DNA Recombination and Extraction Methods by XPCR

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Premise

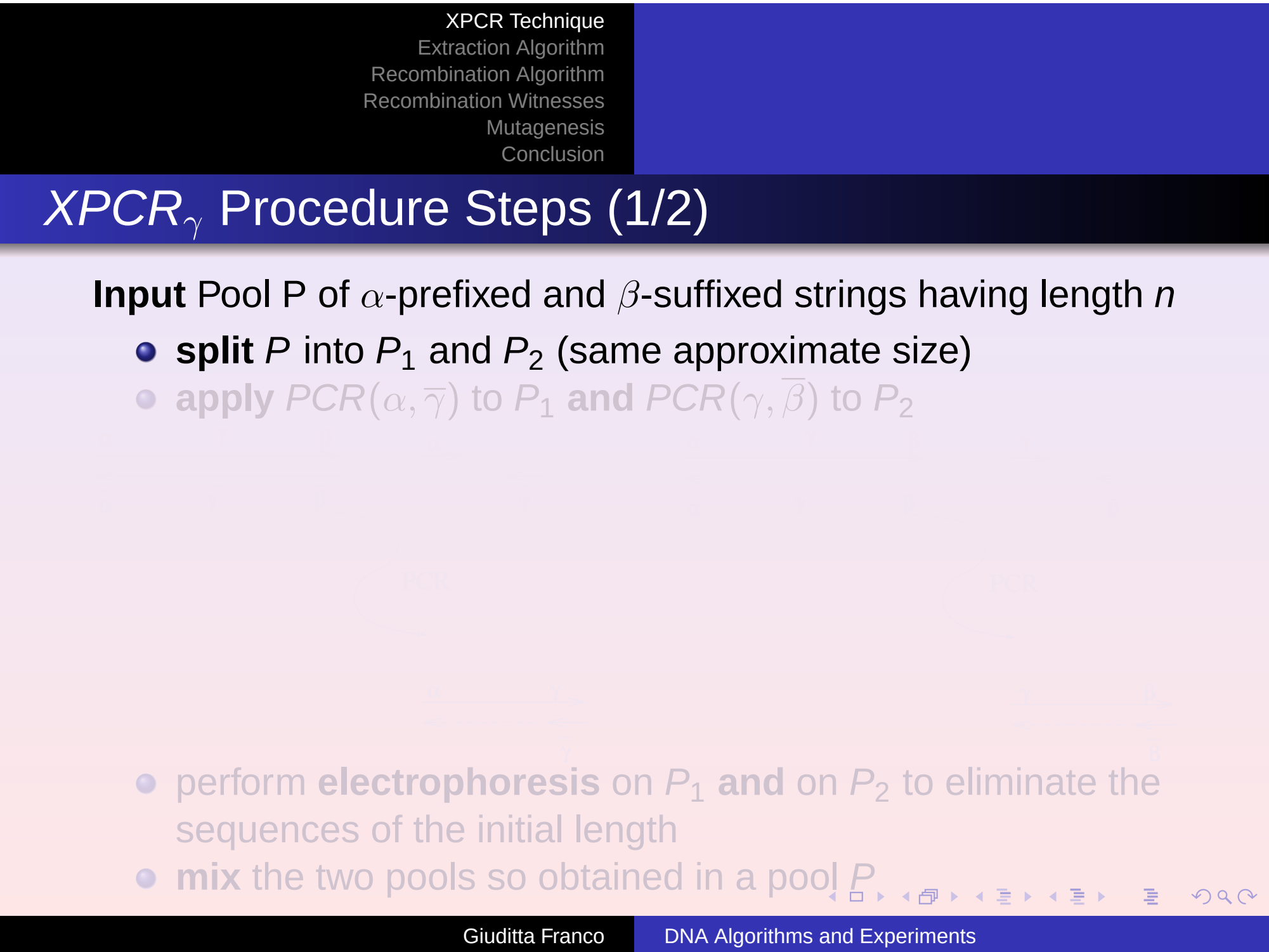
“No amount of experimentation can ever prove me right; a single experiment can prove me wrong.”

