Efficient Two-Stage Group Testing Algorithms for Genetic Screening

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Abstract Efficient two-stage group testing algorithms that are particularly suited for rapid and less-expensive DNA library screening and other large scale biological group testing efforts are investigated in this paper. The main focus is on novel combinatorial constructions in order to minimize the number of individual tests at the second stage of a two-stage disjunctive testing procedure. Building on recent work by Levenshtein (Discrete Math., 266:293–309, 2003) and Tonchev (J. Comb. Optim., 15:1–6, 2008), several new infinite classes of such combinatorial designs are presented.

Keywords Group testing algorithm · Two-stage disjunctive testing · Genetic screening · DNA library · Combinatorial design

1 Introduction

With the completion of genome sequencing projects such as the Human Genome Project, efficient screening of DNA clones in very large genome sequence databases has become an important issue pertaining to the study of gene functions. Very useful tools for DNA library screening are group testing algorithms. The general group testing problem (cf. [9, 10]) can be basically stated as follows: a large population X...
of \( v \) items that contains a small set of defective, or positive, items shall be tested in order to identify the defective items efficiently. For this, the items are pooled together for testing. The group test reports “yes” if for a subset \( S \subseteq X \) one or more defective items have been found, and “no” otherwise. Using a number of group tests, the task of determining which items are defective shall be accomplished. Various objectives could be considered for group testing, e.g., minimizing the number of group tests, limiting the number of pool sizes, or tolerating a few errors. In what follows, we will focus on the first issue.

Of particular practical importance in DNA library screening are one- or two-stage group testing procedures (cf. [18, p. 371]):

“[… ] The technicians who implement the pooling strategies generally dislike even the 3-stage strategies that are often used. Thus the most commonly used strategies for pooling libraries of clones rely on a fixed but reasonably small set on non-singleton pools. The pools are either tested all at once or in a small number of stages (usually at most 2) where the previous stage determines which pools to test in the next stage. The potential positives are then inferred and confirmed by testing of individual clones […].”

In practice, genetic screening based on group testing is often followed by a validation step in which all relevant samples are tested again in ‘conventional’ ways, thus adding the tests required for the second stage of the group testing design may be considered as part of this validation phase. As a consequence, minimizing the number of tests in the second phase is highly desired for DNA library and other large scale biological two-stage group testing procedures.

Disjunctive testing relies on Boolean operations. It aims to find the set of defective items by reconstructing its binary \((0, 1)\)-incidence vector \( x = (x_1, \ldots, x_v) \), where \( x_i = 1 \) if the \( i \)th item is defective (positive), and \( x_i = 0 \) otherwise. Levenshtein [20] (cf. also [28]) has employed a two-stage disjunctive testing algorithm in order to reconstruct the vector \( x \): At Stage 1, disjunctive tests are conducted which are determined by the rows of a binary matrix that is comparable to a parity-check matrix of a binary linear code. After determining what items are positive, negative or unresolved, individual tests are performed at Stage 2 in order to determine which of the remaining unresolved items are positive or negative.

Particularly important with respect to the research objectives in this paper, Levenshtein [20] derived a combinatorial lower bound on the minimum number of individual tests at Stage 2. He showed that this bound is met with equality if and only if a Steiner \( t \)-design exists which has the additional property that the blocks have two sizes differing by one (i.e., \( k \) and \( k + 1 \); cf. Sect. 3). Relying on this result, Tonchev [28] gave a straightforward construction method for such designs, based on specific balanced incomplete block designs (BIBDs). All these results are summarized in Sects. 2 and 3.

In this paper, we build on the work by Levenshtein and Tonchev and construct several further infinite classes of Steiner designs with the desired additional property. Our constructions involve, inter alia, resolvable BIBDs, cyclically resolvable cyclic
BIBDs, 2-resolvable Steiner quadruple systems, and a large set of Steiner triple systems. As a result, we obtain efficient two-stage disjunctive group testing algorithms suited for faster and less-expensive genetic screening.

The paper is organized as follows: Section 2 presents Levenshtein’s two-stage disjunctive group testing algorithm. Section 3 introduces background material on combinatorial structures that is important for our further purposes and gives an overview of the previous combinatorial constructions due to Tonchev. Section 4 is devoted to our new combinatorial constructions. The paper is concluded in Sect. 5.

