac{m}{vN} W_{-1}^{PB_{i}} \right) = C_{i}.$$
(30)

Therefore, Equation (15) is an inactive constraint for $0 \le u_i < -\frac{1}{n} + \frac{m}{vN}$ and $W_{-1}^{PB_i} \leq -1.$

Lemma 3. For $\left(\frac{vN}{mn}\right)e^{\left(-\frac{vN}{mn}+\frac{C_i}{m}\right)}=\frac{1}{e}$ and $0<-\frac{1}{n}+\frac{m}{vN}\leq O_i$, $u_i^*=-\frac{1}{n}+\frac{m}{vN}$ is the optimal solution to (PB - i).

Proof. Since u_i^* satisfies Equations (15) and (16) and is a relative maximum point for the problem (PB - i). As the objective function of (PB - i) is strictly concave, u_i^* is also the optimal solution to (PB - i). \square

Lemma 4. For $-\frac{1}{e} \le -\frac{vN}{mn}e^{\left(-\frac{vN}{mn} + \frac{C_i}{m}\right)} < 0$, $O_i < -\frac{1}{n} + \frac{m}{vN}$, $u_i^* = O_i$ is the optimal solution to (PB-i).

Proof. Since $\frac{\partial}{\partial u_i} [\xi(u_i) - vNu_i] > 0$ and $\xi(u_i) - vNu_i$ is monotonically increasing,

$$\xi(O_{i}) - vNO_{i} = m \ln(1 + nO_{i}) - vNO_{i}$$

$$< m \ln\left[1 + n\left(-\frac{1}{n} + \frac{m}{vN}\right)\right] - vN\left(-\frac{1}{n} + \frac{m}{vN}\right)$$

$$\leq m \ln\left[1 + n\left(-\frac{1}{n} - \frac{m}{vN}W_{-1}^{PB_{i}}\right)\right] - vN\left(-\frac{1}{n} - \frac{m}{vN}W_{-1}^{PB_{i}}\right) = C_{i}.$$
(31)

That is, Equation (15) is an inactive constraint when $0 \le u_i = O_i < -\frac{1}{n} + \frac{m}{vN}$. Therefore, for $O_i < -\frac{1}{n} + \frac{m}{vN}$, $u_i = O_i$ satisfies Equations (15) and (16).

Since $\Psi(u_i)$ is monotonically increasing for $0 \le u_i \le O_i$, $u_i^* = O_i$ is the maximum point, and thus the optimal solution to (PB - i). \square

Hence, Lemmas 3 and 4 provide the optimal solutions to the follower optimization problem (PB - i) for $0 < -\frac{1}{n} + \frac{m}{vN} \le O_i$ and for $O_i < -\frac{1}{n} + \frac{m}{vN}$, respectively.

4.2.3. Optimal Incentive Solution for Federated Egg Banking Blockchain Operations

Based on the optimal solutions from Lemmas 2–4, we developed an iterative scheme to find the optimal incentive solution for the alliance of federated ICEBs. The iterative scheme begins with an initial setting of $v^{(0)} \leftarrow \frac{\rho \xi(O_I)}{NO_I}$, where $v^{(0)}$ is the initial MFR rate per block creation that the alliance \mathbb{A} (the leader) offers to the ICEBs (the followers).

After receiving the offer, each ICEB (\mathbb{B}_i) determines its optimal number of oocytes to participate the alliance \mathbb{A} . Its decision-making process first checks the feasibility of the

offered MFR rate. For $v^{(k)}$ in the kth iteration, if $-\frac{v^{(k)}N}{mn}e^{\left(-\frac{v^{(k)}N}{mn}+\frac{C_i}{m}\right)}<-\frac{1}{e}$, there is no solution in iteration k. The iterative process stops.

On the other hand, if the offered MFR rate is feasible, i.e., $-\frac{v^{(k)}N}{mn}e^{\left(-\frac{v^{(k)}N}{mn}+\frac{C_i}{m}\right)} \ge -\frac{1}{e}$, the optimal number of oocytes is calculated as follows.

$$u_i^{(k+1)} = \begin{cases} O_i, & O_i < -\frac{1}{n} + \frac{m}{v^{(k)}N}, \\ -\frac{1}{n} + \frac{m}{v^{(k)}N}, & \text{otherwise.} \end{cases}$$
(32)

The ICEB \mathbb{B}_i then responds with its optimal number of oocytes, $u_i^{(k+1)}$, to the alliance \mathbb{A} . After collecting the optimal numbers of oocytes, $\{u_i^{(k+1)}\}$, from all the ICEBs, the alliance \mathbb{A} updates the MFR rate per block creation, $v^{(k+1)}$, and offers to each ICEB for the next iteration, k+1.

The iterative process ends when there is no further improvement on v. Pseudo-code in Algorithm 1 describes the iterative scheme for optimal design to find the federated egg banking incentive solution (FEBIS).

The FEBIS algorithm starts from iteration k=0 with $v^{(0)}=\min\{\frac{\rho\xi(O_i)}{NO_i}, \forall i=1,\cdots,I\}=\frac{\rho\xi(O_I)}{NO_I}$. It updates $v^{(k+1)}$ in each iteration, k+1, after all the values of $u_i^{(k)}, \forall i=1,\cdots,I$, are determined in the kth iteration.