Albert Einstein

$XPCR_\gamma$ Procedure Steps (1/2)

Input Pool P of α-prefixed and β-suffixed strings having length n

- **split** P into P_1 and P_2 (same approximate size)
- **apply** $PCR(\alpha, \overline{\gamma})$ to P_1 **and** $PCR(\gamma, \overline{\beta})$ to P_2



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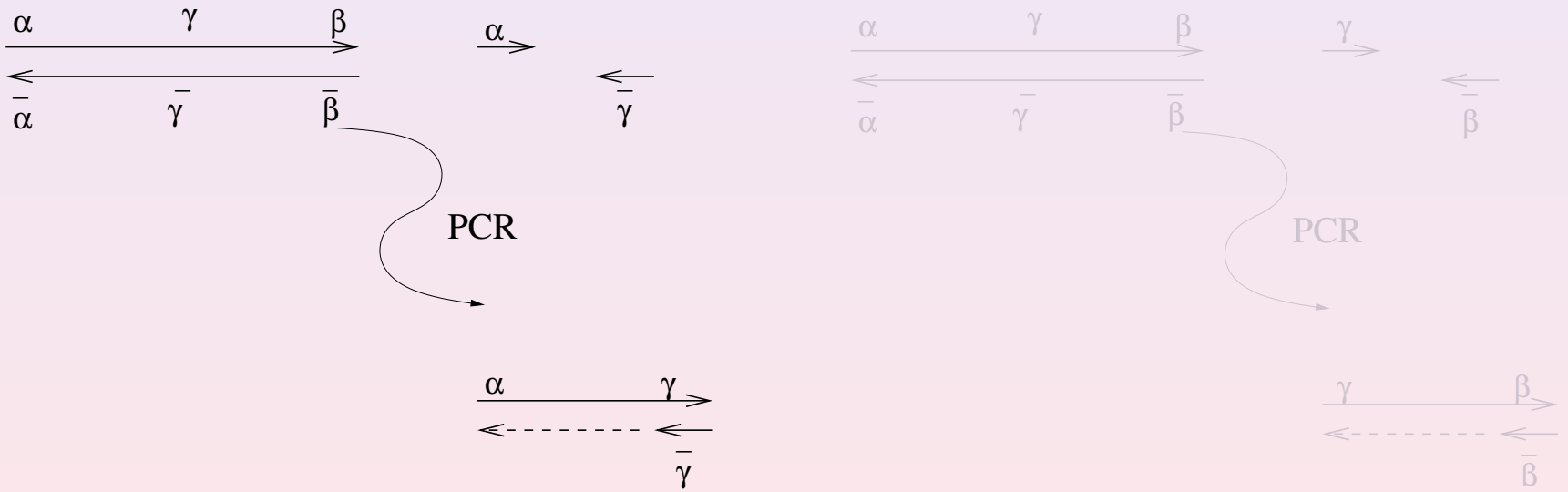

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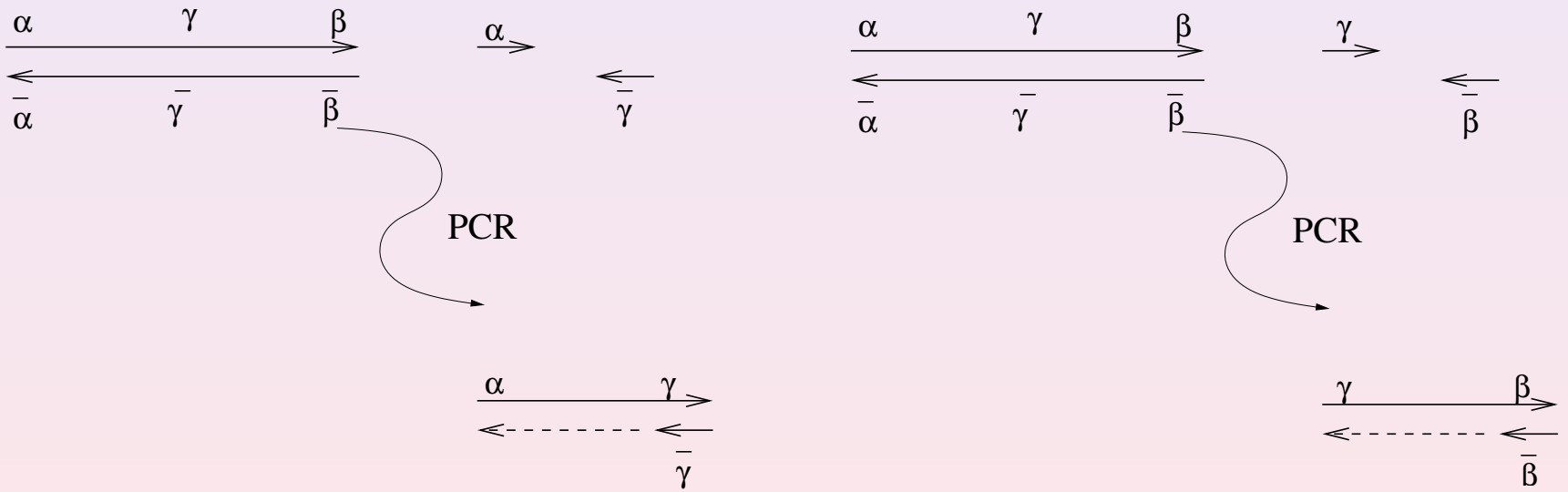