2 Levenshtein’s Two-Stage Disjunctive Group Testing Algorithm

We describe Levenshtein’s two-stage disjunctive group testing procedure and its connection with certain combinatorial designs (cf. [20], see also [28]).

Disjunctive group testing relies on Boolean operations in order to solve the problem of reconstructing an unknown binary vector $x$ of length $v$ using the pool testing procedure [9]. Particularly important for our concerns, Levenshtein has employed a two-stage disjunctive testing algorithm to reconstruct the vector $x = (x_1, ..., x_v)$:

At Stage 1, disjunctive tests are conducted which are determined by the rows $h_i = (h_{i,1}, ..., h_{i,v})$ of a binary $u \times v$ matrix $H$ that is comparable to a parity-check matrix of a binary linear code. A syndrome $s = (s_1, ..., s_u)$ is calculated, where $s_i$ is defined by

$$s_i = \bigvee_{j=1}^{v} x_j \& h_{i,j}, \quad i = 1, ..., u,$$

where $\lor$ and $\&$ denote the logical operations of disjunction and conjunction. The system of $u$ logical equations with $v$ Boolean variables for reconstructing the vector $x = (x_1, ..., x_v)$ does not have a unique solution in general. After determining what items are positive, negative or unresolved, individual tests are performed at Stage 2 in order to determine which of the remaining unresolved items are positive or negative. Formally, let $X = \{1, 2, ..., v\}$. Given a syndrome $s = (s_1, ..., s_u)$, let

$$Q(H, s) = \{ x \in \{0, 1\}^v : s = xH^T \}$$

denote the set of all vectors $x$ having syndrome equal to $s$. For given $H$ and $s$, an item $j \in X$ is positive or negative, respectively, if the $j$th component of all vectors of $Q(H, s)$ is 1 (active) or 0 (inactive), respectively. All remaining $u(H, x)$ items $i \in X$ are called unresolved. Let $h_i$ denote the set of indices of the ones in the test vector $h_i$, called a pool. It can be easily seen that an item $j$ is negative if and only if there exists a pool $h_i$ such that $j \in h_i$ (or $h_{i,j} = 1$) and $s_i = 0$. If for an item $j$ there exists a pool $h_i$ such that $s_j = 1$ and $h_i$ contains $j$ and all other of its indices of the ones (if existent) are negative, then the item $j$ is positive. In the remaining cases either all pools do not contain $j$ or every pool $h_i$, such that $s_j = 1$ and $j \in h_i$, contains also at least one more item that is not negative, in which cases the item $j$ is unresolved. An example is as follows (cf. [20]).
Example 1 Consider the $4 \times 6$ test matrix $H$ and the syndrome $s = (1, 0, 1, 1)$:

| $x_1$ | $x_2$ | $x_3$ | $x_4$ | $x_5$ | $x_6$ | $s$ |
|-------|-------|-------|-------|-------|-------|-----|
| 1     | 1     | 1     | 0     | 0     | 0     | 1   |
| 1     | 0     | 0     | 1     | 1     | 0     | 0   |
| 0     | 1     | 0     | 0     | 1     | 1     | 1   |
| 0     | 0     | 0     | 1     | 1     | 1     | 1   |

Here, items 1, 4 and 5 are negative, item 6 is positive, and items 2 and 3 are unresolved. Moreover, $Q(H, s) = \{(0, 1, 0, 0, 0, 1), (0, 0, 1, 0, 0, 1), (0, 1, 1, 0, 0, 1)\}$.

2.1 Minimum Number of Tests

Assuming that the choice of $x \in \{0, 1\}^v$ is governed by a Bernoulli probability distribution $P$ with parameter $p$, $0 < p < 1$, the efficiency of Levenshtein’s two-stage testing algorithm is characterized by the average number

$$E(H, p) = u + \sum_{x \in \{0, 1\}^v} u(H, x) P(x)$$

of tests used to determine an unknown $x \in \{0, 1\}^v$. The resulting optimization problem is to find the minimum average number

$$E(v, p) = \min E(H, p),$$

where the minimum is taken over all test matrices $H$ with $v$ columns and any number $u \geq 1$ of rows.