Since $\frac{\partial}{\partial v^{(k-1)}} \left[-\frac{1}{n} + \frac{m}{v^{(k-1)}N} \right] < 0$, $-\frac{1}{n} - \frac{m}{v^{(k)}N} \le -\frac{1}{n} - \frac{m}{v^{(k-1)}N}$. From Equation (32), for $-\frac{1}{e} \le -\frac{v^{(k)}N}{mn} e^{(-\frac{vN}{min} + \frac{C_i}{m})}$, $u_i^{(k)} = \min \left\{ -\frac{1}{n} + \frac{m}{v^{(k)}N}, O_i \right\} \le \min \left\{ -\frac{1}{n} + \frac{m}{v^{(k-1)}N}, O_i \right\} = u_i^{(k-1)}$. Hence, $u_i^{(k)}$ is non-increasing in the iterative process. That is, $u_i^{(k)} < u_i^{(k-1)} \le O_i$ or $u_i^{(k)} = u_i^{(k-1)} = O_i$.

In iteration k, for $u_i^{(k)} = u_i^{(k-1)} = O_i$, $\forall O_j \leq O_i < -\frac{1}{n} + \frac{m}{v^{(k-1)}N}$. Hence, $\forall O_j \leq O_i$, $u_j^{(k)} = O_j$. That is, Equation (15) is active in (PB - j), $\forall O_j \leq O_i$ and $u_j^{(k)} = O_j$.

For $u_i^{(k)} < u_i^{(k-1)} \le O_i$, Equation (15) becomes inactive in (PB - i) and the KKT conditions of Equations (23) and (24) are not satisfied in (PB - i). That is, for $u_i^{(k)} < O_i$, $u_i^{(k)}$ is not an optimal solution to (PB - i).

In the first iteration k=0, the algorithm uses the initial setting of $v^{(0)} \leftarrow \frac{\rho \xi(O_I)}{NO_I}$. From Equation (32), for $i=1,\cdots,I, u_i^{(0)}=O_i$ and the corresponding constraint of Equation (15) is active in $(PB-i), \forall i=1,\cdots,I$. In the next iteration $k=1,v^{(1)} \leftarrow \text{Leader}(\mathbf{u}^{(0)}) = \min\left\{\frac{\rho \xi(u_i^{(0)})}{Nu_i^{(0)}}\right\} = \min\left\{\frac{\rho \xi(O_I)}{NO_I}\right\} = \frac{\rho \xi(O_I)}{NO_I} = v^{(0)}$. As $v^{(1)}=v^{(0)}$, there is no further improvement in v, and the iterative process ends in iteration k=1.

Note that as $\forall i=1,\cdots,I, u_i^{(0)}=O_i$ are the optimal solutions to $(PB-i), i=1,\cdots,I,$ respectively, and $v^{(1)}=v^{(0)}=\frac{\rho \xi(O_I)}{NO_I}$ is the optimal solution to (PA), both the leader and followers problems achieve the Stackelberg equilibrium point where both Equations (17) and (18) are satisfied.

Based on the above analysis, the proposed FEBIS algorithm is correct and complete. Its computational complexity is $\mathcal{O}(I^2)$.

Algorithm 1: Federated egg banking incentive solution (FEBIS). **Input:** $I, \rho, N, m, n, \{O_1, \dots, O_I\}, \{C_1, \dots, C_I\}$

```
Output: v^*, \mathbf{u}^* = \{u_1^*, \cdots, u_I^*\}, SolutionOrNot
    /* Initialization
                                                                                                                           */
 1 \ k \leftarrow 0;
 v^{(0)} \leftarrow \frac{\rho \xi(O_I)}{NO_I};
 3 SolutionOrNot ← True;
    /* Main
 4 while k < I do
         /* Call the Follower Subroutine
                                                                                                                           */
         for i \leftarrow 1 to I do
              \begin{array}{l} \textbf{if} - \frac{v^{(k)}N}{mn} e^{\left(-\frac{v^{(k)}N}{mn} + \frac{C_i}{m}\right)} < -\frac{1}{e} \ \textbf{then} \\ \mid \ \textit{SolutionOrNot} \leftarrow \textit{False}; \end{array}
 6
                 break;
 8
            u_i^{(k)} \leftarrow \text{Follower}(v^{(k)}, O_i, C_i);
         /* Call the Leader Subroutine
                                                                                                                           */
         v^{(k+1)} \leftarrow \text{Leader}(\mathbf{u}^{(k)});
10
                                                                            // Update the incentive rate
         /* Check if No Improvements
         if v^{(k+1)} == v^{(k)} then
11
              v^{(I)} \leftarrow v^{(k+1)};
12
              for i \leftarrow 1 to I do
13
               u_i^{(I)} \leftarrow u_i^{(k)};
14
              k \leftarrow I;
15
         k++;
17 if SolutionOrNot = True then
         v^* \leftarrow v^{(I)};
                                                                          // The optimal incentive rate
         \mathbf{u}^* \leftarrow \{u_1^{(I)}, \cdots, u_I^{(I)}\};
                                                                   // The optimal numbers of oocytes
20 return SolutionOrNot;
                                                                                     // End of the algorithm
    /* The Leader Subroutine
                                                                                                                           */
21 Function Leader (\mathbf{u}^{(k)}):
         v^{(k+1)} = \frac{\rho m \ln(1+n)}{N};
                                                                                     // The upper bound of \emph{v}
         for i \leftarrow 1 to I do
23
              if u_i^{(k)} > 0 then
24
                   v^{(k+1)} \leftarrow \min \left\{ \frac{\rho \xi\left(u_i^{(k)}\right)}{Nu_i^{(k)}}, v^{(k+1)} \right\}; \quad \textit{// Get the smallest for } v^{(k+1)}
25
         return v^{(k+1)};
    /* The Follower Subroutine
                                                                                                                           */
27 Function Follower (v, O_i, C_i):
         u_i \leftarrow -\frac{1}{n} + \frac{m}{vN};
                                                                                             // Determine the u_i
28
         if u_i > O_i then
29
          u_i \leftarrow O_i;
                                                                                             // if O_i < -\frac{1}{n} + \frac{m}{vN}
30
31
         return u_i;
```

