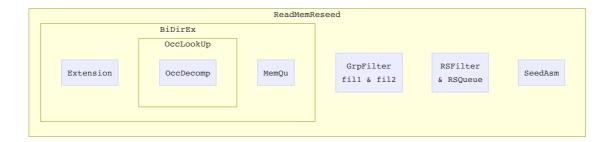
# Implementation of BWA-MEM in FPGA

# 1. System Structure

### 1.1 Read2Seed block

This is a brief introduction of one "Read To Seed" process block, for multi-channel and related memory and cache system, just open the IPI in vivado project.

A "read2seed" block is a complete process block input read and output several seeds.

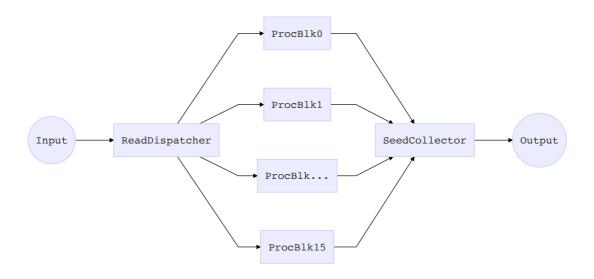


#### Modules:

- Extension: input k0, l0, s0 and bp, output k1, l1 and s1.
- OccLookup & OccDecomp: lookup compressed occ table from memory system and decompress it.
- MemQu: working queue, temporarily store EMs with different intervals produced by forward extension, those EMs will be used by backward extension.
- BiDirEx: do forward ex and backword ex at a specified position of a read, output almost all EMs longer than the specified "min\_mlen" (normally 18).
- GrpFilter: filter out shorter EMs included in another EM with same interval, those "shorter included" MEMs are considered as uninformative.
- RSFilter: pick out EMs should be reseeded.
- SeedAsm: assemble infomations and packed them for uploading to host.
- ReadMemRessed: implements "Simple Forward", "Bidir Seeding" and "Reseeding".

#### 1.2 Process Block x16

16 process blocks combined by read dispatcher and seed collector.



#### Modules:

- ReadDispatcher: dispatch incoming read to the least IDed idle process block.
- SeedCollector: collect seeds from 16 process blocks, seeds with the same read ID will stay together in the output stream.