Concerning the minimum number of individual tests at the second stage, Levenshtein [20] considered the following setting. Let $X(v)$ be the set of all $2^v$ subsets of the set $X = \{1, 2, \ldots, v\}$ and $X_t(v) = \{x \in X(v) : |x| = t\}$. For a fixed $t$ ($1 \leq t \leq v$) consider a covering operator $F : X_t(v) \rightarrow X(v)$ such that $x \subseteq F(x)$ for any $x \in X_t(v)$. Define

$$\mathcal{D} = \{F(x) : x \in X_t(v)\}.$$

For any $T$, $1 \leq T \leq \binom{v}{t}$, consider the decreasing continuous function $g_t(T) = k + \frac{k+1}{T} (1 - \alpha)$ where $k$ and $\alpha$ are uniquely determined by the conditions $T \binom{k}{t} = \alpha \binom{v}{t}$, $k \in \{t, \ldots, v\}$, and $1 - \frac{t}{k+1} < \alpha \leq 1$. Using averaging and linear programing, Levenshtein [20] proved the following inequality:

**Theorem 1** [20]

$$\frac{1}{\binom{v}{t}} \sum_{x \in X_t(v)} |F(x)| \geq g_t(|\mathcal{D}|),$$

and the bound is met with equality if and only if $\mathcal{D}$ is a Steiner $t$-$(v, \{k, k + 1\}, 1)$ design.
As pointed out in [20], one of the main motivations for the above result is to minimize the number of individual tests at the second stage of a two-stage disjunctive group testing algorithm under the condition that the vectors \( x \) are distributed with probabilities \( p_{|x|}(1 - p)^{v - |x|} \) where \( x \in X(v) \) denotes the indices of the ones (defective items) in \( x \). The bound above implies that the expected number of items that remain unresolved after application in parallel of \( u \) pools (any number \( u \geq 1 \)) is not less than

\[
v \sum_{t=1}^{v} \binom{v}{t} p^{t}(1 - p)^{v-t}2^{-\frac{u}{t}} - vp.
\]

Relying on the Shannon theorem on the average length of a prefix code, Berger and Levenshtein [2] derived the following information theoretic bound for the minimum average number

\[
E(v, p) \geq v \left( p \log_2 \frac{1}{p} + (1 - p) \log_2 \frac{1}{1 - p} \right).
\]

This bound implies that the natural desire to achieve \( E(v, p) = o(v) \) as \( v \to \infty \) can be satisfied only if \( p \to 0 \) (cf. [2]). Note that the bound is valid not only for a two-stage testing algorithm but for any adaptive testing algorithm.

The bound (1) is asymptotically better than the information theoretic bound (2) as \( v \to \infty \) when \( p \leq c(\ln v/v) \) with any constant \( c > 0 \). Furthermore, by employing random selection to obtain an upper bound to \( \sum_{x \in \{0,1\}^v} u(H, x) P(x) \), the asymptotic behavior of \( E(v, p) \) can be determined up to a positive constant factor as \( v \to \infty \) when \( p \) is not too small, i.e., \( p > v^{2-\varepsilon} \) with \( \varepsilon > 0 \) arbitrarily small (see [2, 20]).

### 3 Combinatorial Structures and Tonchev’s Constructions

We give some standard notations of combinatorial structures that are important for our further purposes. Let \( X \) be a set of \( v \) elements and \( B \) a collection of \( k \)-subsets of \( X \). The elements of \( X \) and \( B \) are called points and blocks, respectively. An ordered pair \( D = (X, B) \) is defined to be a \( t \)-\((v, k, \lambda)\) design if each \( t \)-subset of \( X \) is contained in exactly \( \lambda \) blocks. For historical reasons, a \( t \)-\((v, k, \lambda)\) design with \( \lambda = 1 \) is called a Steiner \( t \)-design or a Steiner system. Well-known examples are Steiner triple systems (\( t = 2, k = 3 \)) and Steiner quadruple systems (\( t = 3, k = 4 \)). A 2-design is commonly called a balanced incomplete block design, and denoted by BIBD \((v, k, \lambda)\). It can be easily seen that in a \( t \)-\((v, k, \lambda)\) design each point is contained in the same number \( r \) of blocks, and for the total number \( b \) of blocks, the parameters of a \( t \)-\((v, k, \lambda)\) design satisfy the relations

\[
bk = vr \quad \text{and} \quad r(k - 1) = \lambda \left( \begin{array}{c} v-2 \\ t-2 \end{array} \right) \left( \begin{array}{c} k-2 \\ t-2 \end{array} \right) (v - 1) \quad \text{for} \ t \geq 2.
\]

