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**Figure 1:** Adaptive Landscapes for Cefprozil (CPR) at various concentrations: A) 8μg/mL, B) 10μg/mL, C) 12.5μg/mL. Forward arrows signify new mutations and backward arrows signify reversions. Red arrows represent significance with a p-value ≤ 0.05. Black arrows represent non-significance, p-value ≥ 0.05. The global optimum allele is highlighted in red D) Composite of all concentrations, showing only the arrows that remain in the same direction throughout the three concentrations.

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| **C)Macintosh HD:Users:portia:Dropbox:TEM.50:TEM-50 Landscapes:CAZ:CAZ1.25Landscape copy.pdf** | **D)Macintosh HD:Users:portia:Dropbox:TEM.50:TEM-50 Landscapes:Ceph. Composites:CAZComposite copy.pdf** |

**Figure 2:** Adaptive Landscapes for Ceftazidime (CAZ) at various concentrations: A) 0.0625μg/mL, B) 0.1μg/mL, C) 1.25μg/mL. Forward arrows signify new mutations and backward arrows signify reversions. Red arrows represent significance with a p-value ≤ 0.05. Black arrows represent non-significance, p-value ≥ 0.05. The global optimum allele is highlighted in red D) Composite of all concentrations, showing only the arrows that remain in the same direction throughout the three concentrations.

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**Figure 3:** Adaptive landscapes for Piperacillin + Tazobactam (TZP) inhibitor showing only selectivity for the inhibitor resistant mutations (bold). The global optimum is highlighted in red. Red arrows represent significance with a p-value ≤ 0.05. A) Landscape with Tazobactam at 8 μg/mL and Penicillin 128 μg/mL, B) Landscape with Tazobactam at 8 μg/mL Penicillin 256 μg/mL, and C) Landscape with Tazobactam at 8 μg/mL 512 μg/mL.

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**Figure 4:** Adaptive landscapes for Amoxicillin + Clavulanic Acid (AMC) inhibitor showing only selectivity for the inhibitor resistant mutations (bold). The global optimum is highlighted in red. Red arrows represent significance with a p-value ≤ 0.05. A) Landscape with Clavulanic Acid at 8 μg/mL and Amoxicillin at 512 μg/mL, B) Landscape with Clavulanic Acid at 8 μg/mL and Amoxicillin at 1024 μg/mL.

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**Figure 5:** Adaptive landscapes for Amoxicillin + Sulbactam (SAM) inhibitor showing only selectivity for the inhibitor resistant mutations (bold). The global optimum is highlighted in red. Red arrows represent significance with a p-value ≤ 0.05. A) Landscape with Sulbactam at 8 μg/mL and Amoxicillin 8 μg/mL, B) Landscape with Sulbactam at 8 μg/mL Amoxicillin 16 μg/mL, and C) Landscape with Sulbactam at 8 μg/mL and Amoxicillin at 32 μg/mL. D) Landscape with Sulbactam at 8 μg/mL and Amoxicillin at 64 μg.

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**Figure 5:** Adaptive landscapes for Ampicillin + Sulbactam (SAM) inhibitor showing only selectivity for the inhibitor resistant mutations (bold). The global optimum is highlighted in red. Red arrows represent significance with a p-value ≤ 0.05. A) Landscape with Sulbactam at 8 μg/mL and Ampicillin 8 μg/mL, B) Landscape with Sulbactam at 8 μg/mL Ampicillin 16 μg/mL, and C) Landscape with Sulbactam at 8 μg/mL and Ampicillin at 32 μg/mL. D) Landscape with Sulbactam at 8 μg/mL and Amoxicillin at 64 μg.

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| A) SAM   |  |  |  |  |  | | --- | --- | --- | --- | --- | |  | **8** | **16** | **32** | **64** | | **8** | - | 53.1% | 59.4% | 50% | | **16** |  | - | 53.1% | 59.4% | | **32** |  |  | - | 59.4% | | **64** |  |  |  | - | | B) TZP   |  |  |  |  | | --- | --- | --- | --- | |  | **128** | **256** | **512** | | **128** | - | 71.8% | 78.1% | | **256** |  | - | 56.2% | | **512** |  |  | - | |
| C) CPR   |  |  |  |  | | --- | --- | --- | --- | |  | **8** | **10** | **12.5** | | **8** | - | 56% | 68% | | **10** |  | - | 68% | | **12.5** |  |  | - |   Composite: 44% | D) CTT   |  |  |  |  | | --- | --- | --- | --- | |  | **0.0312** | **0.0625** | **0.125** | | **0.0312** | - | 66% | 56% | | **0.0625** |  | - | 59% | | **0.125** |  |  | - |   Composite: 41% |
| E) CAZ   |  |  |  |  | | --- | --- | --- | --- | |  | **0.0625** | **0.1** | **0.125** | | **0.0625** | - | 75% | 68% | | **0.1** |  | - | 84% | | **0.125** |  |  | - |   Composite: 66% |  |

**Table 2:** Similarity matrices for five treatments. A) Amoxicillin + Sulbactam B) Piperacillin + Tazobactam. The concentration for the inhibitors stays constant throughout at 8 μg/mL. C) Cefprozil D) Cefotetan and E) Ceftazidime. The concentration of antibiotic is across the top row and left columns in bold, units in μg/mL. The percentage of similarity among the adaptive landscapes for each comparison is shown, and represents the arrows that match in direction between the two concentrations being compared. The percentage of arrows that appear in each composite is also listed under the corresponding tables.

|  |  |  |
| --- | --- | --- |
| **Penicillins** | **Concentration (μg/mL)** | **F: B** |
| **Amoxicillin** | 1024 | 10:22 |
|  | 512 | 17:15 |
|  | 256 | 13:19 |
|  |  |  |
| **Ampicillin 8X** | 256 | 22:10 |
|  | 128 | 18:14 |
|  | 64 | 20:12 |
|  |  |  |
| **Pen + Inhibitors** | **Concentration (μg/mL)** | **F: B** |
| **Piperacillin + Tazobactam** | 8/512 | 15:17 |
|  | 8/256 | 13:19 |
|  | 8/128 | 12:20 |
|  |  |  |
| **Amoxicillin + Clavulanic Acid** | 8/1024 | 16:16 |
|  | 8/512 | 16:16 |
|  |  |  |
| **Ampicillin + Sulbactam** | 8/64 | 17:15 |
|  | 8/32 | 18:14 |
|  | 8/16 | 13:19 |
|  | 8/8 | 24:8 |
|  |  |  |
| **Cephalosporins** | **Concentration (μg/mL)** | **F: B** |
| **Cefprozil** | 12.5 | 17:15 |
|  | 10 | 15:17 |
|  | 8 | 21:11 |
|  |  |  |
| **Cefotetan** | 0.125 | 14:18 |
|  | 0.0625 | 21:11 |
|  | 0.0312 | 18:14 |
|  |  |  |
| **Cefotaxime** | 0.123 | 19:13 |
|  | 0.06 | 17:15 |
|  | 0.05 | 18:14 |
|  | 0.04 | 14:18 |
|  |  |  |
| **Ceftazidime** | 0.125 | 18:14 |
|  | 0.1 | 19:13 |
|  | 0.0625 | 19:13 |
|  |  |  |
| **Cefepime** | 0.0312 | 22:10 |
|  | 0.0156 | 22:10 |

Table 3: List of the ratios, new mutations: reversion, for each antibiotic treatment and concentration used. Antibiotics in first column, concentration in μg/mL in the second column, and ratio in third column.