5. Numerical Results

5.1. A Numerical Example

This section presents a numerical example to demonstrate the optimal design for the federated egg banking blockchain system. In it, there are five ICEBs, $\{\mathbb{B}_1, \mathbb{B}_2, \mathbb{B}_3, \mathbb{B}_4, \mathbb{B}_5\}$, intending to form an egg banking alliance in order to increase their economies of scope and make their customers happier. Data of the five ICEBs and the parameters of coalition for egg banking are shown in Tables 1 and 2, respectively. Algorithm 1 achieved the optimal solution of $v^*=0.00326137$ after one iteration. The optimal numbers of participating oocytes from the five ICEBs were $u_1^*=480, u_2^*=1440, u_3^*=1440, u_4^*=2400, u_5^*=2400, respectively. The result of <math>(PA)$ was $\Phi(\{u_i^*\}, v^*)=67.05704322$ and the results of $(PB-i), i=1,\cdots,5$, were $\Psi(u_1^*)=101.92745259$, $\Psi(u_2^*)=289.78235776$, $\Psi(u_3^*)=289.78235776$, $\Psi(u_4^*)=477.63726293$ and $\Psi(u_5^*)=477.63726293$. All these five ICEBs are to form the egg banking alliance $\mathbb A$, and each ICEB participates in the alliance $\mathbb A$ with the full number of available oocytes included in the ICEB.

Table 1. Data of the five ICEBs to form an alliance.

	\mathbb{B}_1	\mathbb{B}_2	\mathbb{B}_3	\mathbb{B}_4	\mathbb{B}_5
number of oocytes, O_i	480	1440	1440	2400	2400
budget limit for membership fee expenditure, C_i	1000	1500	1600	2500	3000

Table 2. Parameters of Coalition for Egg Banking.

Parameter	Value
total number of ICEBs in \mathbb{A} , I	5
average number of blocks generated by an oocyte, N	60
weighting factor for satisfaction function, α	10.0
weighting factor for utility function for profit, β	8.0
percentage of membership fees allocated for rebate, ρ	0.1
constant coefficient of the satisfaction function, a	0.1
constant coefficient of the participation function, b	0.2
constant coefficient of the membership fee function, m , n	500.0, 5.0
constant coefficient of the utility function for profit, r	0.1

5.2. Adding a New ICEB

Following the numerical results in Section 5.1, consider a new ICEB \mathbb{B}^{\dagger} that intends to participate in the existing egg banking alliance \mathbb{A} . There are two approaches (I and II) to adding a new ICEB. Approach I resumes and uses the existing result of $v^* = 67.05704322$ calculated in Section 5.1. Additionally, approach II re-executes the FEBIS algorithm to achieve a new v^* . Table 3 describes the test data of the new ICEB to \mathbb{A} , where three scenarios (S1, S2, S3) are presented to test approach I and the other three (S4, S5, S6) approach II. S1 and S4 represent the cases in which the new \mathbb{B}^{\dagger} has the least number of oocytes to participate among the incumbent ICEBs of \mathbb{A} . S2 and S5 consider the cases in which \mathbb{B}^{\dagger} has neither the least nor the largest of number of oocytes to participate. Additionally, S3 and S6 illustrate the cases in which the new ICEB \mathbb{B}^{\dagger} has the most oocytes of any incumbent ICEB in the alliance \mathbb{A} .

Table 4 shows the test results of S1–S6. For approach II, S6 was the only scenario whose new v^* changed and decreased to 0.00175102. The results of v^* from the other two scenarios, S4 and S5, are the same as the first 0.00326137, calculated in Section 5.1. For both approaches, the results of $\{u_i^*\}$ are all the same.

Tables 5–7 illustrate the performance analysis of S1 vs. S4, S2 vs. S5 and S3 vs. S6, respectively. Note that, in Table 7, due to the decrease in v^* from re-executing the FEBIS algorithm, all the test results in S6 are less than those in S3. Additionally, note that the differences in $\Psi(u_i^*)$ between S6 vs. S3 enlarge as the resulting u_i^* s increase. In Tables S6 and S6, as the new S6 vs. S6 and S6 remain the same as the existing S6, their results of S6 vs.

and $\Psi(u_i^*)$, $\forall i = 1, \dots, I$ are almost all the same as their counterparts in scenarios S1 and S2, respectively, except for the negligible increase in $\Phi(v^*)$ in S4.

In summary, the results in Tables 5–7 indicate that both approaches perform well in adding a new ICEB with small- or medium-sized numbers of oocytes, among the incumbent ICEBs. However, when a new, big ICEB with more oocytes than other incumbent ICEBs intends to join alliance \mathbb{A} , re-executing the FEBIS algorithm is better than using the existing rate.

Table 3. Data of the new ICEB \mathbb{B}^{\dagger} to join the egg banking alliance \mathbb{A} for scenarios $S1 \sim S6$.

	Approa	ch I. Use the Ex	isting v	Approach I	I. Re-Execute t	he FEBIS
	<i>S</i> 1	S2	<i>S</i> 3	S4	<i>S</i> 5	<i>S</i> 6
O^{\dagger}	240	1500	4800	240	1500	4800
C^{\dagger}	400	1600	4000	400	1600	4000

 $[\]dagger$ denotes the results of the new ICEB \mathbb{B}^{\dagger} .

Table 4. Results of adding a new ICEB \mathbb{B}^{\dagger} to the egg banking alliance \mathbb{A} .