**Example 2** Take as point-set

\[
X = \{1, 2, 3, 4, 5, 6, 7, 8, 9\}
\]
A BIBD is a resolvable t-design, and as block-set
\[ B = \{\{1, 2, 3\}, \{4, 5, 6\}, \{7, 8, 9\}, \{1, 4, 7\}, \{2, 5, 8\}, \{3, 6, 9\}, \{1, 5, 9\}, \{2, 6, 7\}, \{3, 4, 8\}, \{1, 6, 8\}, \{2, 4, 9\}, \{3, 5, 7\}\}.

This gives a BIBD(9, 3, 1), i.e., the unique affine plane of order 3. It can be constructed as illustrated in Fig. 1.

In this paper, we primarily focus on BIBDs. Let \((X, \mathcal{B})\) be a BIBD\((v, k, \lambda)\), and let \(\sigma\) be a permutation on \(X\). For a block \(B = \{b_1, \ldots, b_k\} \in \mathcal{B}\), define \(B^\sigma := \{b_1^\sigma, \ldots, b_k^\sigma\}\). If \(\mathcal{B}^\sigma := \{B^\sigma : B \in \mathcal{B}\} = \mathcal{B}\), then \(\sigma\) is called an automorphism of \((X, \mathcal{B})\). If there exists an automorphism \(\sigma\) of order \(v\), then the BIBD is called cyclic. In this case, the point-set \(X\) can be identified with \(\mathbb{Z}_v\), the set of integers modulo \(v\), and \(\sigma\) can be represented by \(\sigma : i \rightarrow i + 1 \pmod{v}\).

For a block \(B = \{b_1, \ldots, b_k\}\) in a cyclic BIBD\((v, k, \lambda)\), the set \(B + i := \{b_1 + i \pmod{v}, \ldots, b_k + i \pmod{v}\}\) for \(i \in \mathbb{Z}_v\) is called a translate of \(B\), and the set of all distinct translates of \(B\) is called the orbit containing \(B\). If the length of an orbit is \(v\), then the orbit is said to be full, otherwise short. A block chosen arbitrarily from an orbit is called a base block (or starter block). If \(k\) divides \(v\), then the orbit containing the block
\[
B = \left\{0, \frac{v}{k}, \frac{2v}{k}, \ldots, \frac{(k-1)v}{k}\right\}
\]
is called a regular short orbit. For a cyclic BIBD\((v, k, 1)\) to exist, a necessary condition is \(v \equiv 1 \pmod{k(k-1)}\). When \(v \equiv 1 \pmod{k(k-1)}\) all orbits are full, whereas if \(v \equiv k \pmod{k(k-1)}\) one orbit is the regular short orbit and the remaining orbits are full.

A BIBD is said to be resolvable, and denoted by RBIBD\((v, k, \lambda)\), if the block-set \(\mathcal{B}\) can be partitioned into classes \(\mathcal{R}_1, \ldots, \mathcal{R}_r\) such that every point of \(X\) is contained in exactly one block of each class. The classes \(\mathcal{R}_i\) are called resolution (or parallel) classes. A simple example is as follows.

**Example 3** The BIBD\((9, 3, 1)\) from Example 2 is also an RBIBD\((9, 3, 1)\). Each row is a resolution class.

\[
\begin{align*}
\mathcal{R}_1 &= \{1, 2, 3\}, \{4, 5, 6\}, \{7, 8, 9\} \\
\mathcal{R}_2 &= \{1, 4, 7\}, \{2, 5, 8\}, \{3, 6, 9\} \\
\mathcal{R}_3 &= \{1, 5, 9\}, \{2, 6, 7\}, \{3, 4, 8\} \\
\mathcal{R}_4 &= \{1, 6, 8\}, \{2, 4, 9\}, \{3, 5, 7\}
\end{align*}
\]
Generally, an RBIBD($k^2, k, 1)$ is equivalent to an affine plane of order $k$. An RBIBD($v, 3, 1$) is called a Kirkman triple system. Necessary conditions for the existence of an RBIBD($v, k, \lambda$) are $\lambda(v - 1) \equiv 0 \pmod{k-1}$ and $v \equiv 0 \pmod{k}$.