# 2. Definitions

```
typedef logic [2:0] Symbol;
parameter Symbol sym_N = 3'b000;
parameter Symbol sym_$ = 3'b001;
parameter Symbol sym_A = 3'b100;
parameter Symbol sym_C = 3'b101;
parameter Symbol sym_G = 3'b110;
parameter Symbol sym_T = 3'b111;
```

```
Compl = \{s[2], \sim s[1:0]\};
    endfunction
    // // 3-bit Symbol, used only in compressed Occ table and it's
decompress
    // typedef logic [2:0] Sym3b;
                                = 3'b000;
    // parameter Sym3b sym3b $
    // parameter Sym3b sym3b A
                                   = 3'b100;
    // parameter Sym3b sym3b_C
                                   = 3'b101;
    // parameter Sym3b sym3b_G
                                   = 3'b110;
    // parameter Sym3b sym3b_T
                                   = 3'b111;
    // parameter Sym3b sym3b_N
                                   = 3'b001;
    // function automatic Symbol Sym3to4(input Sym3b in);
    // Sym3to4 = {1'b0, in};
    // endfunction
    // function automatic Sym3b Sym4to3(input Symbol in);
    //
          Sym4to3 = in[2:0];
    // endfunction
    // extension direction
    parameter logic DirForward = 1'b0;
    parameter logic DirBackward = 1'b1;
    // working DW of k, l and s, 2^KLS_W = Max BWT Length
    // don't change this unless you are preparing to review all source
code.
    parameter integer KLS_W = 40;
    // 2 * POS W = n * 8, n = 1, 2, ...
    // POS_W >= Ceiling(Log2(READ_LEN + 3))
    parameter integer POS W = 16;
    // width of read id
    parameter integer RID_W = 32;
    // 2^BIDIREX QU AW - 1 = Capacity of working queue in BiDirEmSeek
    // 2^RESEED_QU_AW = Capacity of reseed queue in ReadMemReseed
    // these 2 params:
    // * too small may cause queue overflow (it's fatal error!)
    // * too large ..., make sure you have enough block memory
    // * Carefully choose their values
    parameter integer BIDIREX_QU_AW = 8; // at least $clog2(read_length),
but may not be necessary
    parameter integer RESEED_QU_AW = 6; // could be smaller than BEX_QU_AW
    // 2^SEEDOUT QU AW = Capacity of output queue of each processing block
    // too small will enlarge the probability of backpressure.
```

```
parameter integer SEEDOUT_QU_AW = 8;
   // used in filters which filter mems to seeds
    // can be OVERRIDED in Read2Seeds instantiation.
   // when set to 2, seeds output will cover 95% of effective seeds in
ref. result,
   // but generate average 12.4 seeds for each read (more redundant
    // when set to 1, seeds output will cover 80% of effective seeds in
ref. result,
   // and generate average 6.1 seeds for each read (more efficient)
    parameter integer FILTER GRP SIZE = 2;
    // block of compressed Occ table
    typedef struct packed {
        logic [31:0][2:0] BwtSlice; // 32 * 3 = 96bit
                               // 40 * 4 = 160bit
       logic [39 : 0] OccT;
       logic [39 : 0] OccG;
                                 // total: 256bit
       logic [39 : 0] OccC;
       logic [39 : 0] OccA;
   } OccBlock;
   typedef struct packed {
        logic [POS_W - 1 : 0] j; // tail position in guarded read
       logic [POS W - 1 : 0] i; // head position in guarded read
       logic [KLS_W - 1 : 0] s; // interval
       logic [KLS_W - 1 : 0] 1; // lower boundary of the reversed
complementary
       logic [KLS_W - 1:0] k; // lower boundary of the original
    } WorkingMem;
    typedef struct packed {
        logic [POS W - 1 : 0] j; // tail position in guarded read
        logic [POS_W - 1 : 0] i; // head position in guarded read
       logic [KLS W - 1 : 0] s; // interval
   } ReseedMem;
    // size of AssemMem must be integer number of bytes
    typedef struct packed {
        logic [POS W - 1 : 0] j; // tail position + 1 in read
       logic [POS W - 1 : 0] i; // head position in read
       logic [KLS_W - 1 : 0] s; // interval will be saturate to [0,255]
       logic [KLS_W - 1 : 0] 1; // lower boundary of the reversed
complementary
        logic [KLS_W - 1 : 0] k; // lower boundary of the original
        logic [RID W - 1 : 0] id;
   } AssemMem;
    // parameter ASMMEM_W = $bits(AssemMem);
```

```
// $bits is not supported by vivado ip packager -_-#
parameter ASMMEM_W = 2*POS_W + 3*KLS_W + RID_W;
endpackage
```

# 3. Modules

# 3.1. Extension (Bi-dir)

Params and ports list

io	type/width	name	description
input	wire	clk	clock
input	wire	rst	synchronous reset, active high
input	Symbol	a_in	new symbol input
input	wire	dir_in	0 - forward, 1- backward
input	wire [KLS_W]	k_in	lower boundary of original seq
input	wire [KLS_W]	l_in	lower boundary of rev-compl seq
input	wire [KLS_W]	s_in	interval of seq
input	wire	start	initiate an extension
output	logic [KLS_W]	k_out	new lower boundary of original seq
output	logic [KLS_W]	1_out	new lower boundary of rev-compl seq
output	logic [KLS_W]	s_out	new interval of seq
output	logic	finish	indicate process finished
output	logic	busy	indicate in processing
input	wire [KLS_W]	acc_cnt_in[4]	C table value, 0-A, 1-C, 2-G, 3-T
input	wire [KLS_W]	pri_pos_in	the position of '\$' in BWT
input	wire	bwt_params_valid	update acc_cnt and pri_pos
output	logic [KLS_W]	occ_k	k for lookup Occ table
output	logic [KLS_W]	occ_ks	k+s for lookup Occ table
output	logic	occ_lookup	initiate an lookup
input	wire [KLS_W]	occ_val_k[4]	lookup result of Occ[x, k] x: 0-'A', 1-'C', 2-'G', 3-'T'
input	wire [KLS_W]	occ_val_ks[4]	lookup result of Occ[x, k+s] x: 0-'A', 1-'C', 2-'G', 3-'T'
input	wire	occ_val_valid	indicate lookup result of 'A', 'C', 'G' and 'T' valid