	Approach I. Use the Existing v			Approach II. Re-Execute the FEBIS		
	<i>S</i> 1	S2	S3	S4	<i>S</i> 5	<i>S</i> 6
v^*	0.00326137	0.00326137	0.00326137	0.00326137	0.00326137	0.00175102
u_1^*	240 [†]	480	480	240 [†]	480	480
u_2^*	480	1440	1440	480	1440	1440
u_{2}^{*} u_{3}^{*}	1440	1440	1440	1440	1440	1440
u_{4}^{*}	1440	1500 [†]	1440	1440	1500 [†]	2400
u_5^*	2400	2400	2400	2400	2400	2400
$u_{4}^{*} \\ u_{5}^{*} \\ u_{6}^{*}$	2400	2400	4800 [†]	2400	2400	4800 [†]
$\Phi(v^*)$	67.34656880 [†]	68.74263723	71.67874412	67.34656887 †	68.74263723	71.67844205
$\Psi(u_1^*)$	54.96372629	101.92745259	101.92745259	54.96372629	101.92745259	58.42925388
$\Psi(u_2^*)$	101.92745259	289.78235776	289.78235776	101.92745259	289.78235776	159.28776163
$\Psi(u_3^{\overline{*}})$	289.78235776	289.78235776	289.78235776	289.78235776	289.78235776	159.28776163
$\Psi(u_4^*)$	289.78235776	301.5232893 †	477.63726293	289.78235776	301.5232893 †	260.14626938
$\Psi(u_5^*)$	477.63726293	477.63726293	477.63726293	477.63726293	477.63726293	260.14626938
$\Psi(u_6^*)$	477.63726293	477.63726293	947.27452586 †	477.63726293	477.63726293	512.29253876 †

[†] denotes the results of the new ICEB \mathbb{B}^{\dagger} .

Table 5. Performance analysis: *S*1 vs. *S*4.

Objective Function Value	<i>S</i> 1	<i>S</i> 4	$\frac{S1-S4}{S4}$ (%)
$\Phi(v^*)$	67.34656880	67.34656887	-0.00000010
$\Psi(u_1^*)^{\dagger}$	54.96372629 [†]	54.96372629 [†]	0
$\Psi(u_2^*)$	101.92745259	101.92745259	0
$\Psi(u_3^*)$	289.78235776	289.78235776	0
$\Psi(u_4^*)$	289.78235776	289.78235776	0
$\Psi(u_5^*)$	477.63726293	477.63726293	0
$\Psi(u_6^3)$	477.63726293	477.63726293	0

[†] denotes the results of the new ICEB \mathbb{B}^{\dagger} .

Objective Function Value	S2	<i>S</i> 5	$\frac{S2-S5}{S5}(\%)$
$\Phi(v^*)$	68.74263723	68.74263723	0
$\Psi(u_1^*)$	101.92745259	101.92745259	0
$\Psi(u_2^*)$	289.78235776	289.78235776	0
$\Psi(u_2^*)$	289.78235776	289.78235776	0

301.5232893 †

477.63726293

477.63726293

0

0

0

301.5232893 †

477.63726293

477.63726293

Table 6. Performance analysis: *S*2 vs. *S*5.

 $\Psi(u_4^*)$

 $\Psi(u_5^*)$

Table 7. Performance analysis: *S*3 vs. *S*6.

Objective Function Value	S3	<i>S</i> 6	$\frac{S3-S6}{S6}$ (%)
$\Phi(v^*)$	71.67874412	71.67844205	0.00042142
$\Psi(u_1^*)$	101.92745259	58.42925388	74.44592532
$\Psi(u_2^*)$	289.78235776	159.28776163	81.92380557
$\Psi(u_3^*)$	289.78235776	159.28776163	81.92380557
$\Psi(u_4^*)$	477.63726293	260.14626938	83.60334901
$\Psi(u_5^*)$	477.63726293	260.14626938	83.60334901
$\Psi(u_6^*)^{\dagger}$	947.27452586 [†]	512.29253876 [†]	84.90890539

[†] denotes the results of the new ICEB \mathbb{B}^{\dagger} .

6. Blockchain-Based, Automated, Biomedical Implementation for Egg Saving (BABIES) Platform

Based on the proposed federated blockchain approach, we continued on to develop a Blockchain-based, Automated, Biomedical Implementation for Egg Saving (BABIES) platform to seamlessly adopt blockchain technology in egg banking business. Figure 7 depicts its system architecture. BABIES utilizes distributed ledgers and smart contracts which are a collection of self-executing code and states, together with automatic identification and data capture (AIDC) technology for the integration and automation of data exchange of the eggs and their data. BABIES provides middleware for data exchange between BABIES and various data sources from hospital information systems (HIS) of the federated ICEBs, autoID (RFID or barcode) devices or automated instruments, IVF Laboratory Information Management Systems (LIMS) and public health data repositories. Critical data are all encrypted with symmetric encryption/decryption. Transaction data are structured into distributed ledgers and stored in the local storage.

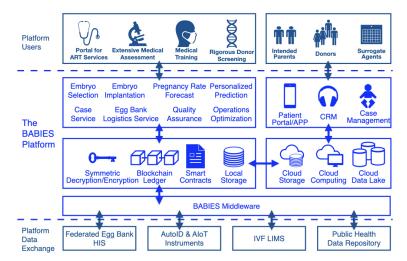


Figure 7. BABIES system architecture.

 $[\]frac{\Psi(u_6^*)}{\text{† denotes the results of the new ICEB }\mathbb{B}^{\text{†}}}.$

Infertility treatments with ART involve complex clinical operations and laboratory procedures. During an ART cycle, a large number of data can be gathered to reflect the competence for clinical practice and laboratory work in ART. The complexity of the ART process demands handling myriad data streams, monitoring a large number of parameters and acquiring sufficient information to demonstrate, analyze and improve ART outcomes. Monitoring ART performance is crucial for evaluating current activities and also for predicting further development. BABIES exploits massive, timed sensory data from IoT and AIoT devices/instruments during the egg banking process. While there are no gold standards to test the success of the birth of a healthy singleton child, recently, some performance indicators (PIs) have been identified for evaluating critical healthcare domains of patient safety, effectiveness, equity, patient-centeredness, timeliness and efficiency for ART laboratory [21] and clinical practice [22]. Based on their recommendations, BABIES has selected and designed a set of ART PIs for evaluation of the ART performance. The ART PIs are made based on the consolidated data that were gathered from federated ICEB HIS, AutoID and AIoT instruments, IVF LIMS and a public health data repository.