If $R_r$ is a resolution class, define $R_{r}^\sigma := \{B^\sigma : B \in R_r\}$. An RBIBD is called cyclically resolvable if it has a non-trivial automorphism $\sigma$ of order $v$ that preserves its resolution $\{R_1, \ldots, R_r\}$, i.e., $\{R_{1}^\sigma, \ldots, R_{r}^\sigma\} = \{R_1, \ldots, R_r\}$ holds. If, in addition, the design is cyclic with respect to the same automorphism $\sigma$, then it is called cyclically resolvable cyclic, and denoted by CRCBIBD($v, k, \lambda$). An example is as follows (cf. [12]).

**Example 4** A CRCBIBD($21, 3, 1$) is given in Table 1. The base blocks are $\{1, 4, 16\}$, $\{19, 20, 3\}$, $\{1, 11, 19\}$, and $\{0, 7, 14\}$. There are three full orbits and one regular short orbit. Each row is a resolution class. One orbit of resolution classes is $\{R_0, \ldots, R_6\}$, and another orbit is $\{R_0', R_1', R_2'\}$.

Mishima and Jimbo [23] classified CRCBIBD($v, k, 1$)s into three types, according to their relation with cyclic quasi-frames, cyclic semiframes, or cyclically resolvable group divisible designs. They can only exist when $v \equiv 1 \pmod{k-1}$.

In a cyclic BIBD($v, k, 1$), we can define a multiset $\Delta B := \{b_i - b_j : i, j = 1, \ldots, k; i \neq j\}$ for a base block $B = \{b_1, \ldots, b_k\}$. Let $\{B_i\}_{i \in I}$, for some index set $I$, be all the base blocks of full orbits. If $v \equiv 1 \pmod{k-1}$, then clearly

$$\bigcup_{i \in I} \Delta B_i = \mathbb{Z}_v \setminus \{0\}.$$  

The family of base blocks $\{B_i\}_{i \in I}$ is then called a (cyclic) difference family in $\mathbb{Z}_v$, denoted by CDF($v, k, 1$).

Let $k$ be an odd positive integer, and $p \equiv 1 \pmod{k-1}$ a prime. A CDF($p, k, 1$) is said to be radical, and denoted by RDF($p, k, 1$), if each base block is a coset of the $k$-th roots of unity in $\mathbb{Z}_p$ (cf. [4]). A link to CRCBIBDs has been established by Genma, Mishima and Jimbo [12] as follows.

**Theorem 2** If there is an RDF($p, k, 1$) with $p$ a prime and $k$ odd, then there exists a CRCBIBD($pk, k, 1$).
The notion of resolvability holds in the same way for \( t-(v,k,\lambda) \) designs with \( t \geq 2 \). A Steiner quadruple system \( 3-(v,4,1) \) is called \textit{2-resolvable} if its block-set can be partitioned into disjoint Steiner \( 2-(v,4,1) \) designs. A large set of \( t-(v,k,\lambda) \) designs is a partition of a Steiner \( k-(v,k,1) \) design (i.e., the set of all \( k \)-subsets of a \( v \)-set) into block-sets of \( t-(v,k,\lambda) \) designs. The number of designs in the large set is \( \binom{v-t}{k-t}/\lambda \).

For encyclopedic references on combinatorial designs, we refer the reader to [3, 8]. A comprehensive book on RBIBDs and related designs is [11]. Highly regular designs are treated in the monograph [15]. A recent survey on various connections between error-correcting codes and algebraic combinatorics is given in [16]. For an overview of numerous applications of combinatorial designs in computer and communication sciences, see, e.g., [6, 7, 17].

3.1 Known Infinite Classes of Combinatorial Constructions

Tonchev [28] straightforwardly gave a non-trivial construction method to obtain Steiner designs which have the additional property that the blocks have two sizes differing by one.