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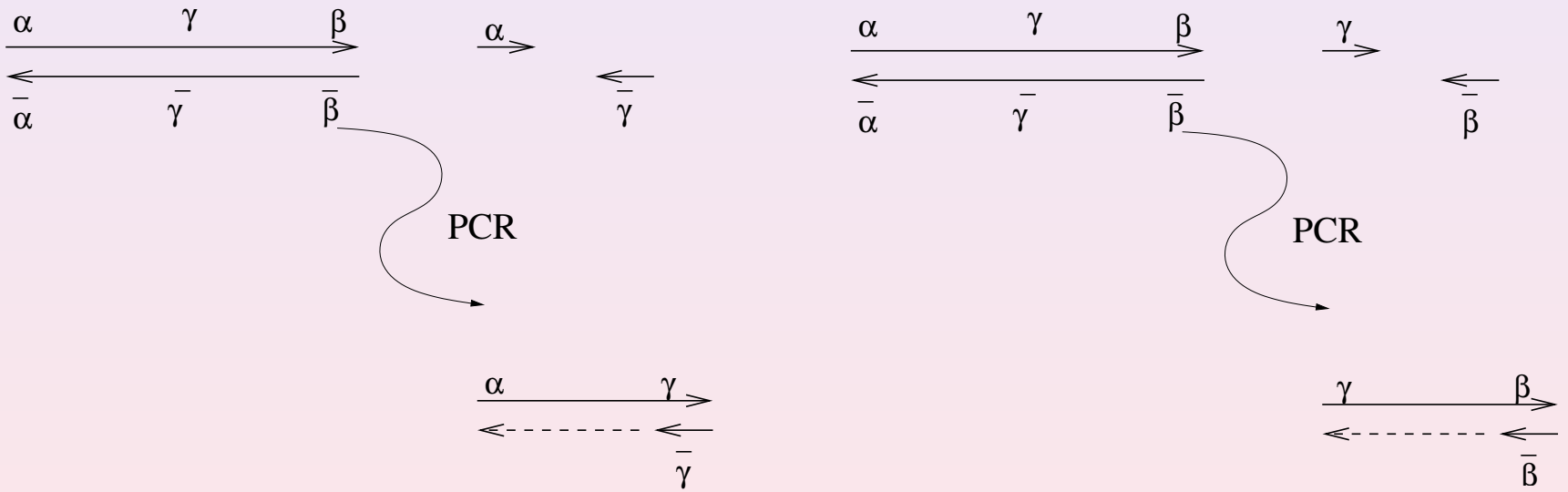