BABIES adopts many machine learning (ML) or deep learning (DL) algorithms to support smart IVF services for embryo selection, embryo implantation, pregnancy rate forecasting, personalized prediction, case service, egg bank logistics service, quality assurance and operations optimization. Some encrypted data and the federated egg banking blockchains are duplicated and stored in cloud storage, from which cloud data lakes are generated and organized by cloud computing. Systems such as Patient Portal, application programs, Customer Relationship Management (CRM) and Case Management, utilize such data and the federated egg banking blockchain in the cloud data lakes to provide secure and private information to platform users, such as intended parents, donors, surrogate agents and so on.

BABIES also provides useful software packages to professional platform users, such fertility specialists, embryologists and laboratory operators. These software packages include a portal for ART services, extensive medical assessment, medical training and rigorous donor screening functionalities.

Figure 8 depicts the software stack of the BABIES platform. At the bottom of the software stack, data from the AIoT devices, ICT infrastructure and automated instruments in the public and proprietary domains are collected and modeled by analytics and empirical approaches. On top of that, distributed ledgers of the transactions of the data are stored and managed with blockchain and cloud/edge computing technology. On top of that, ML and DL algorithms, libraries and frameworks are used to provide smart IVF operations and decisions. On top of that, user experience (UX) functionalities are provided for enduser's interaction with the egg banking services. The highest level of the software stack encompasses all the BABIES egg banking services, including embryo selection, embryo implantation, pregnancy rate forecast, personalized prediction, case service, egg bank logistics service, quality assurance, operations optimization and so on.

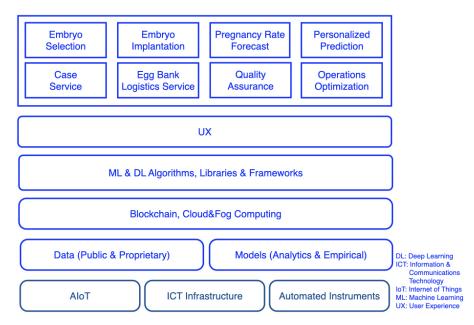


Figure 8. BABIES Software Stack.

7. Conclusions

We presented a novel federated approach that utilizes blockchain technology for smarter egg banking of fertility preservation and assisted reproduction in smart cities. This paper first identified the requirements and business opportunities that exploit hi-tech systems for smarter egg banking. We then proposed a federated egg banking business model for fertility preservation and assisted reproduction in smart cities. The federated blockchain approach intends to form coalition for integrated commercial egg banks (ICEBs) to create more customer satisfaction and encourage more member participation. We designed a membership-fee-rebate (MFR) mechanism to offer incentives to the ICEBs for blockchain operations. We formulated the MFR problem into a leader-followers Stackelberg game problem. At the leader (the alliance) level, the objective is to maximize the benefits of forming the alliance; at in the follower (the ICEB) level, the objective of each ICEB is to maximize the benefits of the ICEB. With a given set of parameters for the membership fee functions and the average number of blocks generated for operations of an oocyte, the optimal MFR is designed, based on the optimal numbers of participating oocytes of the ICEBs. We developed an iterative algorithm, FEBIS, that uses mathematical programming techniques to find the optimal incentive solution for the federated, integrated egg banking alliance. A numerical example demonstrated the feasibility and applicability of the developed methodology for the optimal design of the MFR mechanism. Numerical results also indicated that the FEBIS algorithm performs well in adding a small- or medium-sized new ICEB to the existing alliance with an existing MFR rate. On the other hand, to add a new ICEB with a larger number participating oocytes, re-execution of the algorithm is better. However, a lower MFR rate thus incurs after the joining of a new big one.

Following this research, we continued on to develop the Blockchain-based, Automated, Biomedical Implementation for Egg Saving (BABIES) platform to effectively adopt blockchain technology for egg banking operations and services. The development of BABIES is in progress. This paper outlines the components and functionalities in its system architecture and software stacks. The detailed design of the BABIES platform will be presented in the future. Furthermore, BABIES is implementing a set of the performance indicators (PIs) which are identified in [21,22] for ART laboratory and clinical practice. The performance evaluations of these PIs and the benchmarks will be presented in the future.

Unlike other smart cities projects that may receive government subsidies or money from taxpayers to adopt new technologies, the formation of a coalition of ICEBs urges sufficient incentives to motivate the ICEBS to participate and cooperate to improve citizen

welfare in a smart city. This research initiates the design of a membership-fee–rebate mechanism and adopts four functions, Equations (1)–(4), as the objective functions for modeling the optimal incentive problem. Future research directions include the development of more creative incentive mechanisms for the coalition of ICEBs; the customization of more comprehensive objective functions in incentive problem formulation; and the use of more advanced data and system modeling technologies to integrate the sophisticated fertility preservation and assisted reproduction operations and provide more services and citizen welfare in smart cities applications.

Funding: This research received no external funding.

Data Availability Statement: Not applicable.

Acknowledgments: The author thanks the academic editor and anonymous reviewers for their insightful comments and suggestions. Additionally, the author would like to thank Ming-I Hsu and the embryologists in HuaYu Fertility Center, Taipei, Taiwan, for their valuable discussion.

Conflicts of Interest: The author declares no conflict of interest.