**Proposition 1 [28]** Suppose that \( \mathcal{D} = (X, \mathcal{B}) \) is a Steiner \( t-(v,k,1) \) design that contains a Steiner \( (t-1)-(v,k,1) \) subdesign \( \mathcal{D}' = (X, \mathcal{B}') \), where \( \mathcal{B}' \subseteq \mathcal{B} \). Then, the blocks of \( \mathcal{D}' \), each extended with one new point \( x \notin X \), together with the blocks of \( \mathcal{D} \) that do not belong to \( \mathcal{D}' \), form a Steiner \( t-(v+1,\{k,k+1\},1) \) design. In particular, if there exists an RBIBD\((v,k,1)\), then there exists a Steiner \( 2-(v+1,\{k,k+1\},1) \) design.

Relying on resolvable BIBDs from affine geometries and Kirkman triple systems, Tonchev derived from the above result the following infinite classes:

**Theorem 3 [28]** There exists

- a Steiner \( 2-(q^e+1,\{q,q+1\},1) \) design for any prime power \( q \) and any positive integer \( e \geq 2 \),
- a Steiner \( 2-(6a+4,\{3,4\},1) \) design for any positive integer \( a \).

Based on results on 2-resolvable Steiner quadruple systems by Baker [1] and Semakov et al. [24] and by Teirlinck [26], Tonchev obtained this way also two infinite classes for \( t > 2 \). The third class had already been constructed earlier by Tonchev [27].

**Theorem 4 [27, 28]** There is

- a Steiner \( 3-(2^{2e}+1,\{4,5\},1) \) design for any positive integer \( e \geq 2 \),
- a Steiner \( 3-(2 \cdot 7^e+3,\{4,5\},1) \) design for any positive integer \( e \),
- a Steiner \( 4-(4^e+1,\{5,6\},1) \) design for any positive integer \( e \geq 2 \).
4 New Infinite Classes of Combinatorial Constructions

We present several constructions of new infinite families of Steiner designs having the desired additional property that the blocks have two sizes differing by one. Our constructions involve, inter alia, resolvable BIBDs, cyclically resolvable cyclic BIBDs, 2-resolvable Steiner quadruple systems, and a large set of Steiner triple systems. As a result, we obtain efficient two-stage disjunctive group testing algorithms suited for faster and less-expensive DNA library and other large scale biological screenings.

4.1 CRCBIBD-Constructions

Relying on various infinite classes of cyclically resolvable cyclic BIBDs, we obtain the following result:

**Theorem 5** Let $p$ be a prime. Then there exists a Steiner $2-(pk + 1, \{k, k + 1\}, 1)$ design for the following cases:

1. $(k, p) = (3, 6a + 1)$ for any positive integer $a$,
2. $(k, p) = (4, 12a + 1)$ for any odd positive integer $a$,
3a. $(k, p) = (5, 20a + 1)$ for any positive integer $a$ such that $p < 10^3$, and furthermore
3b. $(k, p) = (5, 20a + 1)$ for any positive integer $a$ satisfying the condition stated in (ii) in the proof,
4. $(k, p) = (7, 42a + 1)$ for any positive integer $a$ satisfying the condition stated in (iii) in the proof,
5. $(k, p) = (9, p)$ for the values of $p \equiv 1 \pmod{72} < 10^4$ given in Table 2.

Moreover, there exists a Steiner $2-(qk + 1, \{k, k + 1\}, 1)$ design for the following cases:

6. $(k, q)$ for $k = 3, 5, 7, \text{ or } 9$, and $q$ is a product of primes of the form $p \equiv 1 \pmod{k(k - 1)}$ as in the cases above,
7. $(k, q) = (4, q)$ and $q$ is a product of primes of the form $p = 12a + 1$ with $a$ odd.