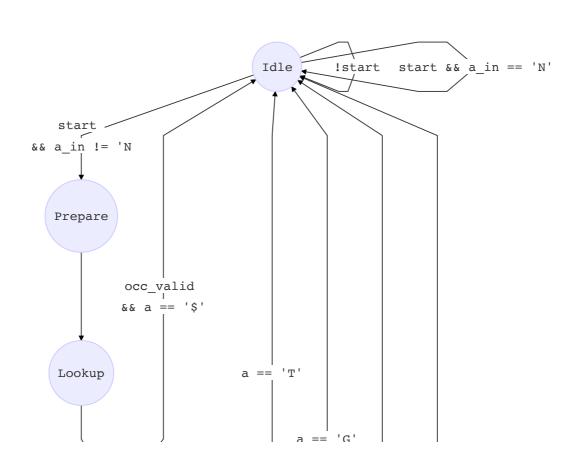
#### **Calculation sequence**

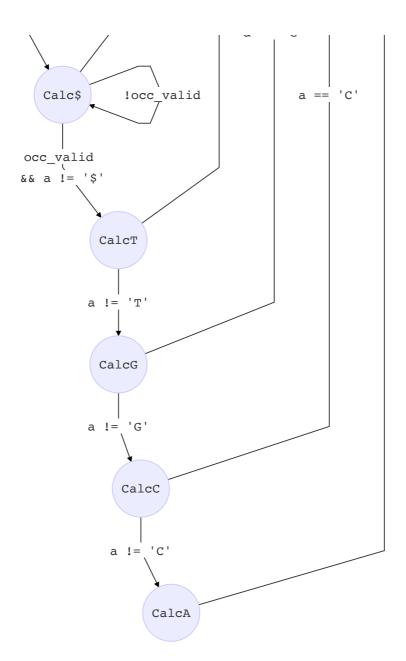
Calculate procedure (dependences among variables are concerned):

- 1. Calc. sumks = k + s Store (take care of forward and backward) k, 1, s
- 2. Lookup O(, k), O(, k+s)
- 3. Calc. 1['\$']=1 Calc. k['\$']=C('\$')+Occ('\$', k) (= k > pos\\$? 1 : 0) Calc. s['\$']=Occ('\$', k+s)-Occ('\$', k) (= (k+s > pos\\$ && k <= pos\\$)? 1 : 0) \*\* if(a == '\\$') finish! \*\*
- 4. wait all other O(, k) and O(, k+s) valid Calc. I['T'] = I['\$'] + s['\$'] Calc. k['T'] = C('T') + Occ('T', k) Calc. s['T'] = Occ('T', k+s) Occ('T', k) \*\* if(a == 'T') finish! \*\*
- 5. Calc. 1['G'] = 1'T' + s'T' Calc. k['G'] = C('G') + Occ('G', k) Calc. s['G'] = Occ('G', k+s) Occ('G', k) \*\* if(a == 'G') finish! \*\*
- 6. Calc 'C'
- 7. Calc **'A'**