Abbreviations

The following abbreviations are used in this paper:

AIDC Automatic Identification and Data Capture

AIoT Artificial Intelligence of Things

APP Application Program

ART Assisted Reproduction Technology

AutoID Automated Identification CEB Commercial Egg Bank

CRM Customer Relationship Management

DL Deep Learning
EBA Egg Banking Alliance
HIS Hospital Information System

ICEB Integrated Commercial Egg Banking

IoT Internet of Things
IT Information Technology

IVF in vitro Fertility

LIMS Laboratory Information Management System

MFR Membership Fee Rebate
ML Machine Learning

RFID Radio Frequency Identification

References

- 1. Finance & Economics. Why the Demographic Transition is Speeding Up. *The Economist*, 11 December 2021. Available online: https://www.economist.com/finance-and-economics/2021/12/11/why-the-demographic-transition-is-speeding-up (accessed on 23 February 2022).
- 2. Barrera, N.; Omolaoye, T.S.; Du Plessis, S.S. A contemporary view on global fertility, infertility, and assisted reproductive techniques. In *Fertility, Pregnancy, and Wellness*; Elsevier: Amsterdam, The Netherlands, 2022; pp. 93–120. [CrossRef]
- 3. Infertility: Symptoms, Treatment, Diagnosis. UCLA Health. Available online: https://www.uclahealth.org/obgyn/infertility (accessed on 23 February 2022).
- 4. Mayo Clinic. Infertility: Symptoms & Causes. Available online: https://www.mayoclinic.org/diseases-conditions/infertility/symptoms-causes/syc-20354317 (accessed on 23 February 2022).
- 5. Centers for Disease Control and Prevention. Infertility FAQs, Reproductive Health. Available online: https://www.cdc.gov/reproductivehealth/infertility/index.htm (accessed on 23 February 2022).
- 6. Ismagilova, E.; Hughes, L.; Dwivedi, Y.K.; Raman, K.R. Smart cities: Advances in research—An information systems perspective. *Int. J. Inf. Manag.* **2019**, *47*, 88–100. [CrossRef]
- 7. Maheswaran, M.; Badidi, E. Handbook of Smart Cities; Springer: Cham, Switzerland, 2018; ISBN 978-3-319-97271-8.
- 8. Ismagilova, E.; Hughes, L.; Rana, N.P.; Dwivedi, Y.K. Security, Privacy and Risks within Smart Cities: Literature Review and Development of A Smart City Interaction Framework. *Inf. Syst. Front.* **2020**, 1–22. [CrossRef] [PubMed]

9. Khan, L.U.; Yaqoob, I.; Tran, N.H.; Kazmi, S.A.; Dang, T.N.; Hong, C.S. Edge-Computing-enabled Smart Cities: A Comprehensive Survey. *IEEE Int. Things J.* **2020**, *7*, 10200–10232. [CrossRef]