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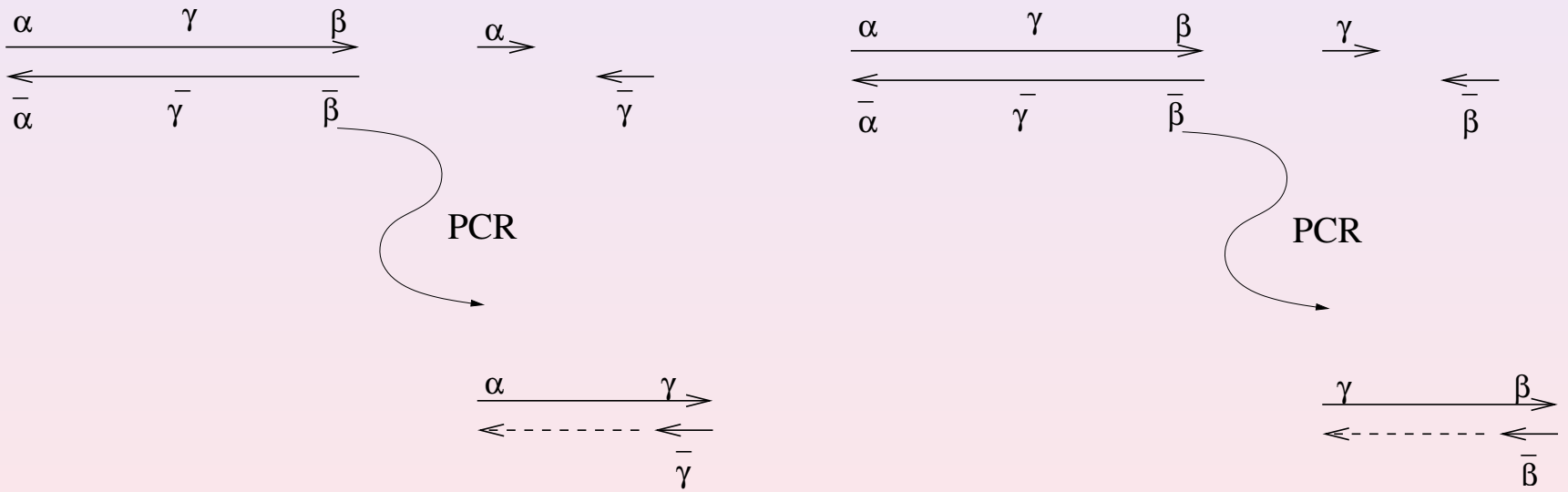
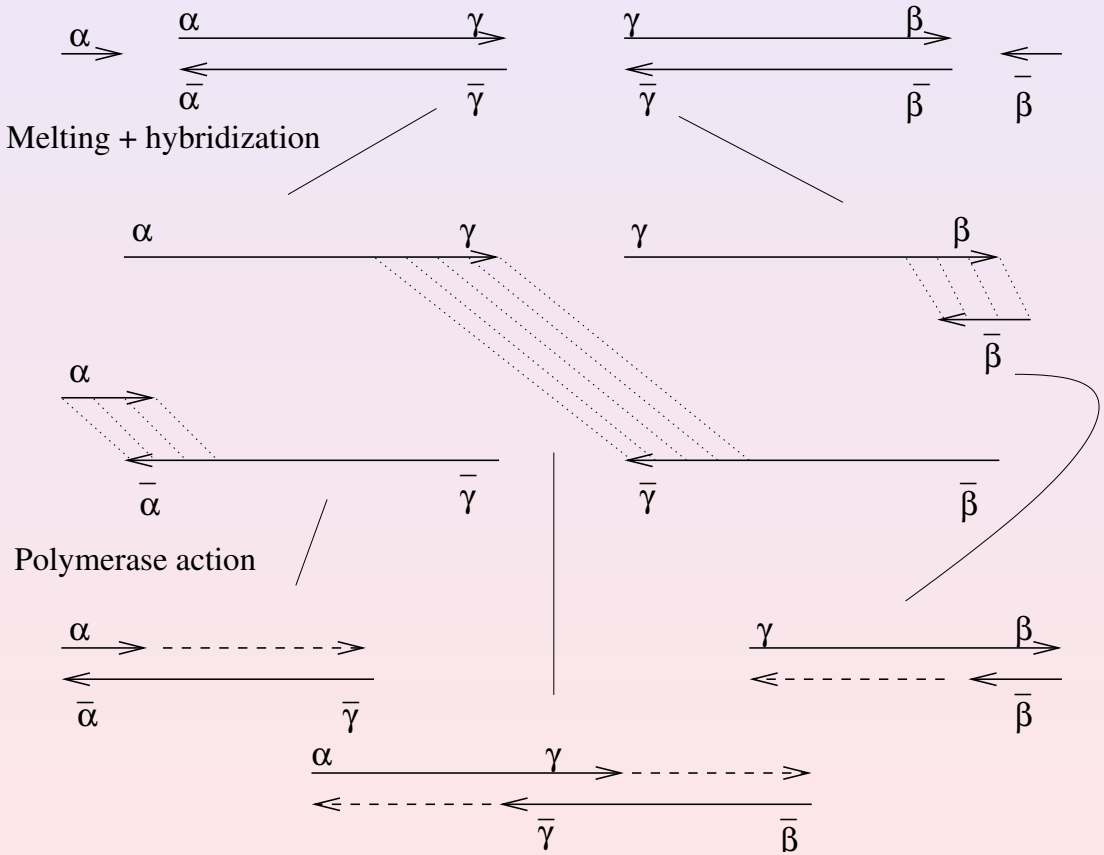