#### **State machine**

#### State machine chart

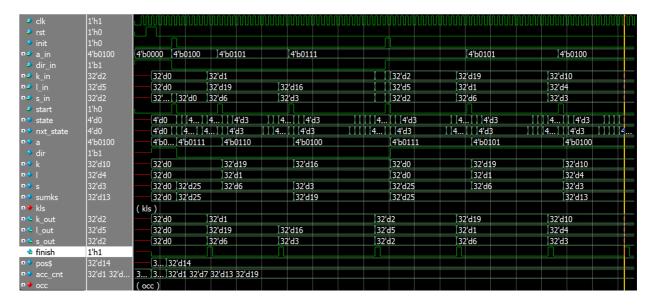




#### State machine table

state	event	nxt_state	do(may be incomplete)
Idle	!start	Idle	
Idle	start && a_in == 'N'	Idle	latch k_out , 1_out , s_out , finish
Idle	start && a_in !=	Prepare	latch a, k, 1, s, sumks
Prepare		Lookup	occ_lookup = 1
Lookup		Calc\$	<pre>1\$ &lt;= 1 k\$ &lt;= k &gt; pos\$? 1 : 0, s\$ &lt;= (k+s &gt; pos\$ &amp;&amp; k &lt;= pos\$)? 1 : 0</pre>
Calc\$	!occ_valid	Calc\$	
Calc\$	occ_valid && a ==	Idle	latch k_out , 1_out , s_out , finish
Calc\$	occ_valid && a !=	CalcT	<pre>lT &lt;= l\$ + s\$  kT &lt;= acc_cnt[3] + occ_val_k[3],  sT &lt;= occ_val_ks[3] - occ_val_k[3]</pre>
CalcT	a == 'T'	Idle	latch k_out, l_out, s_out, finish
CalcT	a != 'T'	CalcG	<pre>lG &lt;= lT + sT  kG &lt;= acc_cnt[2] + occ_val_k[2],  sG &lt;= occ_val_ks[2] - occ_val_k[2]</pre>
CalcG	a == 'G'	Idle	<pre>latch k_out , l_out , s_out , finish</pre>
CalcG	a != 'G'	CalcC	<pre>lc &lt;= lG + sG kc &lt;= acc_cnt[1] + occ_val_k[1], sc &lt;= occ_val_ks[1] - occ_val_k[1]</pre>
CalcC	a == 'C'	Idle	latch k_out, 1_out, s_out, finish
CalcC	a != 'C'	CalcA	<pre>lA &lt;= lC + sC  kA &lt;= acc_cnt[0] + occ_val_k[0],  sA &lt;= occ_val_ks[0] - occ_val_k[0]</pre>
CalcA	a == 'A'	Idle	latch k_out , 1_out , s_out , finish

### Sim result



## 3.2. BiDirEmSeek2 (obs.)

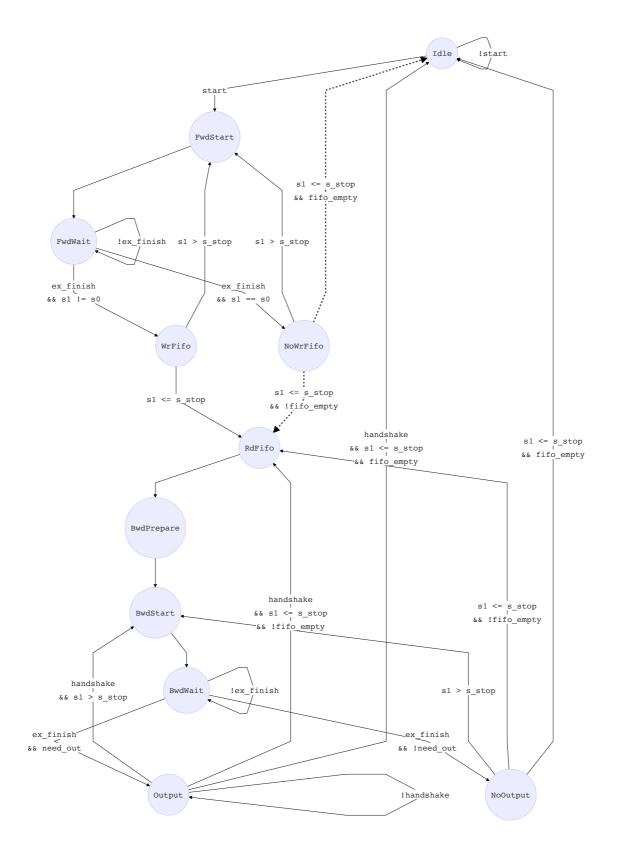
Bi-directional exact match seek (**NOT** compatible with simple forward extension phase)