**Proof** The constructions are based on the existence of a CRCBIBD $(pk, k, 1)$ in conjunction with Proposition 1. We first assume that $k$ is odd. Then the following infinite

| Table 2 | Existence of an RDF $(p, k, 1)$ with $k = 5$, $p < 10^3$, and $k = 7$ or $9$, $p < 10^4$ |
|---------|----------------------------------|
|         | $k = 5$                          |
|         | 41  61  241  281  401  421  601  641  661 |
|         | 701  761  821  881               |
|         | $k = 7$                          |
|         | 337  421  463  883  1723  3067  3319  3823  3907 |
|         | 4621  4957  5167  5419  5881  6133  8233  8527  8821 |
|         | 9619  9787  9829               |
|         | $k = 9$                          |
|         | 73  1153  1873  2017  6481  7489  7561 |

We remark that further parameters are given in [4] for RDF $(p, k, 1)$s with $k = 7$ or $9$ and $10^4 \leq p < 10^5$. 

\[ \text{ Springer} \]
(i) An RDF\( (p, 3, 1) \) exists for all primes \( p \equiv 1 \pmod{6} \).
(ii) Let \( p = 20a + 1 \) be a prime, let \( 2^e \) be the largest power of 2 dividing \( a \) and let \( \varepsilon \) be a 5-th primitive root of unity in \( \mathbb{Z}_p \). Then an RDF\( (p, 5, 1) \) exists if and only if \( \varepsilon + 1 \) is not a \( 2^{e+1} \)-th power in \( \mathbb{Z}_p \), or equivalently \( (11 + 5\sqrt{5})/2 \) is not a \( 2^{e+1} \)-th power in \( \mathbb{Z}_p \).
(iii) Let \( p = 42a + 1 \) be a prime, and let \( \varepsilon \) be a 7-th primitive root of unity in \( \mathbb{Z}_p \). Then an RDF\( (p, 7, 1) \) exists if and only if there exists an integer \( f \) such that \( 3^f \) divides \( a \) and \( \varepsilon^2 + \varepsilon^2 + \varepsilon + 1 \), \( \varepsilon^2 + \varepsilon + 1 \), \( \varepsilon^2 + \varepsilon + 1 \varepsilon + 1 \) are \( 3^f \)-th powers but not \( 3^f+1 \)-th powers in \( \mathbb{Z}_p \).
(iv) An RDF\( (p, 9, 1) \) exists for all primes \( p < 10^4 \) displayed in Table 2.

Theorem 2 yields the respective CRCBIBD\( (pk, k, 1) \)s. Moreover, in [12] a recursive construction is given that implies the existence of a CRCBIBD\( (qk, k, 1) \) whenever \( q \) is a product of primes of the form \( p \equiv 1 \pmod{k(k-1)} \). In addition, a CRCBIBD\( (5p, 5, 1) \) has been shown [5] to exist for any prime \( p \equiv 1 \pmod{20} < 10^3 \).

We now consider the case when \( k \) is even: In [19], a CRCBIBD\( (4p, 4, 1) \) is constructed for any prime \( p = 20a + 1 \), where \( a \) is an odd positive integer. Furthermore, via the above recursive construction, a CRCBIBD\( (4q, 4, 1) \) exists whenever \( q \) is a product of primes of the form \( p = 12a + 1 \) and \( a \) is odd. The result follows. □

Example 5 Values of \( p \) for which an RDF\( (p, k, 1) \) exists with \( k = 5, p < 10^3 \), and \( k = 7 \) or 9, \( p < 10^4 \) are displayed in Table 2 (cf. [8]). For example, if we take an RDF\( (41, 5, 1) \), then we obtain a Steiner 2-(206, \{5, 6\}, 1) design. If we take an RDF\( (61, 5, 1) \), then we obtain a Steiner 2-(306, \{5, 6\}, 1) design.

4.2 RBIBD-Constructions

By considering various infinite classes of resolvable BIBDs, we establish the following result:

**Theorem 6** Let \( v \) be a positive integer. Then there exists a Steiner 2-(\( v + 1 \), \{\( k, k + 1 \)\}, 1) design for the following cases:

1. \( (k, v) = (2, 2a) \) for any positive integer \( a \),
2. \( (k, v) = (3, 6a + 3) \) for any positive integer \( a \),
3. \( (k, v) = (4, 12a + 4) \) for any positive integer \( a \),
4. \( (k, v) = (5, 20a + 5) \) for any positive integer \( a \) with the possible exceptions given in Table 3,
5. \( (k, v) = (8, 56a + 8) \) for any positive integer \( a \) with the possible exceptions given in Table 3.