- 10. Kuru, K.; Ansell, D.T. CitySmartF: A Comprehensive Systematic Framework for Transforming Cities into Smart Cities. *IEEE Access* **2020**, *8*, 18615–18644. [CrossRef]
- 11. Xie, J.; Tang, H.; Huang, T.; Yu, F.R.; Xie, R.; Liu, J.; Liu, Y. A Survey of Blockchain Technology Applied to Smart Cities: Research Issues and Challenges. *IEEE Commun. Surv. Tutorials* **2019**, 21, 2794–2830. [CrossRef]
- 12. Majeed, U.; Khan, L.U.; Yaqoob, I.; Kazmi, S.A.; Salah, K.; Hong, C.S. Blockchain for IoT-based Smart Cities: Recent Advances, Requirements, and Future Challenges. *J. Netw. Comput. Appl.* **2021**, *181*, 103007. [CrossRef]
- 13. Donnez, J.; Dolmans, M.M. Fertility Preservation in Women. N. Engl. J. Med. 2017, 377, 1657–1665. [CrossRef]
- 14. Flink, D.M.; Sheeder, J.; Kondapalli, L.A. A Review of the Oncology Patient's Challenges for Utilizing Fertility Preservation Services. *J. Adolesc. Young Adult Oncol.* **2017**, *6*, 31–44. [CrossRef]
- 15. Gunnala, V.; Schattman, G. Oocyte Vitrification for Elective Fertility Preservation: The Past, Present, and Future. *Curr. Opin. Obstet. Gynecol.* **2017**, 29, 59–63. [CrossRef]
- 16. Argyle, C.E.; Harper, J.C.; Davies, M.C. Oocyte Cryopreservation: Where Are We Now? *Hum. Reprod. Update* **2016**, 22, 440–449. [CrossRef]
- 17. Baldwin, K. *Egg Freezing, Fertility and Reproductive Choice: Negotiating Responsibility, Hope and Modern Motherhood;* Emerald Group Publishing: Bingley, UK, 5 September 2019; ISBN 978-1-78756-484-8
- 18. Mintziori, G.; Veneti, S.; Kolibianakis, E.M.; Grimbizis, G.F.; Goulis, D.G. Egg Freezing and Late Motherhood. *Maturitas* **2019**, 125, 1–4. [CrossRef] [PubMed]
- 19. Kushnir, V.A.; Darmon, S.K.; Barad, D.H.; Gleicher, N. New National Outcome Data on Fresh vs. Cryopreserved Donor Oocytes. *J. Ovarian Res.* **2018**, *11*, 1–4. [CrossRef] [PubMed]
- 20. Quaas, A.M.; Pennings, G. The Current Status of Oocyte Banks: Domestic and International Perspectives. *Fertil. Steril.* 2018, 110, 1203–1208. [CrossRef] [PubMed]
- ESHRE Special Interest Group of Embryology and Alpha Scientists in Reproductive Medicine. The Vienna Consensus: Report of An Expert Meeting on the Development of Art Laboratory Performance Indicators. Reprod. Biomed. Online 2017, 35, 494–510.
 [CrossRef]
- 22. ESHRE Clinic PI Working Group; Vlaisavljevic, V.; Apter, S.; Capalbo, A.; D'Angelo, A.; Gianaroli, L.; Griesinger, G.; Kolibianakis, E.M.; Lainas, G.; Mardesic, T.; et al. The Maribor Consensus: Report of An Expert Meeting on the Development of Performance Indicators for Clinical Practice in ART. *Hum. Reprod. Open* **2021**, 2021, hoab022. [CrossRef]
- 23. Tozzo, P. Oocyte Biobanks: Old Assumptions and New Challenges. BioTech 2021, 10, 4. [CrossRef]
- 24. Couture, V.; Delisle, S.; Mercier, A.; Pennings, G. The Other Face of Advanced Paternal Age: A Scoping Review of Its Terminological, Social, Public Health, Psychological, Ethical and Regulatory Aspects. *Hum. Reprod. Update* **2021**, 27, 305–325. [CrossRef]
- 25. Rimon-Zarfaty, N.; Kostenzer, J.; Sismuth, L.K.; de Bont, A. Between "Medical" and "Social" Egg Freezing. *J. Bioethical Inq.* **2021**, 18, 1–17. [CrossRef]
- 26. Bhutta, M.N.M.; Khwaja, A.A.; Nadeem, A.; Ahmad, H.F.; Khan, M.K.; Hanif, M.A.; Song, J.; Alshamari, M.; Cao, Y. A Survey on Blockchain Technology: Evolution, Architecture and Security. *IEEE Access* **2021**, *9*, 61048–61073. [CrossRef]
- 27. Peck, M.E. Blockchain World-Do You Need A Blockchain? This Chart Will Tell You If the Technology Can Solve Your Problem. *IEEE Spectr.* **2017**, *54*, 38–60. [CrossRef]
- 28. Chowdhury, M.J.M.; Colman, A.; Kabir, M.A.; Han, J.; Sarda, P. Blockchain versus database: A critical analysis. In Proceedings of the 2018 17th IEEE International Conference On Trust, Security Additionally, Privacy In Computing Additionally, Communications/12th IEEE International Conference on Big Data Science Additionally, Engineering (TrustCom/BigDataSE), New York, NY, USA, 1–3 August 2018; pp. 1348–1353. [CrossRef]
- 29. Bhushan, B.; Khamparia, A.; Sagayam, K.M.; Sharma, S.K.; Ahad, M.A.; Debnath, N.C. Blockchain for Smart Cities: A Review of Architectures, Integration Trends and Future Research Directions. *Sustain. Cities Soc.* **2020**, *61*, 102360. [CrossRef]
- 30. Esposito, C.; Ficco, M.; Gupta, B.B. Blockchain-based Authentication and Authorization for Smart City Applications. *Inf. Process. Manag.* **2021**, *58*, 102468. [CrossRef]
- 31. Hakak, S.; Khan, W.Z.; Gilkar, G.A.; Imran, M.; Guizani, N. Securing Smart Cities through Blockchain Technology: Architecture, Requirements, and Challenges. *IEEE Netw.* **2020**, *34*, 8–14. [CrossRef]
- 32. Leible, S.; Schlager, S.; Schubotz, M.; Gipp, B. A Review on Blockchain Technology and Blockchain Projects Fostering Open Science. *Front. Blockchain* **2019**, 2, 16. [CrossRef]
- 33. Rao, K.A.; Krishna, D. *Principles and Practice of Assisted Reproductive Technology*, 2nd ed.; Jaypee Brothers Medical Publishers ltd.: New Delhi, India, 2019; Volumes 1–3, ISBN 978-93-5270-503-0.
- 34. Centers for Disease Control and Prevention. State-Specific Assisted Reproductive Technology Surveillance. Available online: https://www.cdc.gov/art/state-specific-surveillance/index.html (accessed on 23 February 2022).
- 35. Pai, H.D.; Baid, R.; Palshetkar, N.P.; Pai, A.; Pai, R.D.; Palshetkar, R. Oocyte Cryopreservation-Current Scenario and Future Perspectives: A Narrative Review. *J. Hum. Reprod. Sci.* **2021**, *14*, 340–349. Available online: https://www.jhrsonline.org/text.asp? 2021/14/4/340/334531 (accessed on 23 February 2022).

36. Niederberger, C.; Pellicer, A.; Cohen, J.; Gardner, D.K.; Palermo, G.D.; O'Neill, C.L.; Chow, S.; Rosenwaks, Z.; Cobo, A.; LaBarbera, A.R.; et al. Forty Years of IVF. Fertil. Steril. 2018, 110, 185–324. [CrossRef]