- perform **electrophoresis** on P_1 **and** on P_2 to eliminate the sequences of the initial length
- **mix** the two pools so obtained in a pool *P*

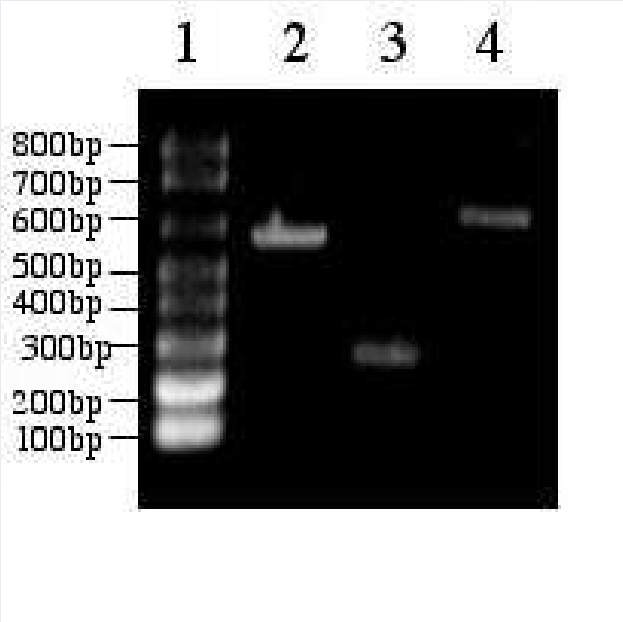
$XPCR_\gamma$ Procedure Steps (2/2)

- **apply** $PCR(\alpha, \overline{\beta})$ to P



Output The pool P resulting from the previous step.

Experiment for Testing the XPCR



Electrophoresis results. 1: molecular size marker ladder (100b). 2: $\alpha\phi\gamma\psi$-strands of human RhoA (582bp), 3: $\gamma\psi\beta$-strands (253bp), 4: cross pairing amplification of $\alpha\phi\gamma\psi\beta$-strands (606bp): 606 = 582 +253 - 229.

$XPCR - Extract(P, \gamma)$

1. $S := \emptyset$; $L := length(P)$;
2. **for each** $n \in L$ **do**
   1. $R_1 := \emptyset, R_2 := \emptyset, Q := \emptyset, P_1 := \emptyset, P_2 := \emptyset$;
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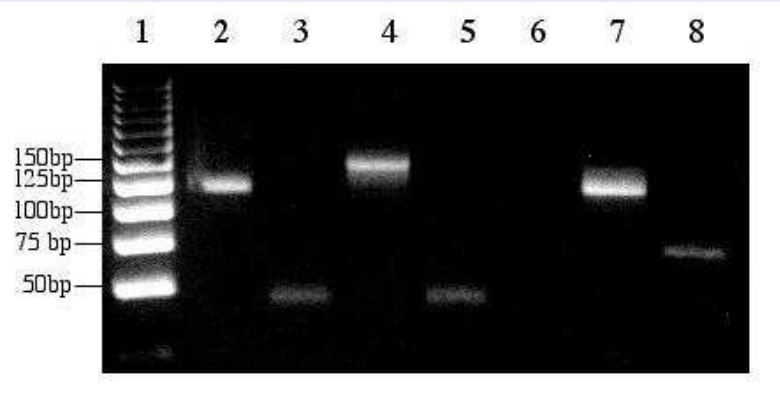

Electrophoresis results. 1: molecular size marker ladder (50 bp). 2: amplification of $\alpha \ldots \gamma$ strands (120 bp); 3: amplification of $\gamma \ldots \beta$ strands (45 bp); 4: cross pairing amplification of $\alpha \ldots \gamma$ and $\gamma \ldots \beta$ (150 bp). 5: positive control by PCR($\gamma, \bar{\beta}$), with γ at position -45; 6: negative control by PCR($\gamma', \bar{\beta}$); 7, 8: positive controls by PCR($\gamma_1, \bar{\beta}$) and PCR($\gamma_2, \bar{\beta}$) respectively, with γ_1 at position -125 and γ_2 at position -75.