**Proof** The constructions are based on the existence of an RBIBD\( (v, k, 1) \) in conjunction with Proposition 1. The following infinite series of resolvable balanced incomplete block designs are known (cf. [8, 13] and the references therein):

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Possible exceptions:

An RBIBD\((v, k, 1)\) with \(k = 5\) or \(8\) is not known to exist for the following values of \(v \equiv k \pmod{k(k-1)}\):

| \(k = 5\)  | 45  | 345 | 465 | 645 |
|-------------|-----|-----|-----|-----|
|             | 176 | 624 | 736 | 1128|
|             | 1240| 1296| 1408| 1464|

| \(k = 8\)  | 1520| 1576| 1744| 2136|
|-------------|-----|-----|-----|-----|
|             | 2416| 2640| 2640| 2920|
|             | 2920| 2976|     |     |

Table 3

(i) When \(k = 2, 3\) and \(4\), respectively, an RBIBD\((v, k, 1)\) exists for all positive integers \(v \equiv k \pmod{k(k-1)}\) (the case \(k = 2\) is trivial since an RBIBD\((v, 2, 1)\) is a one-factorization of the complete graph on \(v\) vertices).

(ii) An RBIBD\((v, 5, 1)\) exists for all positive integers \(v \equiv 5 \pmod{20}\) with the possible exceptions given in Table 3.

(iii) An RBIBD\((v, 8, 1)\) exists for all positive integers \(v \equiv 8 \pmod{56}\) with the possible exceptions given in Table 3.

This proves the theorem.

We remark that Case (2) has already been covered in Theorem 3.

Example 6

Choosing for example an RBIBD\((65, 5, 1)\), we get a Steiner 2-(66, \(\{5, 6\}\), 1) design. If we choose an RBIBD\((105, 5, 1)\), then we obtain a Steiner 2-(106, \(\{5, 6\}\), 1) design.

Theorem 7

If \(v\) and \(k\) are both powers of the same prime, then a Steiner 2-(\(v+1, \{k, k+1\}, 1\)) design exists if and only if \((v-1) \equiv 0 \pmod{(k-1)}\) and \(v \equiv 0 \pmod{k}\).

Proof

It has been shown in [14] that, for \(v\) and \(k\) both powers of the same prime, the necessary conditions for the existence of an RBIBD\((v, k, \lambda)\) are sufficient. Hence, the result follows via Proposition 1 when considering an RBIBD\((v, k, 1)\).

4.3 3-Design-Constructions

Based on further results on 2-resolvable Steiner quadruple systems as well as on a large set of Steiner triple systems, we obtain this way three infinite classes for \(t > 2\).

Theorem 8

There exists
• a Steiner 3-(2 \cdot 31^e + 3, \{4, 5\}, 1) design for any positive integer e,
• a Steiner 3-(2 \cdot 127^e + 3, \{4, 5\}, 1) design for any positive integer e.

**Proof**  By [26], for any positive integer e there exist 2-resolvable Steiner quadruple systems 3-(2 \cdot 31^e + 2, 4, 1) and 3-(2 \cdot 127^e + 2, 4, 1). Thus the constructions follow via Proposition 1.

**Theorem 9** There exists a Steiner 3-\((v + 1, \{3, 4\}, 1)\) design if and only if \(v \equiv 1 \text{ or } 3 \pmod{6}\), \(v \neq 7\).

**Proof**  A large set of Steiner triple systems 2-(\(v, 3, 1\)) exist if and only if \(v \equiv 1 \text{ or } 3 \pmod{6}\), \(v \neq 7\), due to the work of Lu [21, 22] and Teirlinck [25]. Applying Proposition 1 again yields the result.

5 Conclusion

Group testing algorithms are very useful tools for genetic screening. For practical reasons, it is desirable to have at most two-stage group testing procedures. Building on recent work by Levenshtein and Tonchev, we have constructed in this paper new infinite classes of combinatorial structures, the existence of which are essential for attaining the minimum number of individual tests at the second stage of a two-stage disjunctive testing algorithm. This results in efficient two-stage disjunctive group testing algorithms suited for faster and less-expensive DNA library screening and other large scale biological group testing efforts.

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