### Params and ports list

10	Type/Width	Name	Description
param	integer	GD_REAK_LEN	len of the input "guarded read"
input	wire	clk	clock
input	wire	rst	synchronous reset, active high
input	wire Symbol	gd_read[GD_READ_LEN]	"guarded read"
input	wire [POS_W]	pos_in	position to start
input	wire	bi_dir	0 - for simple forward ex 1 - for bi-dir ex
input	wire	start	initiate an operation
output	logic [POS_W]	pos_out	break bp position
output	logic	finish	
output	logic	busy	
Axi4Streamlf.source		m_axis_emout	output of seek result(EMs)
Axi4Litelf.master		m_axi_occlu	mm master for occ lookup
input	wire [KLS_W]	acc_in[4]	acc count table
input	wire	acc_valid	
input	wire [KLS_W]	pri_pos_in	position of '\$' in bwt
input	wire	pri_pos_valid	
input	wire [POS_W]	min_mlen_in	minimum length of output EMs
input	wire	min_mlen_valid	
input	wire [KLS_W]	bwt_len_in	length of BWT(including '\$')
input	wire	bwt_len_valid	
input	wire [KLS_W]	min_intv_in	interval to stop ex.
input	wire	min_intv_valid	

## **State machine**

#### fsm chart

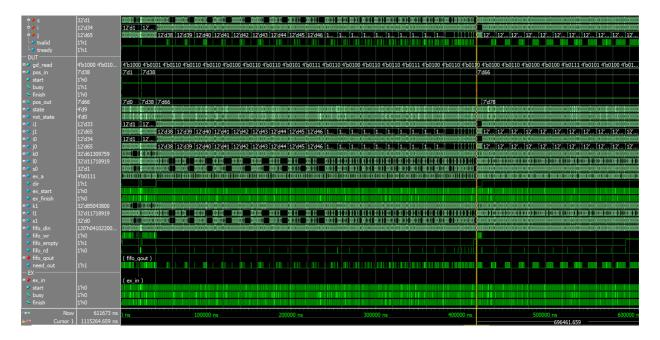


### State machine table

state	event	nxt_state	do (may be incomplete)
Idle	!start	Idle	
Idle	start	FwdStart	<pre>read &lt;= read_in  i1 &lt;= pos</pre>
FwdStart		FwdWait	ex_start = 1
FwdWait	!ex_finish	FwdWait	
FwdWait	ex_finish && s1 != s0	WrFifo	
FwdWait	ex_finish && s1 == s0	nWrFifo	
WrFifo	s1 != 0	FwdStart	fifo_wr = 1 j1 <= j1 + 1 {i0, j0} <= {i1, j1} kls0 <= kls1
WrFifo	s1 == 0	RdFifo	latch pos_out
NoWrFifo	s1 != 0	FwdStart	j1 <= j1 + 1 {i0, j0} <= {i1, j1} kls0 <= kls1

NoWrFifo	s1 == 0 && !fifo_empty	RdFifo	latch pos_out
NoWrFifo	s1 == 0 && fifo_empty	Idle	latch finish , pos_out
RdFifo		BwdPrepare	fifo_rd = 1
BwdPrepare		BwdStart	<pre>i1 &lt;= fifo_q[] - 1 j1 &lt;= fifo_q[] {i0, j0} &lt;= {i1, j1} kls0 &lt;= fifo_q[] dir &lt;= DirBackward</pre>
BwdStart		BwdWait	ex_start = 1
BwdWait	!ex_finish	BwdWait	
BwdWait	ex_finish && need_out	Output	<pre>m_axis_data, valid &lt;=</pre>
BwdWait	ex_finish &&!need_out	NoOutput	
Output	!handshake	Output	tvalid = 1
Output	handshake && s1 != 0	BwdStart	i1 <= i1 - 1 kls0 <= kls1 tvalid = 1
Output	handshake && s1 == 0 && !fifo_empty	RdFifo	tvalid = 1
Output	handshake && s1 == 0 && fifo_empty	Idle	tvalid = 1
NoOutput	s1 != 0	BwdStart	i1 <= i1 - 1 kls0 <= kls1
NoOutput	s1 == 0 && !fifo_empty	RdFifo	
NoOutput	s1 == 0 && fifo_empty	Idle	