XPCR-Based Recombination Algorithm

Goal: to generate the combinatorial library of n binary numbers

$$\{\alpha_1 \cdots \alpha_n \mid \alpha_i \in \{X_i, Y_i\},\ i = 1, \ldots, n\}.$$

The method starts from I_1, I_2, I_3 I_4 (extended by prefix α and suffix β), and generates the whole library, in linear time and by using essentially polymerase extension.

1. *Positive*: $I_1 = X_1X_2X_3X_4X_5X_6$,
2. *Negative*: $I_2 = Y_1Y_2Y_3Y_4Y_5Y_6$,
3. *Positive-Negative*: $I_3 = X_1Y_2X_3Y_4X_5Y_6$,
4. *Negative-Positive*: $I_4 = Y_1X_2Y_3X_4Y_5X_6$.

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XPCR-Based Recombination Algorithm

Goal: to generate the combinatorial library of n binary numbers

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Recombination Algorithm

- **Let** P_1 and P_2 be two copies of the pool

$$\{\alpha I_1 \beta,\ \alpha I_2 \beta,\ \alpha I_3 \beta,\ \alpha I_4 \beta\}$$

- **for** $i = 2, 3, 4, 5$ **do**
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Example: $I_1,\ I_4 \xrightarrow{r_{X_2}} X_1X_2Y_3X_4Y_5X_6,\ Y_1X_2X_3X_4X_5X_6,$
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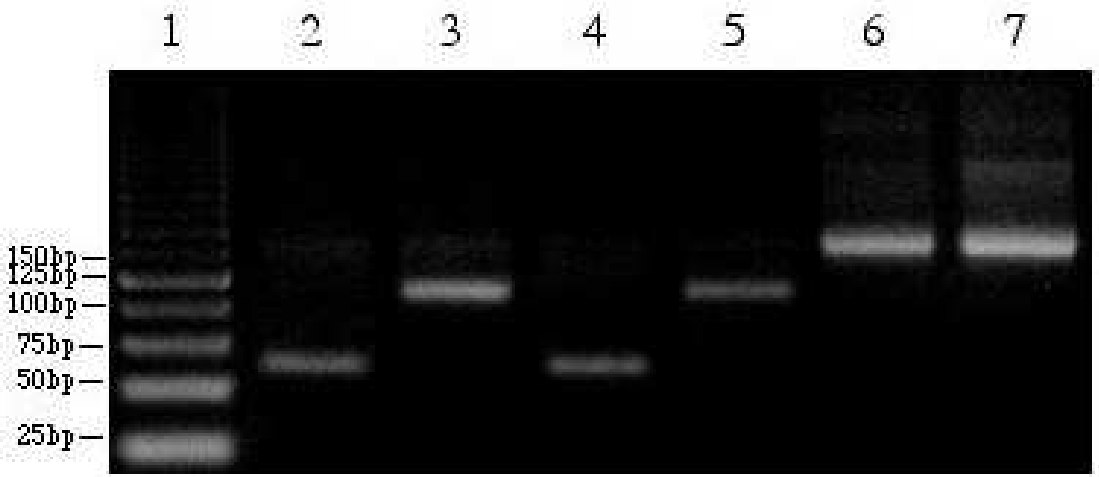
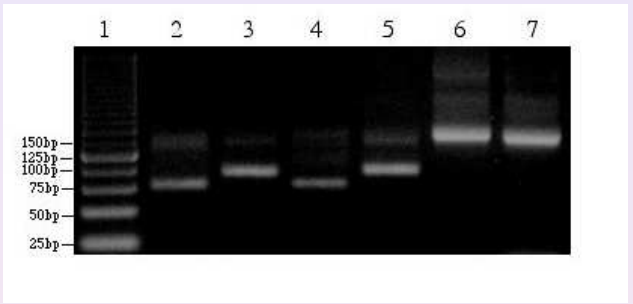
Experiment for Testing Recombination (1/2)