- 37. Karavani, G.; Wasserzug-Pash, P.; Mordechai-Daniel, T.; Bauman, D.; Klutstein, M.; Imbar, T. Age-Dependent in vitro Maturation Efficacy of Human Oocytes—Is There an Optimal Age? *Front. Cell Dev. Biol.* **2021**, *9*, 1638. [CrossRef]
- Mayes, C.; Williams, J.; Lipworth, W. Conflicted Hope: Social Egg Freezing and Clinical Conflicts of Interest. Health Sociol. Rev. 2018, 27, 45–59. [CrossRef]
- 39. Hudson, N.; Culley, L.; Herbrand, C.; Pavone, V.; Pennings, G.; Provoost, V.; Coveney, C.; Funes, S.L. Reframing Egg Donation in Europe: New Regulatory Challenges for A Shifting Landscape. *Health Policy Technol.* **2020**, *9*, 308–313. [CrossRef]
- 40. Go, K.J.; Dwan, P.; Hillis, L. Establishing and managing donor oocyte banking. In *In Vitro Fertilization*; Springer: Cham, Switzerland, 2019; pp. 721–726.
- 41. Go, K.J.; Nagy, Z.P.; Chang, C.C. Cryopreserved oocyte banking: Its prospects and promise. In *Biennial Review of Infertility*; Springer: New York, NY, USA, 2013; pp. 155–161.
- 42. Quaas, A.M.; Melamed, A.; Chung, K.; Bendikson, K.A.; Paulson, R.J. Egg Banking in the United States: Current Status of Commercially Available Cryopreserved Oocytes. *Fertil. Steril.* 2013, 99, 827–831. [CrossRef]
- 43. Angraal, S.; Krumholz, H.M.; Schulz, W.L. Blockchain Technology: Applications in Healthcare. *Circulation* **2017**, *10*, e003800. [CrossRef] [PubMed]
- 44. Kuo, T.T.; Kim, H.E.; Ohno–Machado, L. Blockchain Distributed LedgerTechnologies for Biomedical and Healthcare Applications. J. Am. Med Informatics Assoc. 2017, 24, 1211–1220. [CrossRef] [PubMed]
- 45. Engelhardt, M.A. Hitching Healthcare to the Chain: An Introduction to Blockchain Technology in the Healthcare Sector. *Technol. Innov. Manag. Rev.* **2017**, *7*, 22–34. Available online: https://www.timreview.ca/article/1111 (accessed on 23 February 2022). [CrossRef]
- 46. Hickman, C.F.L.; Alshubbar, H.; Chambost, J.; Jacques, C.; Pena, C.A.; Drakeley, A.; Freour, T. Data Sharing: Using Blockchain and Decentralized Data Technologies to Unlock the Potential of Artificial Intelligence: What Can Assisted Reproduction Learn from Other Areas of Medicine? Fertil. Steril. 2020, 114, 927–933. [CrossRef]
- 47. Benchoufi, M.; Ravaud, P. Blockchain Technology for Improving Clinical Research Quality. Trials 2017, 18, 1–5. [CrossRef]
- 48. Curchoe, C.L.; Malmsten, J.; Bormann, C.; Shafiee, H.; Farias, A.F.S.; Mendizabal, G.; Chavez-Badiola, A.; Sigaras, A.; Alshubbar, H.; Rosenwaks, Z.; et al. Predictive Modeling in Reproductive Medicine: Where will the Future of Artificial Intelligence Research Take Us? Fertil. Steril. 2020, 114, 934–940. [CrossRef]
- 49. Curchoe, C.L. The Paper Chase and the Big Data Arms Race. J. Assist. Reprod. Genet. 2021, 38, 1613–1615. [CrossRef]
- 50. Yaqoob, I.; Salah, K.; Jayaraman, R.; Al-Hammadi, Y. Blockchain for Healthcare Data Management: Opportunities, Challenges, and Future Recommendations. *Neural Comput. Appl.* **2021**, 1–16. [CrossRef]
- 51. Liu, Z.; Luong, N.C.; Wang, W.; Niyato, D.; Wang, P.; Liang, Y.C.; Kim, D.I. A Survey on Blockchain: A Game Theoretical Perspective. *IEEE Access* **2019**, *7*, 47615–47643. [CrossRef]
- 52. Wahab, O.A.; Bentahar, J.; Otrok, H.; Mourad, A. A Stackelberg Game for Distributed Formation of Business-driven Services Communities. *Expert Syst. Appl.* **2016**, *45*, 359–372. [CrossRef]
- 53. Bai, Y.; Hu, Q.; Seo, S.H.; Kang, K.; Lee, J.J. Public Participation Consortium Blockchain for Smart City Governance. *IEEE Int. Things J.* **2021**, *9*, 2094–2108. [CrossRef]
- 54. Xiong, Z.; Feng, S.; Wang, W.; Niyato, D.; Wang, P.; Han, Z. Cloud/Fog Computing Resource Management and Pricing for Blockchain Networks. *IEEE Int. Things J.* **2018**, *6*, 4585–4600. [CrossRef]
- 55. Ding, X.; Guo, J.; Li, D.; Wu, W. Pricing and Budget Allocation for IoT Blockchain with Edge Computing. *arXiv* 2020, arXiv:2008.09724.
- 56. Hu, M.; Wu, D.; Zhou, Y.; Chen, X.; Chen, M. Incentive-Aware Autonomous Client Participation in Federated Learning. *IEEE Trans. Parallel Distrib. Syst.* **2022**, *33*, 2612–2627. [CrossRef]
- 57. Kashaninejad, N.; Shiddiky, M.J.A.; Nguyen, N.T. Advances in Microfluidics-based Assisted Reproductive Technology: From Sperm Sorter to Reproductive System-on-A-Chip. *Adv. Biosyst.* **2018**, *2*, 1700197. [CrossRef]
- 58. Zonis, R.M. Development of An Automated Microfluidic System for the Loading and Unloading of Cryoprotectants from Mammalian Oocytes. Doctoral Dissertation, Massachusetts Institute of Technology, Cambridge, MA, USA, 2020. Available online: http://dspace.mit.edu/handle/1721.1/7582 (accessed on 23 February 2022).
- 59. Castro, M.; Liskov, B. Practical byzantine fault tolerance. In Proceedings of the Third Symposium on Operating Systems Design and Implementation, New Orleans, LA, USA, 22 February 1999; Volume 99, pp. 173–186. Available online: https://people.csail.mit.edu/alinush/6.824-spring-2015/papers/pbft.pdf (accessed on 23 February 2022).
- 60. Luenberger, D.G.; Ye, Y. Linear and Nonlinear Programming, 4th ed.; Springer: Cham, Switzerland, 2016; ISBN 978-3319188416.