## Sim result



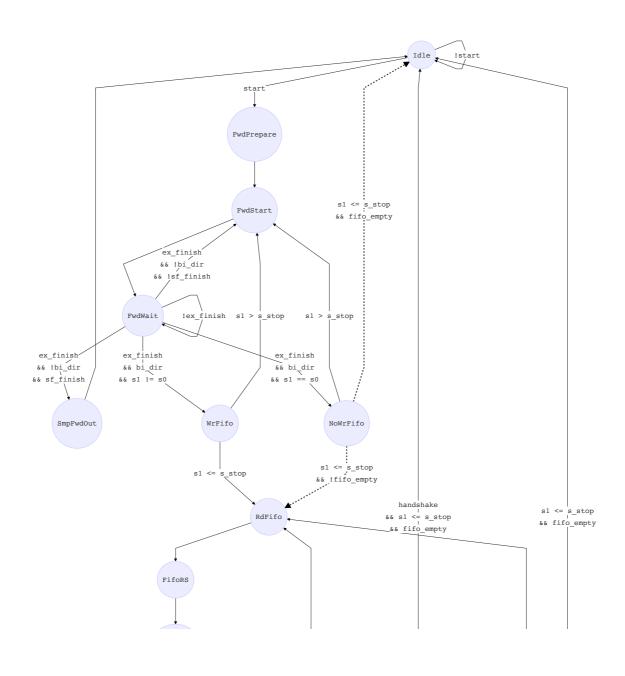
# 3.3. BiDirEmSeek3

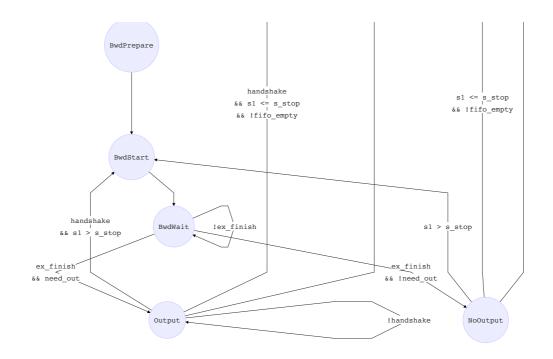
Same as BiDirEmSeek, but with reseed and "simple forward phase" compatible

# Params and ports list

10	Type/Width	Name	Description
param	integer	GD_REAK_LEN	len of the input "guarded read"
input	wire	clk	clock
input	wire	rst	synchronous reset, active high
input	wire Symbol	gd_read[GD_READ_LEN]	"guarded read" read prefixed and suffixed with 'N'
input	wire [POS_W]	pos_in	position to start
input	wire	bi_dir_in	0 - for simple forward ex 1 - for bi-dir ex
input	wire	start	initiate an operation
output	logic [POS_W]	pos_out	break bp position
output	logic	finish	
output	logic	busy	
Axi4Streamlf.source		m_axis_emout	output of seek result(EMs)
Axi4LiteIf.master		m_axi_occlu	mm master for occ lookup
input	wire [KLS_W]	acc_cnt_in[4]	acc count table
input	wire [KLS_W]	pri_pos_in	position of '\$' in bwt
input	wire [KLS_W]	bwt_len_in	length of BWT(including '\$')
input	wire	bwt_params_valid	update acc_cnt, pri_pos & bwt_len
input	wire [POS_W]	min_mlen_in	minimum length of output EMs
input	wire	min_mlen_valid	
input	wire [KLS_W]	min_intv_in	interval to stop ex.
input	wire	min_intv_valid	
input	wire	sf_mlen	length of MEM in Simple Forward
input	wire	sf_max_intv	max. interval of MEM in Simple Forward
input	wire	sf_params_valid	

# FSM chart





# 3.4. Mem Filter 1

Filter output effective EMs within a backward group (a group produced in backward extension and with a same end position in read)

Examples of backward group & fiter1 group (see next section):



### 3.5. Mem Filter 2

Filter output effective EMs from the last N by N array within a filter1 group (when filter1 output a EM has different start pos & end pos from it's N-th previous one, we call this EM starts a new filter1 group and the previous one ends the last filter1 group).

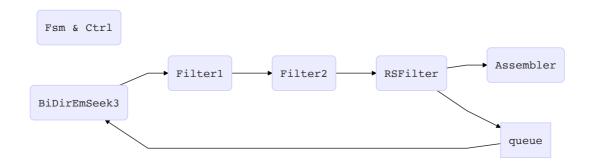
MemFilter2 also generate tlast for the last mem within mems with same read id.