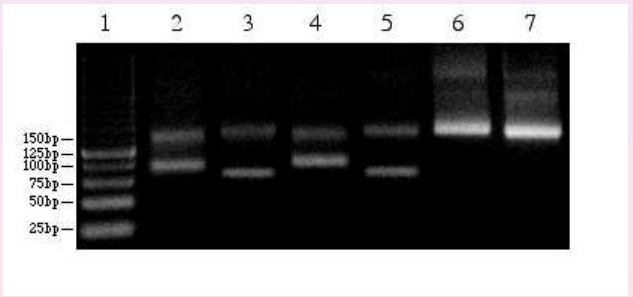
1: Marker (25bp). 2: $\alpha \cdots X_2$ (60bp), 3: $X_2 \cdots \beta$ (105bp), 4:$\alpha \cdots Y_2$ (60bp), 5: $Y_2 \cdots \beta$ (105bp). 6: $XPCR_{X_2}$ and 7: $XPCR_{Y_2}$ with X_2 and Y_2 15 long.

Experiment for Testing Recombination (2/2)

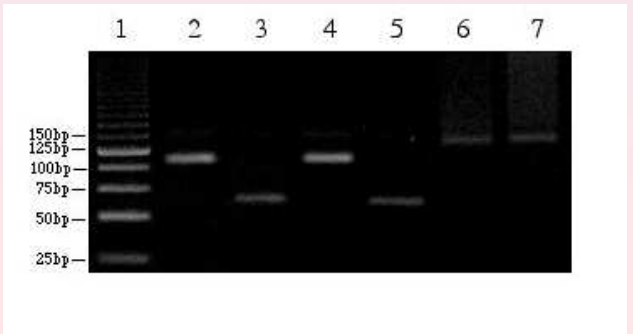
Results $XPCR_{X_i}$ and $XPCR_{Y_i}$ for i=3:



Results $XPCR_{X_i}$ and $XPCR_{Y_i}$ for i=4:



Results $XPCR_{X_i}$ and $XPCR_{Y_i}$ for i=5:



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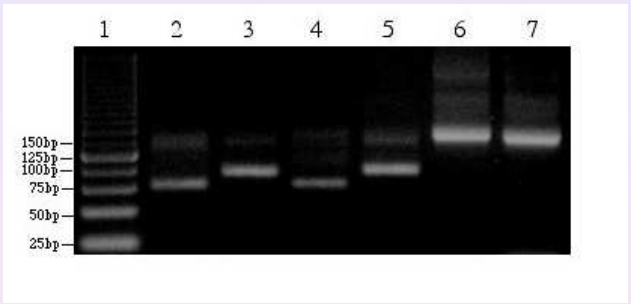
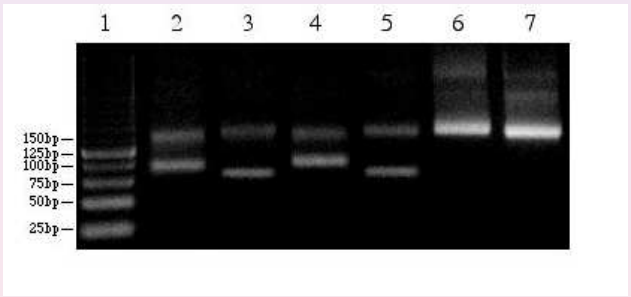


Results $XPCR_{X_i}$ and $XPCR_{Y_i}$ for i=4:



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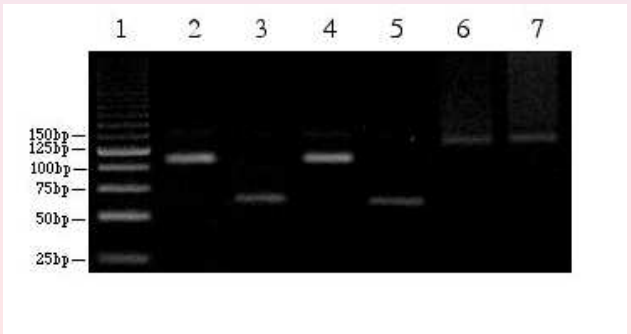

Experiment for Testing The Witnesses Presence

For each $Z_1Z_2Z_3Z_4Z_5Z_6$ of the recombination witnesses W_1 and W_2, its presence was checked in the final pool by means of the following steps:

1. **perform** $PCR(Z_1, \overline{Z_6})$, then **electrophoresis** selecting shortest strands

$$\alpha \underline{Z_1 \ldots Z_6} \beta$$

2. **perform** $PCR(Z_2, \overline{Z_5})$, then **electrophoresis** selecting shortest strands

$$Z_1 \underline{Z_2 \ldots Z_5} Z_6$$

3. **perform** $PCR(Z_3, \overline{Z_4})$

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Success

Marker (25bp). 2: PCR $(X_1, \overline{X_6})$ (90bp), 3: $PCR(X_2, \overline{X_5})$ (60bp), 4: $PCR(Y_3, \overline{Y_4})$ (30bp), 5: $PCR(Y_1, \overline{Y_6})$ (90bp), 6: $PCR(Y_2, \overline{Y_5})$ (60pb), 7: $PCR(X_3, \overline{X_4})$ (30pb).

$XPCR - Mutagenesis(P, \gamma, \delta)$

let $Type(P) = \{< \alpha\gamma\beta >\}$;

1. **input** $Q : \{< \alpha[-18, -1]\ \delta\ \beta[1, 20] >\}$;
2. $(P_1, P_2) := split(P)$;
3. $P_1 := PCR(P_1, \alpha[1, 18], mir(\alpha[-18, -1]))$;
4. $P_2 := PCR(P_2, \beta[1, 20], mir(\beta[-20, -1]))$;
5. $P_1 := separate(P_1, |\alpha|)$; $P_2 := separate(P_2, |\beta|)$;
6. $P_1 := mix(P_1, Q)$;
7. $P_1 := PCR(P_1, \alpha[1, 18], mir(\beta[1, 20]))$;
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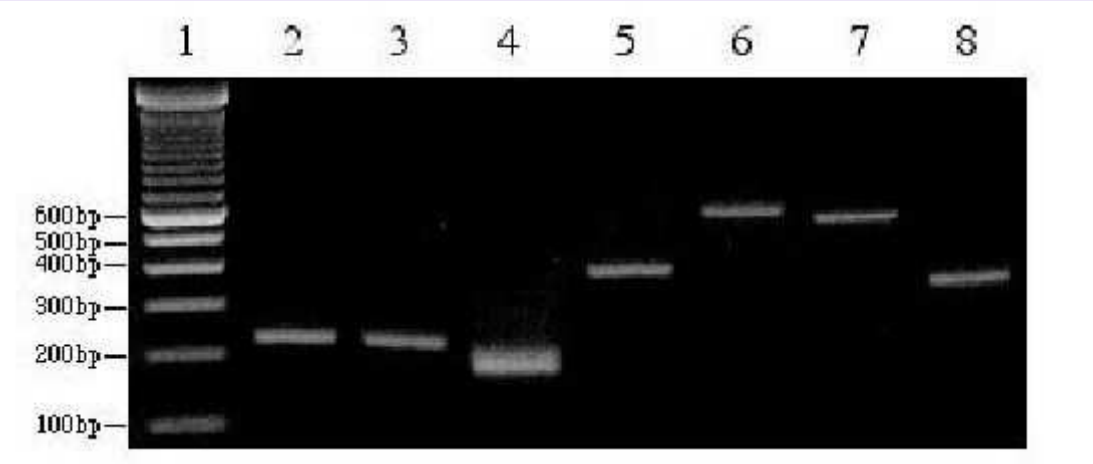
7. $P_1 := PCR(P_1, \alpha[1, 18], mir(\beta[1, 20]))$;
8. $P_1 := separate(P_1, |\alpha| + |\delta| + 20)$;
9. $P := mix(P_1, P_2)$;
10. $P := PCR(P, \alpha[1, 18], mir(\beta[-20, -1]))$;
11. $P := separate(P, |\alpha| + |\beta| + |\delta|)$;
12. **output** P.

Experiment for Testing Mutagenesis



DNA Mutagenesis. *1*: molecular size marker ladder (100bp). *2*: amplification of strand α (230bp). *3*: amplification of strand β (229bp). *4*: amplification of strand $\alpha[-18,-1]\delta\beta[1,20]$ (188bp). *5*: cross pairing amplification of α and $\alpha[-18,-1]\delta\beta[1,20]$ (400bp). *6*: cross pairing amplification of β and $\alpha\delta\beta[1,20]$ (609bp). *7*: RhoA (582bp). *8*: positive control by $PCR(\alpha[26,46],\beta[-20,-1])$ 354 bp. All PCRs at 58°C.

References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