### 3.6. Mem Assembler

Assemble infomations, see definition of "AssemMem".

# 3.7. ReadMemReseed2 (obs.)

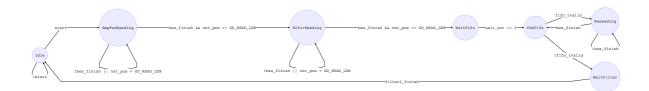
Find Seeds of a read.



# Params and ports list

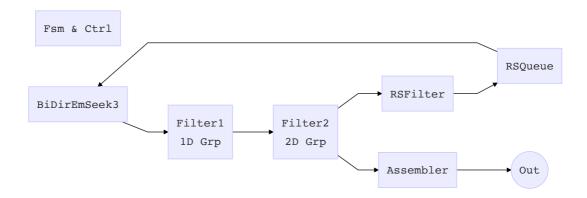
1/0	Type/Width	Name	Descr.
input	wire [POS_W]	min_rslen_in	

# **State Machine**



# 3.7. ReadMemReseed3

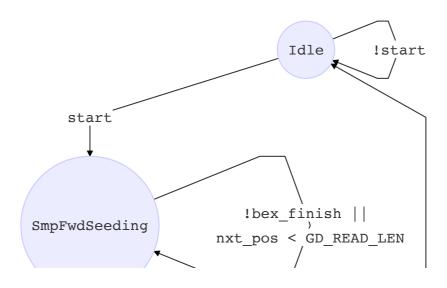
Find Seeds of a read.

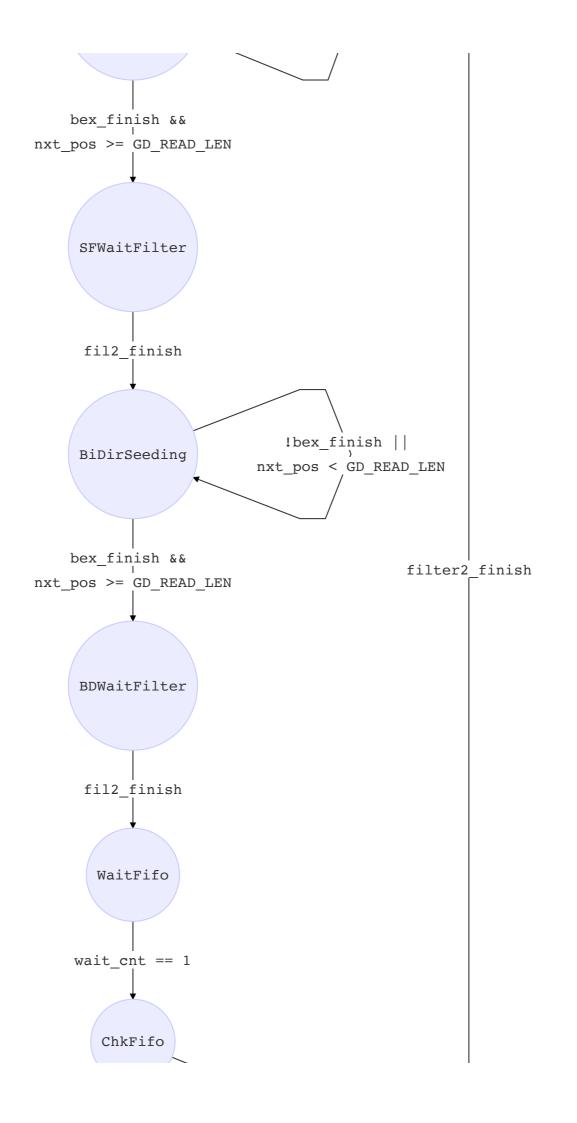


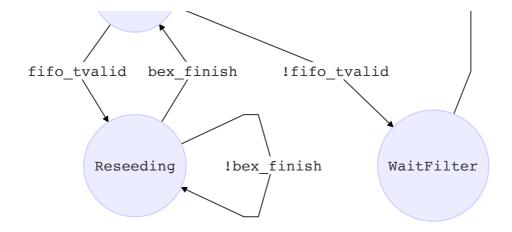
# Params and ports list

1/0	Type/Width	Name	Descr.
input	wire [POS_W]	min_rslen_in	

### **State Machine**



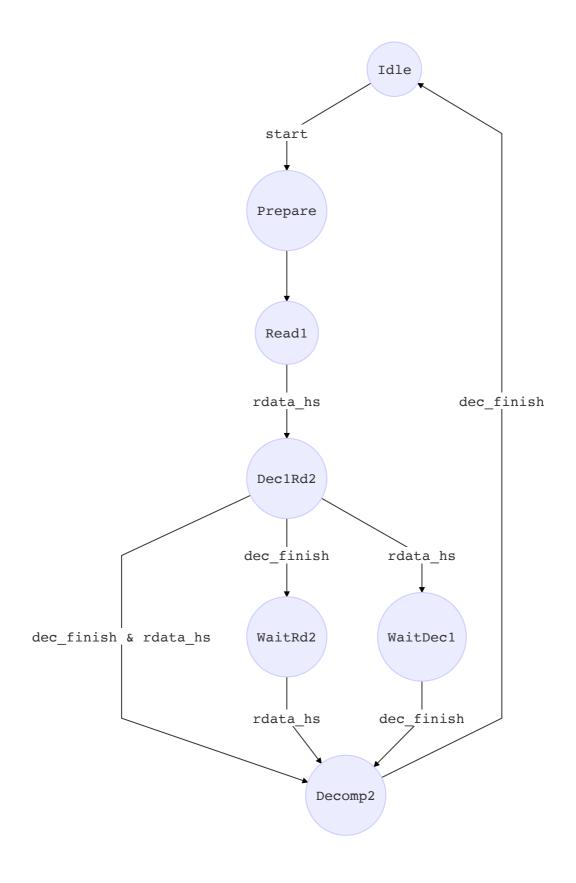




# 3.8. OccLookup

Lookup Compressed Occ Block, and use decompress module to convet it to Occ values of A, C, G, T.

### **State Machine**



## 3.9. OccDecompress

### **Extra Ultilities**

#### bwt2cocc

Command line tool wrote in C++, convert bwt file to compressed occ table file used by FPGA.

#### **BWT File**

bwt file format (described in c struct, little-endian)

### **Occ Table (and Compress)**

The (uncompressed) Occ table is constructed from BWT string **with '\$'**, and has (BwtLenght + 1) element using the definition:

$$occ(a,i) = \big| \{0 \leq j < i \big| BWT[j] = a\} \big|$$

Becaulful of the "less than" sign, it's different from definitions in some papers.

Compressed file is an array of blocks witch contains 4 40-bit AccuCount values ('A', 'C', 'G' and 'T') and 32 3-bit symbols in BWT.

Compressed block format (described in SystemVerilog struct, little-endian):

```
// Total lenght 256 bits, 32 bytes
// be aware of that verilog struct place the first element in MSB
typedef struct packed {
    logic [31:0][2:0] BwtSlice; // 32 * 3 = 96bit
    logic [39 : 0] OccT; // 40 * 4 = 160bit
    logic [39 : 0] OccG; // total: 256bit
    logic [39 : 0] OccC;
    logic [39 : 0] OccA;
} OccBlock;
```

The whole compressed file will have  $\lfloor BwtLength/32 \rfloor + 1$  blocks. The last one have at least one dummy symbols at the end if the BwtLength is not a multiple of 32. If BwtLength is a multiple of 32, the last block will be full of dummy symbols, this is intended to maintain consistency of decompress procedure. Compressed file size in bytes:

$$32 imes (\lfloor BwtLength/32 
floor + 1)$$

Regardless of the 4 Accucount\_? s, symols in all blocks make up the complete BWT string with '\$'.

AccuCount\_? s are occurrences of symbol? in all symbols before the block which it resides in.

#### **Decompress procedure**

For looking up Occ(a, i):

- 1. Get block = CompressedOccBlock[i / 32] at byte address i & 40'hF\_FFFF\_FFFE0 (40-bit address)
- 2. c = block.AccuCount <a>, s = block.Symbols
- 3.  $Occ(a,i)=c+\left|\{0\leq j< \mathrm{rem}(i,32)\big|s[j]=a\}\right|$  (c plus the count of 'a' before(exc.) rem(i, 32)).